Epilepsy and Developmental Impairments Following Severe Malaria in Kenyan Children: A Study of their Prevalence, Relationships, Clues to Pathogenesis and Service Requirements

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Abstract

Falciparum malaria produces a range of neurological manifestations, of which seizures in children is the most common. A smaller proportion progress to coma, ie cerebral malaria (CM). Neuro-cognitive impairments have been reported after CM but not in the much larger group of children presenting with seizures without coma. Many of these seizures are complicated (focal, prolonged or repetitive) and potentially damaging. The aim of this study was to determine the prevalence of impairments, including epilepsy, in children with a history of severe malaria, with specific reference to malaria and complicated seizures (M/S). An assessment battery was developed to detect impairments, particularly in language, memory and behaviour but also including non-verbal functioning, motor skills, hearing and vision. Three groups of children were recruited: children previously admitted with CM (n=152) or M/S (n=156) and children unexposed to either condition (n=179).

There was an increased prevalence of epilepsy in children with previous CM (OR=4.4 95%C.I.=1.42 - 13.69 p=0.01) and M/S (OR=6.1 95%C.I.=2.02 - 18.25 p=0.001) compared to the unexposed group. Children exposed to CM had a poorer group performance on most of the developmental assessments, while poorer performance in the M/S group was concentrated on pragmatics, phonology and behaviour. Twenty-four percent of the CM and M/S groups had at least one impairment on any of the domains measured in the study. In both groups, children with active epilepsy had lower scores on assessment than those without epilepsy.

CM and M/S are associated with an increased prevalence of epilepsy and developmental impairments. Current figures on the neuro-cognitive consequences of severe malaria are likely to be underestimates: this has profound public health implications in terms of education and development for children in sub-Saharan Africa.

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Members of the assessment team

For Andrew,

Who made it possible and makes it all worthwhile

Glossary of Assessment Terms

The glossary below presents terminology as used in the assessment batteries:

- **Syntax:** sentence structure (word order) and rules of grammar
- **Morphology:** morphemes are the smallest units of linguistic meaning
- **Lexical semantics:** a person's lexicon comprises the number of words they know (their vocabulary) and the meanings of those words
- **Minor lexeme/word component:** (refers to lexical semantics assessment) the grammatical or functional words in a sentence
- **Major lexeme/word component:** (refers to lexical semantics assessment) the content words in a sentence
- **Higher level language:** the level at which the basic aspects of language integrate and interact
- **Pragmatics:** rules of language use and non-verbal communication
- **Phonology:** the organisation of the sound system
- **Phoneme:** contrastive units of sound
- **Paraphasia:** the substitution of words or sounds in words, resulting in reduced intelligibility and obscure meaning
- **Neologism:** meaningless, novel words
- **Circumlocution:** circuitous description of unrecalled words

Chapter One: Elements of the Study

1.1 Overview of the thesis

This thesis investigates the hypotheses that the prevalence of epilepsy is increased in children following severe forms of falciparum malaria and that epilepsy in this context is associated with impairments in language, memory, behaviour and motor function.

The first part of the thesis describes the background to the study. Chapter Two presents a systematic review of neurological impairments associated with infections of the central nervous system (CNS), highlighting the paucity of reports of long-term deficits associated with cerebral malaria (CM). The literature on falciparum malaria reviewed in the chapter confirms that there are no published studies of impairments associated with other neurological manifestations of the disease, including malaria with seizures. In addition, there are few data on epilepsy and no reports comparing the prevalence of epilepsy in children with a history of severe malaria to that in children unexposed to the condition, despite the fact that epilepsy is shown to be commonly associated with other infectious diseases reviewed. The findings of the review indicate that impairments in cognition and motor functions are the most common, persisting deficits associated with CNS infections. This includes more subtle problems, which may be difficult to detect on gross neurological assessment but may still be deleterious to the child's social and educational functioning.

Chapter Three examines the complex relationship between epilepsy and developmental impairments. Epidemiological studies have consistently suggested a link between epilepsy and impairments in cognition and behaviour. Epilepsy affects the development of children in several domains and may best be viewed as a syndrome, one part of which is the seizure disorder. Seizures are common in CM: multiple and prolonged seizures are associated with the subsequent development of neurological impairments. In addition to those occurring during CM, seizures are common in children with otherwise uncomplicated malaria in whom consciousness is rapidly regained after the seizure. Such seizures were traditionally considered to be simple febrile seizures but findings from previous studies in Kenya and Thailand indicate that many occur in afebrile children and have complex features and that seizures may be twice as likely to occur in children with falciparum than vivax malaria. In the context of febrile seizures, complex seizures are associated with neurological damage, principally to the temporal lobe, and the subsequent development of epilepsy, particularly complex partial seizures. Children with complex partial seizures may have deficits in language, memory and behavioural functions.

The second part of the thesis details the context of the study, beginning with demographic information on the study site, Kilifi District on the coast of Kenya, in Chapter Four. This chapter also discusses issues relating to the perception and remediation of disability in resource-poor countries and the purpose of the current study in a situation with little existing rehabilitative provision. The term 'resource-poor countries' will be used in preference to 'developing countries', or similar terms, throughout the thesis in recognition of the fact that many of the issues pertinent to the study participants and by extension, this thesis, are related to lack of financial, educational and health resources. Despite the lack of immediate rehabilitative provision for children with impairments participating in this study, the characterisation of developmental impairments associated with severe malaria will provide an estimation of the cost of the disease to society and allow governmental and other agencies to address the issues of schooling and rehabilitation services and facilitate the development of appropriate remedial measures.

Chapter Five outlines the complex interaction between factors associated with conditions of economic deprivation on child development, concentrating on five factors particularly relevant to the Kilifi context: protein energy malnutrition, iron deficiency anaemia, parasitic infections other than malaria, socioeconomic conditions and HIV-related encephalopathy. The chapter discusses the evidence for their deleterious effects on child development and describes how each factor was accounted for in the current study.

Chapter Six highlights the importance of culturally valid assessment tools and procedures as a means by which study participants can fairly demonstrate their skills. In comparison to the number of published assessments in the UK, there are very few available assessments designed for the rural Kenyan context, therefore novel instruments and procedures had to be designed for certain elements of the study, most notably the speech and language battery. This chapter outlines factors germane to this process, including evidence for the influence of culture on development and performance and aspects of coastal Kenyan culture that may have particular relevance to the assessment procedure. The chapter concludes with a description of the specific measures employed in the study to construct culturally-valid assessment tools.

Chapter Seven presents a brief outline of Kigiryama, the language spoken by the majority of participants in the study and the medium of assessment. The chapter aims to provide a context in which to present the development of the speech and language battery (Chapters Nine to Eleven) and more specifically, to elucidate alterations described in those chapters to the grammatical content of assessments originating in the UK.

Part Three of the thesis concentrates on methodology and assessment development, beginning with Chapter Eight, which presents the design and methodology of the study. Three groups of children were recruited: children previously admitted with CM or with malaria and complicated seizures (M/S) and a group unexposed to either condition. The assessment battery is described, which included tests designed to measure performance across the range of developmental domains. Assessments of epilepsy, motor skills, hearing and vision were based on international, standardised techniques whilst cognitive and behavioural assessments were mostly based on instruments previously established in Kilifi. There are few language assessment resources in Kigiryama, thus the development of culturally-appropriate, reliable and valid speech and language assessments is the focus of Chapters Nine to Eleven.

Chapter Nine describes the development of a theoretical framework of speech and language functions to take into account potential neurological damage and its hypothesised effects on language, while accommodating the constraints set by the context. The current level of knowledge of Kigiryama necessitates a broad classificatory framework, which encompasses the universal aspects of language content, form and use. This framework is used in the development and initial validation of the speech and language assessment battery, described in Chapter Ten. This chapter concludes with a description of the speech and language pilot study, which aimed to examine the cultural validity of the tools, their suitability for children in this context and discriminatory ability. The results of the pilot study suggested that deficits in speech and language may persist for up to six years post-malaria and that impairments may be associated with manifestations of severe malaria other than CM.

Chapter Eleven concludes the third part of the thesis, outlining refinements and alterations made to the speech and language battery following the pilot study results. The assessments were analysed using quantitative (item difficulty, response distributions and item endorsement) and qualitative (acceptance and response of participants) techniques for indications of areas for refinement. Psychometric measures indicate that the assessments have an acceptable level of construct validity, internal consistency and reliability.

Part Four presents the findings of the study, their interpretation and possible implications for clinical practice across sub-Saharan Africa. This study aimed to provide a broad overview of impairments associated with malaria across the spectrum of developmental domains, therefore the level of detailed analysis possible in a more narrowly-focussed study was not performed in these chapters.

Chapter Twelve provides background information on the 487 children (152 in the CM group; 156 in the M/S group and 179 unexposed to either condition) recruited to the study. An *a priori* decision was made to adjust all estimates for age, sex and schooling, nutritional and socio-economic status. The chapter presents data on demographic, medical and socioeconomic measures relevant to the study. The findings suggest that the groups are comparable on most of the major determinants of cognitive and language development, although certain variables, notably schooling status, exhibited group differences.

Chapter Thirteen presents the results of the epilepsy questionnaire, electroencephalogram, neurological examination and visual acuity and hearing screening. Chapter Fourteen reports the results of the speech and language assessment battery, which comprised eight assessments measuring receptive grammar, receptive vocabulary, syntax, lexical semantics (expressive vocabulary), higher level language, pragmatics, phonology and word finding. The cognitive and behavioural assessment results, the former comprising the Kilifi Creek Behavioural Memory Test (KCBMT) and assessments of attention and non-verbal functioning, are presented in Chapter Fifteen.

The data presented in these chapters indicate a significant increase in the prevalence of epilepsy in children who had previously been admitted with CM or M/S, compared to the unexposed group. The results of the developmental assessments suggest a general depression of functions among children with previous CM. There were significant differences in performance between the CM and unexposed groups on the assessments of higher level language, lexical semantics, pragmatics and non-verbal functioning. In contrast, areas of reduced functioning among children with previous M/S were more circumscribed, with significantly poorer performance on measures of phonology, pragmatics and behaviour relative to the unexposed group. There was no evidence of specific hippocampal damage or dysfunction in the M/S group on KCBMT subtests, although the scores of the CM group were significantly poorer than those of the unexposed group on several subtests linked to hippocampal functioning. No severe impairments were detected on the hearing test and visual screening identified no impairments in either of the exposed groups

The performance of the active epilepsy group was reduced relative to that of the group without epilepsy on measures across the domains of language, memory, cognition, behaviour and motor skills and was significantly lower on the assessments of receptive grammar, receptive vocabulary, syntax, pragmatics, word finding, memory, attention, behaviour and motor skills. Children with inactive epilepsy did not have the same level of poor performance as children with active epilepsy. They had lower estimated scores than children without epilepsy in attention, behaviour and selected areas of language functioning. Their performance was significantly lower than that of the no epilepsy group on the measure of non-verbal functioning.

There was a trend towards lower mean/median and minimum scores in the exposed groups on assessments in which there were no significant group differences, indicative of the existence of a group of outliers with poor performance in the context of average group performance. Chapter Sixteen describes a subgroup of children categorised as having impairments in at least one of the domains measured in the study. Twenty-four percent of the CM and M/S groups had at least one impairment, suggesting that although there were fewer differences in group performance in the M/S group than in the CM group, the number of children performing at the lower end of the spectrum was similar. However, children with previous CM presented with a more extensive pattern of impairments. Nineteen percent of the CM impairment group, 16% of the M/S impairment group and 6% of the unexposed impairment group had epilepsy.

Chapter Seventeen concludes the thesis, discussing the implications of the findings for children and communities in malaria-endemic regions. The results suggest that the impact of malaria on child development is more extensive than suggested in previous studies, with persisting impairments apparent up to 9 years after the acute episode. The findings also indicate that children with active epilepsy are at additional risk of developmental impairments, possibly with a specific target in domains unaffected by or recovered from deficits associated with severe malaria. Alternatively, epilepsy may simply be a manifestation of more extensive damage associated with malaria, or other factors. The chapter concludes with a discussion of possibilities for further study and the proposition that the data represent an even greater impetus for identifying such children and making provision for follow-up after malaria.

1.2 The candidate's role in the study

The specific contributions of the candidate to the study presented in this thesis are detailed below.

Background and preparation

- Involved in the original conception of the study and the generation of the hypotheses.
- Wrote initial proposals for funding to The Wellcome Trust and for ethical approval to the Kenya Medical Research Institute Ethics Committee.
- Design and planning of both the pilot and main studies

Preparation of tools and assessor training

- Design of all speech and language assessment tools. Modification of these tools following piloting.

- Conducted a pilot study of speech and language assessment tools, including design of the protocol and administration of observational assessments included in the protocol.
- Design and production of speech and language assessment manuals.
- Assisted in the design of the epilepsy questionnaire.
- Ran a training programme for two speech and language assessors and three fieldworkers.
- Ran a training programme for one fieldworker in visual screening and audiometry

Procedure

- Design of the protocol for the main study to assess 487 children using tests of speech and language, cognition, motor skills, behaviour, vision, hearing and an EEG.
- Management of the assessment procedure and team, comprising four full-time assessors, three part-time assessors and four full-time fieldworkers.
- Quality control, involving cross-checking of all assessments, regular observation of assessment procedures, organisation of weekly team meetings and 'assessment refresher days'.
- Administration of the majority of audiometric and visual acuity screening tests.

Data storage and analysis

- Assisted in the creation of a FoxPro database for data storage.
- Cleaned all of the data before analysis.
- Design of the protocol for statistical analysis.
- Statistical analysis, with advice from a statistician.
- Writing publications (Appendix 30) and presentation of the results at conferences.

Part One: Background to the Study

Falciparum malaria produces a range of neurological manifestations in children: seizures are the most common but cerebral malaria (CM) is the defined end of the spectrum. Neuro-cognitive impairments associated with CM were first recognised over 40 years ago (Murphy and Breman, 2001), although their long-term effects are poorly characterised and their importance to the burden of malaria rarely discussed. There have been no reports of the prevalence of neuro-cognitive impairments in the much larger group of children presenting with seizures without coma. This thesis is concerned with the potential impact of these manifestations of falciparum malaria on the development of children in sub-Saharan Africa and their possible association with the onset of epilepsy. Epilepsy has been associated with developmental impairments in its own right, resulting in several interconnecting strands to the study. For the sake of clarity, the background to the work presented in the thesis has been divided into two introductory chapters, the first examining the association between malaria and neuro-cognitive deficits (Chapter Two) and the second (Chapter Three), concentrating on the role of epilepsy in the genesis of developmental impairments.

Chapter Two: Neuro-cognitive Impairment Following CNS Infections

2.1 Introduction

This chapter will provide a broad overview of the epidemiology and clinical features of malaria and the neurological impairments associated with CM. In the absence of a body of literature on deficits following other forms of severe malaria or on persisting impairments post-CM, the greater part of the chapter will comprise a systematic review of the wider literature on neurological impairment associated with common CNS infections. A systematic review methodology was chosen in order to select high quality reports of the most relevance to the current study from the sizeable body of literature on this subject (Mulrow, 1994). The chapter will conclude with a summary of the implications of the review findings for the current study.

2.2 Infectious diseases

Infectious diseases are the most important causes of mortality in infants and young children: they cause more than 13 million deaths per year, one in every two deaths in resource-poor countries (WHO, 2002). Six infectious diseases account for half of all premature deaths: pneumonia, tuberculosis, diarrhoeal diseases, malaria, measles and HIV/AIDS (WHO, 1999). Acute bacterial meningitis (ABM) and CM are the most common infections of the CNS. Apart from epidemics, there are 1.2 million cases of ABM per year, 135,000 of which are fatal (WHO, 1998). The epidemiology of malaria is discussed in section 2.3.1.

The issue of whether impairments found after an illness are primary or sequelae is not always clear but in the case of infective illnesses, the mechanism has always been considered to be causative. The morbid consequences of infectious disease are often overlooked in the face of high mortality rates, particularly in resource-poor countries where resources for detecting such problems may be limited. Neurological impairment subsequent to CNS infections may have a devastating impact on the development of the child and by the nature of cerebral impairments, the economic and structural development of countries. For example, the effect of malaria on the gross domestic product (GDP) of Africa over the past 35 years is estimated to be equivalent to the loss of US$100 billion annually (WHO, 2002). In 1998 alone, malaria resulted in the loss of 39 million disability adjusted life years (DALYs) (WHO, 1999), although the precise contribution of CM to these figures is unclear.

2.2.1 Mechanisms of CNS damage

CNS infections may cause focal or global damage that can lead to subsequent neurological impairment. Impairments may be specific to a primary insult from organisms invading the brain parenchyma or the result of secondary pathophysiological events. Focal damage is usually of infective or vascular origin, the latter typically associated with an area of partial and total ischaemia, which results in neuronal necrosis or impaired function. Global damage may be hypoxic-ischaemic, inflammatory, metabolic (for example, hypoglycaemia) or seizure-related. Reversible global ischaemia, although affecting the whole brain, often produces damage to particular regions that are more susceptible to neuronal damage (Tasker, 1999). In infections, inflammatory mediators, for example cytokines, may be important but it is often difficult to differentiate the deleterious from the beneficial effects.

CNS infections can produce neuronal damage by any one of these mechanisms but the pattern of damage is determined by the localisation of the organism within the brain and the secondary pathophysiological processes initiated, for example seizures. Other factors such as age and previous CNS disease may also influence the pattern of damage and recovery.

2.3 Malaria

Malaria is defined as an acute febrile illness with parasitaemia, although this may not be detectable, depending upon local capability for parasitologic confirmation (Breman, 2001). Four species of protozoal plasmodia – *Plasmodium falciparum, P. vivax, P. ovale* and *P. malariae* – can cause human malaria, transmitted by the female *Anopheles* mosquito when biting for a blood meal. Infectious sporozoites contained in the mosquito's saliva circulate in the bloodstream before entering the liver, unless eliminated by phagocytic cells. Asexual reproduction (schizogony) in the liver culminates in the release of thousands of merozoites into the bloodstream, where they invade red blood cells, developing into ring forms (trophozoites). Mature trophozoites (schizonts) undergo a further stage of schizogony, multiplying to infect new red blood cells. The schizonts of *P. falciparum* preferentially sequester in the microvascular beds of internal organs. Rupture of the parasitised red blood cells releases merozoites into the bloodstream and the cycle thereby repeats until increasing parasitaemia is prevented by immunity, chemotherapy or the death of the host.

2.3.1 Epidemiology of malaria

Over 40% of the world's population from more than 90 countries live with the risk of malaria. The World Health Organisation (WHO) estimates that there are 300-400 million clinical cases of malaria each year, resulting in the deaths of over one million people, 90% of whom are children under 5 years in sub-Saharan Africa (WHO, 2002). There is evidence that mortality risks have increased since the 1980s, linked to the rise in resistance to chloroquine, the first-line treatment in many areas (Snow, et al., 1999). The majority of severe disease and mortality is due to *P. falciparum.* An estimated 2.9 million children are admitted with malaria each year in endemic regions of sub-Saharan Africa, although this represents only a minority of clinical cases, as more than 80% of patients have no contact with formal health services (Breman, 2001; Murphy and Breman, 2001). Many deaths from malaria occur at home, making the establishment of reliable health statistics difficult.

Malaria transmission patterns in sub-Saharan Africa are not homogeneous, varying from intermittent epidemic malaria to stable holo-endemic disease, according to ecological variations in both vectors and humans (Marsh and Snow, 1999). In areas of stable transmission, children may present with clinical malaria from the age of 4 months and the highest mortality occurs in the 1-3 year age group. There are three main syndromes of severe malaria in children in endemic areas: impaired consciousness (Blantyre coma score of ≤4, compared to the strict definition of CM, outlined in section 2.3.2, which specifies a Blantyre coma score of ≤2), respiratory distress and severe anaemia (Marsh, et al., 1995). The age spectra of the three syndromes are different. Children with respiratory distress have been found to be significantly younger than children with impaired consciousness (Marsh, et al., 1995). Reports of severe anaemia consistently demonstrate that the mean age of illness is lower than that of CM. Consequently, in areas of high transmission where children are exposed to malaria at a younger age, the majority of severe cases presenting to hospital are young infants with malarial anaemia, while in lower transmission settings, there appears to be an increased proportion of older children with CM (Marsh and Snow, 1999; Snow, et al., 1999). The gradual acquisition of immunity, although not conferring complete protection from the disease, means that children above the age of 5 years are not usually at risk of death, provided they maintain constant exposure. However, the morbid consequences of malaria appear to increase with age, although data from African studies are limited (Marsh and Snow, 1999).

2.3.2 The spectrum of malarial disease

In endemic areas, almost every child is infected with the malaria parasite but most carry it asymptomatically. Although there is an association between high levels of parasitaemia and clinical disease, the total lifetime experience of malarial disease, as defined by the number of clinical episodes, has been found to be similar in areas of high and low transmission intensity (Marsh and Snow, 1999). The relationship between level of exposure, the incidence of severe disease and death is controversial. The factors determining the development of severe disease in a child resident in a malaria-endemic area who is likely to have had repeated exposure to infection are unclear but are postulated to include the dose and virulence of the parasite and genetic, immunological, nutritional and sociological variants in the host (Greenwood, et al., 1991).

The clinical features of uncomplicated malaria – fever, diarrhoea, headache, generalised aching and vomiting – are non-specific and describe the symptoms of a variety of febrile illnesses prevalent in malaria-endemic areas. Approximately 1-2% of clinical infections result in severe disease (Greenwood, et al., 1991), which is characterised by the presence of life-threatening complications, operationally defined as any malaria syndrome associated with high mortality (>5%) despite appropriate hospital treatment (Newton and Krishna, 1998). The risk of death depends on the age, background immunity and genotypic predisposition of the patient, as well as access to appropriate treatment. Of the major clinical syndromes of severe malaria, impaired consciousness and respiratory distress generally present the greatest risk of death (Newton and Krishna, 1998).

CM is the most severe complication of the disease, defined as the presence of a peripheral asexual parasitaemia, inability to localise a painful stimulus (Blantyre coma score ≤2) and the exclusion of other encephalopathies, particularly bacterial meningitis and locally prevalent viral encephalitides (Newton, et al., 2000). Other complications may co-occur with CM, particularly lactic acidosis or hypoglycaemia. CM presents as a diffuse encephalopathy: alterations in level of consciousness, ranging from drowsiness to deep coma, are often precipitated by seizures, which are reported in the histories of 50-80% of children (Molyneux, et al., 1989; Schmutzhard and Gerstenbrand, 1984). Children often present with abnormal posturing, pupillary changes, absent corneal reflexes, abnormal respiratory rhythms and gaze abnormalities (Newton and Krishna, 1998).

Marsh and colleagues (1996) postulate that the clinical syndrome of CM may comprise four overlapping but distinct syndromes, all meeting the WHO definition of CM. First, children with secondary coma due to an abnormally prolonged post-ictal state (up to six hours) or second, due to covert status epilepticus. A third group comprises children with coma due to metabolic abnormalities such as hypoglycaemia or acidosis. The final group represents half of all cases in Kilifi fulfilling the WHO criteria for CM: these children do not present with gross metabolic disturbances or anaemia and although they have seizures, the coma persists for 24-48 hours after the resolution of the seizure. Marsh and colleagues comment that in these children, the coma is more likely to be a primary brain event rather than a secondary manifestation of a more general insult. These syndromes have differing prognoses and may result in different profiles of recovery and subsequent impairment in survivors (Boivin, in press). Mortality rates are difficult to determine as most endemic areas are rural. In research settings, the median mortality rate for strictly defined CM is 18.6% (95% C.I. 16.3-21.0) (Newton and Krishna, 1998), most deaths occurring within 24 hours of inception of treatment. However, most series are small and mortality in the community is likely to be higher.

2.3.3 Neurological impairment following severe malaria

Most survivors of severe falciparum malaria are reported to make a full neurological recovery, although neurological impairment has increasingly been associated with CM in reports over the past decade. Estimates of its prevalence vary according to the definition of the disease, length of follow-up and nature of the assessment techniques. In African children with CM, neurological deficits have been estimated to occur in 10.9% (95% C.I. 8.3 – 13.5%) of survivors (Newton and Krishna, 1998), although few comprehensive and detailed studies have been reported. Estimates of prevalence from studies since 1962 indicate that there is a trend towards higher levels of impairment over time, suggesting variously that diagnostic awareness has improved, follow-up and referral have increased, falciparum parasites have become more virulent or rising drug resistance has effected increased morbidity (Murphy and Breman, 2001). Two recent reviews have attempted to estimate the burden of persisting deficits associated with CM in sub-Saharan Africa. Snow and colleagues (1999) estimated that 30,000 children under 10 years of age have suffered residual disabling effects, such as epilepsy and motor deficits, associated with CM in the past decade. Murphy and Breman (2001) estimated that each year, between 9,000 and 19,000 children under the age of 5 years experience neurological complications following CM, which last more than 6 months.

Neurological impairment following CM has been associated with prolonged or focal seizures (Bondi, 1992; Brewster, et al., 1990; Meremikwu, et al., 1997; van Hensbroek, et al., 1997); deep coma (van Hensbroek, et al., 1997); prolonged coma (Bondi, 1992; Brewster, et al., 1990; Meremikwu, et al., 1997; van Hensbroek, et al., 1997); raised intracranial pressure (Newton, et al., 1997); hypoglycaemia (Bondi, 1992; Brewster, et al., 1990) and severe anaemia (Brewster, et al., 1990), although the latter finding has not been replicated in other studies (Bondi, 1992). Van Hensbroek and colleagues (1997) found that hypoglycaemia and lactic acidosis, strong predictors of fatality, were not independently predictive of neurological impairment. Depth and length of coma and multiple convulsions were the only independent risk factors for subsequent neurological deficits, suggesting that morbidity and mortality may not share a common pathologic pathway.

The impairments most commonly associated with CM are ataxia, paresis, cortical blindness and speech and language deficits (Bondi, 1992; Brewster, et al., 1990; Carme, et al., 1993; Meremikwu, et al., 1997; Molyneux, et al., 1989; van Hensbroek, et al., 1997). Children with severe neurological impairments, such as spastic tetraparesis or vegetative states, often die at home within months of discharge, thus do not present at follow-up (Newton, et al., 2000). Impairments generally fall into two categories: transient and persisting. For example, ataxia is commonly reported at discharge but usually resolves rapidly. Cortical blindness and hemiparesis often improve within the first 6 months but may not completely resolve. Ataxia and paresis have been associated with the presence of multiple abnormalities (van Hensbroek, et al., 1997). Speech and language deficits are reported to be among the most commonly occurring neuro-cognitive impairments (Bondi, 1992; Brewster, et al., 1990; Meremikwu, et al., 1997): they are not characterised in these studies but are presumed to be the gross impairments most easily detectable on general neurological assessment. Neurological disorders such as epilepsy or behavioural problems may develop after discharge. Epilepsy is often reported after CM but there have been no studies investigating its prevalence (Newton and Krishna, 1998).

Few studies have carried out long-term follow-up of survivors of CM or attempted to describe the nature and severity of persisting deficits. The evidence for persisting cognitive deficits following CM is sparse and appears contradictory. A case-control study focussing on the measurement of non-verbal functions in 36 pairs of Gambian children found no significant impairments in children after an average follow-up of 3.4 years (Muntendam, et al., 1996). A group difference of borderline significance was detected on a test of balance, with poorer performance among children with previous CM. A larger case-control series from Kilifi administered a detailed battery of cognitive and behavioural assessments and a brief language assessment to children with a history of severe malaria with impaired consciousness and found a significant sub-group (14%) with impairments in cognitive functions, language and behaviour (Holding, et al., 1999). Group differences were found on measures of attention, syntax, articulation and behaviour, suggestive of possible impairments in higher order (executive) functions.

Falciparum malaria produces a range of other neurological manifestations. CM is merely the defined end of the spectrum: clinically discrete and comparatively easy to identify, it has been the subject of most reports. Other neurological manifestations such as multiple, prolonged or focal seizures with rapid recovery of consciousness after the seizure are more common than CM (Waruiru, et al., 1996). Despite this, the prevalence and characteristics of acquired neurological impairment following such manifestations are not known. The origin and possible ramifications of these seizures are discussed in section 3.6.2.

Due to the paucity of data on persisting neuro-cognitive impairments following severe forms of malaria, a systematic review of the wider literature on neurological impairment associated with common CNS infections was conducted and is described below.

2.4 Systematic Review: Methodology

2.4.1 Data sources and search strategy

Observational studies of neurological outcome following malaria, meningitis (bacterial, viral, tuberculous), encephalitis or tetanus with a cohort, case-control or cross-sectional design were eligible for inclusion in the review. HIV/AIDS was not considered, as the mechanism of damage is progressive, in contrast to those operating in the other infections. Single cases and case series were excluded. Literature searches were carried out using three databases: MEDLINE (1966-8/2001) and EMBASE (1980-9/2001) on WinSPIRS 2.1 and PsycINFO (1887-10/2001) on WebSPIRS 4.3. To increase the sensitivity and specificity of the search, two trial searches were conducted before the final search strategy was reached.

The strategy was developed by breaking down the review question into elemental facets – exposure, outcome, population, publication language and key words - according to the recommendations of the National Health Service Centre for Reviews and Dissemination (Khan, et al., 2001) (table 2.1). Publication language was restricted to English and French. The bibliographies of key references were later hand-searched to identify articles missed in the database search.

Search element	MEDLINE	EMBASE	PSYCINFO
Exposure	**Thesaurus terms exploded:** Meningitis Malaria Encephalitis Tetanus **+ subheadings:** complications diagnosis epidemiology aetiology mortality prevention/control psychology rehabilitation therapy	**Thesaurus terms exploded:** Meningitis Malaria Encephalitis Tetanus Newborn Tetanus **+ subheadings:** complications diagnosis epidemiology aetiology rehabilitation therapy	**Thesaurus terms exploded:** Meningitis Malaria Encephalitis Tetanus
Key words	Sequela* OR Outcome* OR Morbidity OR Prognos* OR Impairment* OR Deficit* OR Follow-up OR Long-term OR Incidence OR Prevalence		
Outcome	**Thesaurus terms exploded:** Dyskinesias Gait disorders Neurobehavioural manifestations Neuromuscular manifestations Paralysis Paresis Reflex-abnormal Seizures Sensation disorders Voice disorders **+ subheadings:** (as above)	**Thesaurus terms exploded:** Gait disorder Behaviour disorder Learning disorder Mental deficiency Thought disorder Motor dysfunction Epilepsy Sensory dysfunction **+ subheadings:** (as above)	**Thesaurus terms exploded:** Developmental disabilities Epilepsy Pervasive developmental disorders Mental disorders due to general medical conditions Mental disorders Memory disorders Learning disorders Communication disorders Behaviour disorders Articulation disorders Neuromuscular disorders Movement disorders
Population	Age = Child Child-preschool Infant Infant-newborn Adolescence	Age = Child* Infan* Adolescen*	Age = Adolescence Childhood Infancy Neonatal
Language	Language = English or French		

Table 2. 1: Description of the search strategy

2.4.2 Study selection

The on-line abstracts of studies identified from the database search were reviewed and reprints of potentially eligible studies obtained. Inclusion criteria were:

1. Follow-up at least 6 months after exposure to exclude transient impairments and include later-developing impairments.
2. The use of standardised tests or controls in the assessment of cognition or language.
3. Verification of the infection using appropriate and clearly described diagnostic methods (see table 2.2).
4. At least 80% of the group originally identified, located for follow-up.
5. Study participants below the age of 19 years or in studies of both adults and children, clear delineation between the groups.

CNS infection	Diagnostic methods
Aseptic meningitis	All of the following criteria fulfilled for a diagnosis: • Fever, fully conscious • Symptoms and signs of meningism (ie. neck stiffness, headache, neck pain) • Evidence of virus in the CSF (culture, PCR for DNA)
Viral encephalitis	Both of the following criteria fulfilled for a diagnosis: • Impaired level of consciousness • Evidence of virus in the CSF (culture, PCR for DNA)
ABM (Berkley, et al., 2001)	Evidence of bacterial infection in the CSF, either: • Growth of bacteria in CSF culture • Gram stain positive • Antigen tests positive
Tuberculous meningitis	Evidence of bacterial infection in the CSF, either: • Growth of *Mycobacterium tuberculi* from CSF culture • Zeil Neilson stain positive
Tetanus	Clinical diagnosis based upon the presence of: • Trismus • Spasms • Refusal to feed
CM (Newton, et al., 2000)	All of the following criteria fulfilled for a diagnosis: • Presence of *Plasmodium falciparum* asexual parasites in the peripheral blood • Impaired consciousness • Exclusion of other causes of encephalopathy

Table 2. 2: Acceptable diagnostic methods for systematic review studies

Key:
CSF cerebrospinal fluid
PCR polymerase chain reaction

2.4.3 Data extraction

Many of the studies gave little detail on the nature of impairments encountered after CNS infections, so data were organised into seven broad categories: cognition/language, behaviour, special senses, epilepsy, motor, movement and general development.

To provide a more detailed review of patterns of impairment following CNS infection, a methodological quality assessment was carried out to identify a sub-selection of papers of high quality, assessing a broad spectrum of developmental domains. These were selected from the studies used in the overview according to criteria evaluating the scope of the study, selection and attrition bias and external validity:

1. The study includes assessment of cognition/language, behaviour, special senses, epilepsy and motor/movement.
2. The data is presented in sufficient detail to be re-analysed.
3. The cohort is representative of the population or the controls were selected from the source of the case population.
4. The groups are comparable on important confounding factors (age, sex, level of schooling).
5. Where a control group is used, assessors are blinded to the exposure status of the child.
6. Where a control group is used, follow-up rates and losses are comparable (<5% difference) in each group.
7. In case-control studies, there is no overmatching on factors related to exposure.

2.5 Results

The process of study selection is shown in figure 2.1. After the abstracts were reviewed, 146 potentially eligible citations remained from the 608 identified by the search strategy.

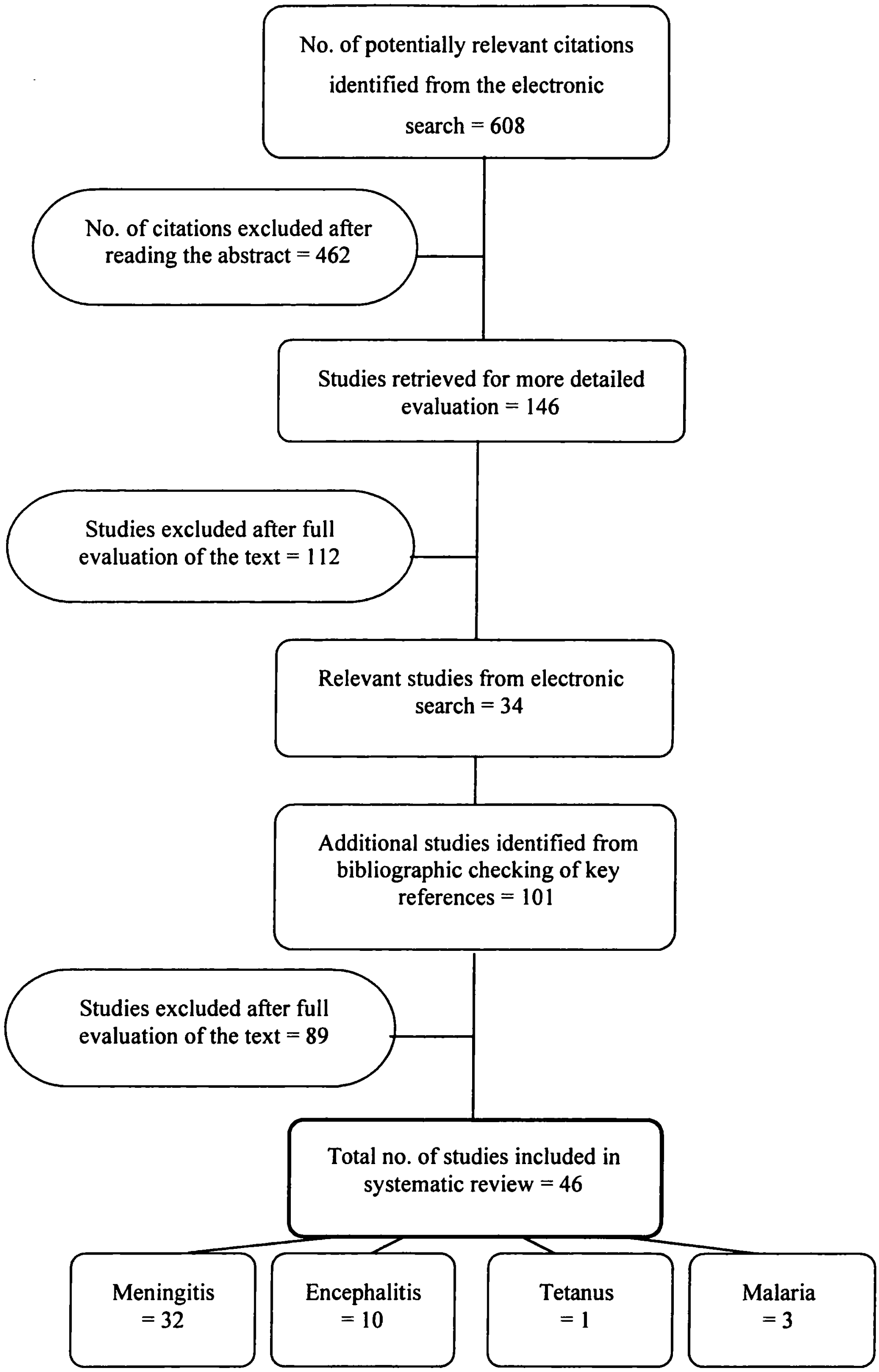

Figure 2. 1: Selection of studies for the systematic review

After evaluation of the full text, 112 studies were excluded, usually because they did not meet the review criteria (sometimes more than one criterion per study was not met). Reasons for exclusion were: the follow-up period was less than 6 months (n=29); the number assessed was less than 80% of the original cohort (n=29); the diagnostic technique was not adequate or was not described sufficiently to ensure confidence in the accuracy of the diagnosis (n=30); adults were included in the study (n=13) or neither controls or standardised assessments were used (n=11). Additional studies were excluded because the relevant data could not be extracted from the text (n=7) or the study was a review, single case, case series or contained duplicate data to an included study (n=22).

In some instances, a sub-selection of the participants in particular studies was included in the systematic review. For example, if both adults and children were assessed, the children's data were selected out where possible. In cases in which only some of the diagnostic methods were acceptable, those diagnosed satisfactorily were selected out if the presentation of the data permitted.

2.6 Overview

The majority (63%) of studies eligible for inclusion in the overview evaluated sequelae following ABM. There were very few eligible publications in the areas of malaria and tetanus and none on tuberculous meningitis. This may reflect the fact that these areas are under-researched, either because of lack of resources or the view that morbidity is not as important as mortality. All of the studies followed children up for at least 6 months, providing evidence that neurological impairment persists after CNS infection. Many children live with potentially debilitating impairments years after the infectious episode.

A quantitative data synthesis was inappropriate because there is considerable heterogeneity between the studies in this review. There is clinical heterogeneity in source populations, baseline disease severity, methods of assessment, types of impairment investigated and duration of follow-up. Furthermore, although a minimum threshold for study quality was set by eliminating studies with high losses to follow-up and lack of standardised assessment techniques, differences in patient selection procedures result in enough methodological heterogeneity to contraindicate meta-analysis.

The results of the overview are presented in table 2.3. Empty cells indicate that the domain in question was not investigated in that study.

Reference	CNS infection	Country of study	No. adm	No. follow -up	Length follow-up	No sequelae (%)	Cognition Language	Behaviour	Special Senses	Epilepsy	Motor	Movemt	General dev.
Bondi, 1992	Cerebral malaria	Nigeria	78	62	12-15 mths	6 (9.7)	1		1	1	4		
Holding, et al., 1999	Severe malaria with impaired consciousness	Kenya	106	87	42-70 mths	12 (13.8)	12						
van Hensbroek, et al., 1997	Cerebral malaria	The Gambia	624	452	6 mths	20 (4.4)	4	4	5	1	12		4
Teknetzi, et al., 1983	Neonatal tetanus	Greece	73	38	5-12 yrs	4 (10.5)	4	3			1		3
Annegers, et al., 1988 ***	Aseptic meningitis	USA	-	181	10 yrs av	4 (2.2)				4			
Bergman, et al., 1987	Enteroviral meningitis	USA	45	33	21m – 16y	3 (9.1)	1	0	1	1	0	0	0
Guiscafre, et al., 1984	Viral meningitis	Mexico	94	75	6 mths	2 (2.7)			2				
Balkhy and Schreiber, 2000	La Crosse encephalitis	USA	6	5	1 yr	3 (60.0)		1		2			
Chun, et al., 1968	California encephalitis	USA	35	35	1 yr +	19 (54.3)	2/32			2	15		
Cizman, et al., 1999	Tick-borne encephalitis	Slovenia	133	6	6-17 mths	3 (50.0)			1	1	1		

Corey, et al., 1988	HSV encephalitis	USA	24	24	6m – 3yrs	10 (41.7)	8		11	8	9		8
Domachowske et al., 1996	Epstein-Barr encephalitis	USA	11	10	2-9 yrs	4 (40.0)		2			1		1
Donat, et al., 1980 **	Meningoencephalitis	USA	30	29	1-2 yrs	2 (6.9)		1		1	0	0	
Lahat, et al., 1999	HSV encephalitis	Israel	28	26	2-12 yrs	10 (38.5)	6	4		4	5		
Sabatino and Cramblett, 1968	California encephalitis	USA	14	14	7m – 2yrs	14 (100)	10	14			1		
Shoji, et al., 1994 ***	Japanese encephalitis	Japan	2	2	2ys	1 (50.0)					1		
Wong and Yeung, 1987	Viral encephalitis	Hong Kong	6	6	1-10 yrs	3 (50.0)	3	1		2	2		
Baumgartner, et al., 1983	Bacterial meningitis	USA	24	23	6m – 5yrs	6 (26.1)			2	2	2		
Carroll and Carroll, 1994	Bacterial meningitis	Vanuatu	83	65	17.5m mean	23 (35.4)	12		21	3			
Carstensen, et al., 1985 **	Streptococcal meningitis	Denmark	35	27	9.5m mean	6 (22.2)	2		5		1		
Chin and Fitzhardinge, 1985	Streptococcal meningitis	Canada	27	20	18m +	6 (30.0)	6		4		2		
Dawson, et al., 1988	Bacterial meningitis	New Zealand	143	139	6mths +	10 (7.2)			11		1		1
Edwards, et al., 1985	Streptococcal meningitis	USA	61	38	3yrs +	19 (50.0)	15		8	7	6		

Ellsworth, et al., 1979	Meningococcal meningitis	Canada	43	41	1-5 yrs	10 (24.4)		5	2		3		
Fitzhardinge, et al., 1974	Neonatal meningitis	Canada	37	18	1yr +	13 (72.2)	24*				2		8
Franco, et al., 1992	Neonatal meningitis	USA	26	19	1-14 yrs	13 (68.4)	11		9	3	1		
Grimwood, et al., 1995	Bacterial meningitis	Australia	181	130	6.7y mean	35 (26.9)	2	12	12	7	3		
Habib, et al., 1979 ***	Meningococcal meningitis	Egypt	-	674	6 mths	43 (6.4)			43				
Jadavji, et al., 1986	Bacterial meningitis	Canada	235	171	1yr +	35 (20.5)	8		25	2	5		9
Kavaliotis, et al., 1994	Non-typhoid salmonella meningitis	Greece	8	6	4-7 yrs	1 (16.7)	1						1
Kilpi, et al., 1995 †	Bacterial meningitis	Finland	134	115	6 mths	4 (3.5)				1	3		
Klinger, et al., 2000	Neonatal meningitis	Canada	101	101	1-19 yrs	16 (15.8)			3	3	4		10
Letson, et al., 1992	Bacterial meningitis	Alaska	63	53	35m mean	21 (39.6)	21		6	5	15		
Lindberg, et al., 1977	*Haemophilus* meningitis	Sweden	97	80	6m – 7yrs	22 (27.5)	5	3	15		3		
Munoz, et al., 1983	*Haemophilus* meningitis	Mexico	70	70	6 mths	2 (2.9)			2				
Odio, et al., 1991	Bacterial meningitis	Costa Rica	120	101	6-24 mths	25 (24.8)			10		15		
Pikis, et al., 1996	Pneumococcal meningitis	Greece	90	47	4-23 yrs	14 (29.8)	9	1	9	7	5		

Pomeroy, et al., 1990	Bacterial meningitis	USA	191	172	5 yrs	26 (14.1)	7		20	6	7		
Raivio and Koskiniemi, 1978	*Haemophilus* meningitis	Finland	131	101	1-15 yrs	38 (37.6)			29	9			
Richardson, et al., 1997	Bacterial meningitis	UK	133	124	9 m +	3 (2.4)			3				
Salih, et al., 1991	Bacterial meningitis	Sudan	44	30	3-4 yrs	9 (30)	11	2	6	3	2		
Sell, et al., 1972 ††	*Haemophilus* meningitis	USA	99	56	1-11 yrs	32 (57.1)	15	5	21	3	4		
Sproles, et al., 1969	*Haemophilus* meningitis	USA	40	33	4-13 yrs	15 (45.5)	13	3	4		2		4
Tejani, et al., 1982 ‡	*Haemophilus* meningitis	USA	29	22	6m – 4y	2 (9.1)			3		1		
Wald, et al., 1986	Streptococcal meningitis	USA	74	34	2.5-17.5y	9 (26.5)	8		6	7	5		
Ware and McLaughlin, 1978	*Haemophilus* meningitis	UK	25	17	6m+	4 (23.5)	2	3	0		1		1

Table 2. 3: Results of the overview

* 11 S/L impairments, 13 low IQ
** Only children with confirmed meningitic agents were included
*** Adult patients removed
† Hearing data removed (collected <6 months post-discharge)
†† Questionnaire data (not completed by medical personnel) removed
‡ Cognitive data removed (follow-up <80% children)

The highest levels of neurological sequelae are seen after encephalitis and ABM. Even when studies examining only one developmental domain (Annegers, et al., 1988; Rie, et al., 1973; Shoji, et al.; 1994) or with very low numbers of participants (Balkhy and Schreiber, 2000; Cizman, et al., 1999) are omitted, between one third to one half of children assessed after encephalitis suffered impairments up to 12 years after the infection. The data for neonatal tetanus, CM and aseptic meningitis are difficult to interpret because of low study numbers and the fact that many studies investigated only one developmental domain. However, the results suggest that aseptic meningitis has the lowest rate of impairment of all the CNS infections examined.

Patterns of deficit following particular types of encephalitis are difficult to identify as a number of viral causes are represented amongst the 10 studies. The aetiology of encephalitis appears to affect the outcome. There seems to be little mortality and mild cognitive sequelae following California virus encephalitis (Rie, et al., 1973; Sabatino and Cramblett, 1968), whereas the outcome following Herpes Simplex encephalitis is much more devastating (Lahat, et al., 1999). A disparate pattern of results is seen in the two studies of California encephalitis (Chun, et al., 1968; Rie, et al., 1973; Sabatino and Cramblett, 1968) and may be explained by the fact that both studies included children with minor impairments. Fourteen of the motor deficits in the former study were described as "minimal" and Sabatino and colleagues comment that a specific cognitive deficit did not exist amongst his cohort, although children had visual, motor and perceptual difficulties. These results suggest that California encephalitis may have a more benign prognosis than the review results indicate. This is further supported by the low rates of impairment found in children in Donat and colleagues' (1980) study, almost two-thirds of whom had a diagnosis of California encephalitis. These discrepancies again highlight the heterogeneity in the classification of post-infectious sequelae.

Studies of neonatal meningitis often included meningitis caused by multiple organisms, most commonly by Group B Streptococci and *Escherichia coli.* In two prospective studies, sequelae occurred in 70% of children (Fitzhardinge, et al., 1974; Franco, et al., 1992), whilst in another study in which the data were derived from the medical notes, 15.8% had some form of impairment (Klinger, et al., 2000). There are difficulties in assessing children, particularly within the first two years of life. Some of the studies of neonatal meningitis are confounded by the inclusion of other causes of CNS deficits such as premature birth (Chin and Fitzhardinge, 1985) or congenital abnormalities.

Bacterial aetiology is reported to have a substantial impact on the outcome of ABM: pneumococcal meningitis usually results in higher levels of impairment, followed by *Haemophilus* and meningococcal meningitis (Baraff, et al., 1993; Kaaresen and Flaegstad, 1995). There was only one study solely examining pneumococcal meningitis (Pikis, et al., 1996) eligible for the review so it is difficult to establish such comparisons, particularly when the duration of follow-up in this study was markedly longer than that in other studies. However, five (Carroll and Carroll, 1994; Dawson, et al., 1988; Jadavji, et al., 1986; Kaaresen and Flaegstad, 1995; Kilpi, et al., 1995; Pomeroy, et al., 1990; Woolley, et al., 1999) of the eight studies of generic bacterial meningitis in children (ie. not neonates) showed that pneumococcal meningitis was the most common cause of sequelae. Of the remaining three studies, Odio and colleagues (1991) gave no information comparing aetiology and sequelae, Letson and colleagues' (1992) results are unclear because of small numbers and Richardson and colleagues (1997) found no difference between aetiologies.

In summary, the overview results suggest that cognitive and motor impairments are the most common persisting sequelae of CNS infections. Movement impairments were not found at all, although they were explicitly investigated in few studies,. Impairments in special senses (most commonly hearing) were frequently identified following ABM. However, hearing impairments were generally found at a lower prevalence than language and cognitive sequelae, contrary to the results of a meta-analysis of ABM, which found higher rates of hearing impairment compared to 'mental retardation' (Baraff, et al., 1993).

2.7 Detailed review

Application of the criteria for inclusion in the detailed review resulted in 5 papers from the 46 included in the overview, suggesting that very few papers give clear results covering the full spectrum of developmental domains and are also methodologically sound. Only one report of CM and no reports of tetanus or encephalitis met the inclusion criteria.

As in the overview, the papers for the detailed review have different lengths of follow-up, study sizes and populations. By definition, all have examined each major developmental domain and therefore provide a means of direct comparison between the patterns of impairment.

The results of the detailed review are presented in table 2.4.

Paper	CNS Infection	No. (%) died *	No. (%) deficits **	Cognition Language	Behaviour	Hearing	Vision	Epilepsy	Motor	Minor Neurological Signs ***
van Hensbroek, et al., 1997	Cerebral Malaria	134 (21.5) [1]	20 (4.4)	4 aphasia /dysarthria	4	3 hearing loss	2 visual field defects	1	7 paresis 5 ataxia	
Bergman, et al., 1987	Enteroviral meningitis	3 (6.7)	3 (9.1)	1 IQ<70 ‡	0	1 S-N loss †	0	1 ‡	0	
Grimwood, et al., 1995	Bacterial meningitis	8 (4.4)	32 (24.6)	14 IQ<80 10 unable to read	12	8 S-N loss	1 blind	7	3 spasticity	3 failed a quiet 'speech in noise' (SPIN) test
Pikis, et al., 1996	Pneumococcal meningitis	16 (17.8) [2]	14 (29.8)	9 'mental retardation'	1	8 S-N loss	1	7	4 spastic quadriplegia 1 cranial nerve palsy	
Salih, et al., 1991	Bacterial meningitis	9 (20.5) [3]	9 (30)	2 lang disorder/ delay	2	6 S-N loss	0	3	2 hemiplegia	

Table 2. 4: Results of the detailed review

* number (%) of children who died during hospital admission [died during follow-up period]
** number (%) of children followed-up who were diagnosed with neuro-cognitive deficits
*** Results not included in sequelae calculations
† Child had family history of sensori-neural hearing loss
‡ Control sibling also had the same impairment

2.7.1 Comparative mortality and morbidity

An interesting relationship between mortality, morbidity and numbers of children making a full recovery can be seen in table 2.4 and is illustrated in figure 2.2. The pattern is difficult to deduce in aseptic meningitis because of small numbers in Bergman and colleagues' (1987) study. However, mortality is low and a relatively small number of children are left with debilitating sequelae. CM and ABM, although having similarly high levels of mortality, have differing levels of morbidity with ABM leaving many more children with impairments.

	Mortality	**Morbidity**	**Full Recovery**
CM	⇧	⇩	⇧
ABM	⇧	⇧	⇩
Aseptic meningitis	⇩	⇩	⇧

Figure 2. 2: Comparative mortality and morbidity as suggested by the results of the review

The pattern of mortality and morbidity following CM may be explained by the suggestion that rather than lying on a continuum of severity, the two outcomes result from separate pathologic processes (Newton and Krishna, 1998). As discussed in section 2.3.3, this is supported by the fact that van Hensbroek and colleagues (1997) found that hypoglycaemia and lactic acidosis, strong predictors of fatality, were not independently predictive of sequelae after CM. One implication of this data is that high mortality and low to moderate morbidity may indicate the possibility of reducing death rates without necessarily increasing the rate of impairments. In ABM, children often die from shock and septicaemia but may also die from CNS complications such as raised intracranial pressure and transtentorial herniation. In contrast, children with enteroviral meningitis die from myocarditis (Bergman, et al., 1987) and not from CNS mechanisms. In CM, children may die as a result of cardiorespiratory arrest in the presence of acidosis or brainstem death. Furthermore, it is difficult to differentiate between the direct effects of the infection on the brain and the systemic effects.

2.7.2 Multiple impairments

The results of the review show that following ABM, four children with spastic quadriplegia also had severe learning disabilities (Pikis, et al., 1996) and two with hemiplegia had seizures (Salih, et al., 1991). The results of Grimwood and colleagues' (1995) study are unclear but 15% of children had more than one impairment. Following CM, six of the children with paresis and all five with ataxia had multiple impairments (van Hensbroek, et al., 1997), although the precise nature of the concomitant impairments is not described. These data are similar to those found in children with cerebral palsy, where clustering of epilepsy, cognitive and behavioural impairments occurs, indicating cortical grey matter damage (Amess, et al., 1998; Neville, 2001). The severity of the damage may also be indicated by the occurrence of concomitant deficits: van Hensbroek and colleagues (1997) found that 92% of children with one impairment made a full recovery within 6 months compared to 18% with multiple impairments.

2.7.3 Prevalence and patterns of impairment

The level of epilepsy and cognitive impairments is higher as a result of ABM compared to CM, suggesting that there is more parenchymatous brain damage following ABM, perhaps due to the direct, toxic action of the organisms invading brain matter. As indicated in the overview, bacterial aetiology seems to affect the outcome of ABM. However, differences in study design may have influenced these results, for example the large difference in length of follow-up between the CM and ABM papers. The prevalence of epilepsy after CNS infection increases over time and may develop years after the initial insult (Annegers, et al., 1988; Pikis, et al., 1996; Pomeroy, et al., 1990), although the numbers may be reduced by the increased number of deaths that occur amongst people with epilepsy in resource-poor countries (Snow, et al., 1994).

The pattern of cognitive deficits indicates high rates of learning difficulties as a result of ABM, although differences in methods of assessing cognition may have affected the results. For example, it is unclear whether van Hensbroek and colleagues (1997) or Salih and colleagues (1991) directly assessed cognitive function, whereas the other studies employed some form of formal psychological assessment.

Full-scale IQ scores or descriptions of 'mental retardation' without specific diagnostic criteria give little indication as to whether there is global cognitive impairment or whether individual aspects of cognitive function are distorting the total score. Cognitive impairments may occur as a result of focal damage to specific brain regions or may reflect suboptimal development in earlier stages of growth, rather than specific neurological damage, and may therefore be a function of the age of the child at the time of the infection and the time since onset (Epstein, 1986). In addition, the effects of cognitive impairment on the child's performance may become more pronounced as the child matures and the educational and social demands placed on him/her increase (Cross and Ozanne, 1990).

The most obvious difference in impairment patterns is the level of hearing impairment resulting from each CNS infection. Unsurprisingly, ABM results in a much higher prevalence of sensori-neural hearing loss, particularly severe to profound losses. Cochlear dysfunction is considered to be the reason for the hearing impairment since in one study, all children with sensori-neural hearing loss as a result of meningitis failed to produce otoacoustic emissions (Richardson, et al., 1997). The cochlear dysfunction causing the hearing loss is generally thought to be the result of labyrinthitis or the effects of bacterial toxins or inflammatory mediators on the hair cells of the Organ of Corti. Other possible mechanisms include similar processes acting on the endocochlear potential, metabolic defects secondary to low CSF glucose and the effects of changes in intra-cranial pressure (ICP) transmitted through the cochlear aqueduct (Richardson, et al., 1997). The finding that high levels of hearing impairment are particularly associated with bacterial meningitis further supports the view that the pathogenetic mechanisms behind hearing impairment in ABM are different to those behind neurological impairments.

In contrast, there was a low prevalence of visual impairment following all CNS infections included in the review, suggesting that it is not a long-term deficit commonly associated with CNS infection. As mentioned earlier, cortical blindness often improves in the months following CM (Newton and Krishna, 1998). The highest prevalence is after CM, although few details are given as to the nature of the visual deficit. However, it is possible that in the presence of severe cognitive impairments, visual deficits may not always be discovered.

Focal ischaemic damage secondary to CNS infection predominantly produces three kinds of impairments: partial epileptic seizures, sensory/motor deficits and cognitive deficits. None of the papers specify epilepsy types or as mentioned above, provide detail about cognitive deficits. Language impairments are cited by Salih and colleagues (1991) and van Hensbroek and colleagues (1997), which may be indicative of focal damage following ABM and CM respectively. Cerebellar damage as a result of CM may be suggested by the prevalence of ataxia, although van Hensbroek does not confirm that the cerebellum was the site of damage and no other signs of cerebellar dysfunction are reported. Focal cortical areas of decreased density, compatible with areas of infarction secondary to vasculitis, have been demonstrated by computerised tomography (CT) following ABM (Snyder, et al., 1981). Stenosis or occlusion of the basal cerebral arteries in CM has been demonstrated by angiography and transcranial Doppler (Newton, et al., 2000).

The transient nature of some neurological sequelae may give an indication of the pathogenesis of CNS damage and the relative prevalence of impairments in the current study, which aims to document persisting sequelae. Of the studies describing the prevalence of transient sequelae, Pikis and colleagues (1996) state that five cases of motor impairments (three hemiparesis, one cranial nerve palsy and one ataxia and cranial nerve palsy) and one case of hearing loss recovered, although four of the children were left with other sequelae (three sensori-neural hearing loss and one epilepsy and learning difficulties). Salih and colleagues (1991) report a similar pattern with two cases of hemiplegia recovering but later developing epilepsy. Following CM, van Hensbroek and colleagues (1997) report that some children in each impairment category at discharge recovered, particularly following paresis and ataxia. In contrast, they state that aphasia tended to persist. These results suggest that ischaemia in watershed areas may be more common than focal damage due to arterial stroke, particularly in CM.

2.8 Reliability of review results

The aim of this review was to provide a systematic analysis of persisting neuro-cognitive impairments following common CNS infections. Despite the relatively large number of papers on this subject, there is a dearth of methodologically-sound studies that cover the spectrum of developmental domains in most CNS infections, including CM. However, stringent minimum quality criteria were applied to the overview studies and measures were implemented to maintain the internal and external validity of the studies selected for the detailed review. Consequently, although it is difficult to completely avoid study bias, the consistency of the detailed review results between studies of the same infection suggests that this small number of studies gives some indication of the comparative prevalence of impairments.

The selection criteria may have introduced some elements of bias into the review. There is evidence that studies showing no impairments may be less likely to be published in English or indeed published at all (Khan, et al., 2001). Only published studies in English or French were included, so there is a risk that the effects found may have been overestimated.

The review process highlighted a number of shortcomings common to follow-up studies. Despite the importance of long-term follow-up in the study of persistent post-CNS infection impairments, 20% of the studies reviewed were excluded because the duration of follow-up was less than 6 months and a further 20% were excluded because less than 80% of the original cohort were examined. Inevitably, the longer the follow-up period in a retrospective study, the more likely the loss of study participants, which highlights the dilemma of deciding between prospective or retrospective studies when the former are often prohibitive in time and cost yet produce more reliable and valid results. Another difficult issue in assessment-based studies is what constitutes 'impairment'. This issue is particularly highlighted when standardised assessments cannot be used, for example in studies carried out in countries without such resources. Any classification of 'impairment' is by necessity arbitrary unless there is a control group sufficiently large to provide standardisation. In such cases, it is essential to describe the criteria for impairment to avoid confusion.

2.9 Summary

The review presented in this chapter has highlighted the paucity of published studies of long-term impairments associated with severe malaria. There is only one report offering a comprehensive analysis of persisting impairments associated with CM (van Hensbroek, et al., 1997). This study suggests that deficits in a broad range of developmental domains (cognition/language, behaviour, hearing, vision, epilepsy, motor skills) may be affected following CM. The literature presented in section 2.3.3 has also confirmed that there are no published studies of impairments associated with the other neurological manifestations, including malaria with seizures.

The pattern of relative morbidity indicated that ABM is more frequently associated with neuro-cognitive impairment than CM, although the number of reports was disparate. Epilepsy was a sequela of infectious disease in each of the studies included in the detailed review. However, impairments in cognition and motor function emerged from the review as the most common, persisting sequelae of CNS infections. Grimwood and colleagues' (1995) study also highlighted more subtle cognitive deficits in apparently unaffected survivors of meningitis. These deficits, although difficult to detect on formal assessment, may still adversely affect the child's social and educational functioning. As discussed in section 2.3.3, such impairments are increasingly recognised after severe forms of malaria (Holding, et al., 1999). The burden of impairment as a result of CNS infection, particularly in resource-poor countries, is probably much greater than has previously been recognised.

Chapter Three: Epilepsy and Child Development

3.1 Introduction

Chapter Two demonstrated that epilepsy is a common sequela of CNS infections. Epilepsy itself is associated with developmental impairments, although the interrelationships between epilepsy, cognition and behaviour are complex and causality is unclear. This chapter reviews the literature on epilepsy and child development, describes the various seizure manifestations in severe malaria and possible associations with subsequent impairments in development, discusses the particular issues related to epilepsy in resource-poor countries and concludes with an outline of the central questions of this thesis.

3.2 Definitions and epidemiology

Epilepsy is the most common chronic neurological condition in childhood. The prevalence is estimated to be between 0.5% and 1% of the general world population, with an incidence of between 40 and 70/100 000 per year (Bell and Sander, 2001; Sander and Shorvon, 1996). The most epileptogenic parts of the brain are the limbic system, temporal lobes and frontal lobes (O'Regan, et al., 1998), the neuroanatomical substrates of language and behaviour. An epileptic seizure is a transient clinical event: alterations in behaviour, sensation and/or consciousness resulting from a change in electrical activity in the brain. The clinical manifestations depend on the region of the brain involved, from activity in a single area of the brain resulting in a focal or partial seizure to activity in diffuse areas of the brain, resulting in a generalised seizure. Epilepsy is not a diagnosis in itself but a symptom of an underlying cerebral disturbance, which may occur in isolation or in association with other diagnoses with a wide variety of aetiologies.

Classifications of epilepsy were traditionally based on seizure types, distinguishing between generalised and partial types. The 1989 International League Against Epilepsy (ILAE) classification divides the disorder into syndromes based on clusters of symptoms and signs (Commission, 1989). Within the syndrome classification, the terms idiopathic, symptomatic and cryptogenic are used to refer to likely aetiology. Idiopathic epilepsies have no recognisable associated brain disorder and generally have a good prognosis. Symptomatic epilepsy syndromes have a known underlying cause and cryptogenic syndromes are secondary to an undetermined brain disorder. Due to difficulties inherent in the current classification – for example, the fact that a distinction between simple and complex partial seizures can be both difficult to ascertain and sometimes irrelevant, as both may be associated, or not, with altered consciousness - the ILAE is currently in the process of proposing a new diagnostic scheme (Engel, 2001). However, the ILAE scheme presently in general use will be adopted in the current study.

3.3 Epilepsy and child development

The complex relationship between epilepsy, language, behaviour and cognition is not well understood. However, epidemiological studies have consistently suggested a link between epilepsy and cognitive and behavioural impairments. The UK child health and education survey followed a cohort of over 16000 children born in a particular week in 1970. After follow-up for 10 years, 30% of the children with epilepsy were reported to have a developmental delay or disability, a figure that rose to 73% for children with symptomatic seizures (Verity, et al., 1992). McDermott and colleagues (1995) carried out a population-based study of behaviour problems in US children using data from the 1988 National Health Interview Survey. They found that children with parent-reported seizures were 4.7 times more likely to have behaviour problems than controls. In addition, 21.5% were classified as having a developmental delay and 28.7% had repeated a grade at school. Of those with both seizures and behavioural problems, 57.1% required special education. Studies on African populations have found similar patterns of results. Eighteen percent of Nigerian children with epilepsy were diagnosed as having learning difficulties (Iloeje and Paed, 1989), a rate that was increased in children with early-onset seizures or status epilepticus. Seventy-one percent of a group of rural South African children with epilepsy were found to have developmental disabilities, nearly one quarter of which were moderate to severe (Christianson, et al., 2000).

Epidemiological research has also suggested that difficulties in childhood may have implications for adult life. In a long-term follow-up of adults with early-onset epilepsies, participants with uncomplicated epilepsy had significantly poorer outcomes on social, educational and employment-related variables than matched controls of similar socioeconomic status (Sillanpaa, et al., 1998). These results remained consistent even in participants who were in remission without medication, in some cases for more than 20 years.

3.3.1 Interrelationships between epilepsy, cognition and behaviour

Epilepsy may interact with cognition in a number of different ways:

1. Brain damage or dysfunction causes both epilepsy and cognitive impairments.
2. Epilepsy causes brain damage or dysfunction, which results in cognitive impairments.
3. Epilepsy directly causes cognitive impairments.

The interrelationship between epilepsy and behaviour is more complex and reflects the interaction of biological and psychosocial factors. Besag (2002) recommends a five-fold systematic approach to determining causality in epilepsy-related behavioural disorders. First, the epilepsy itself can cause behavioural changes related to the peri-ictal or post-ictal period, inter-ictal psychoses, focal frontal or temporal lobe discharges or frequent absence seizures. The effects of antiepileptic medication on behaviour and cognition are well-recognised (Aldenkamp, 2001; Kalviainen, et al., 1996; Kwan and Brodie, 2001), as are negative reactions from others, both in the form of teasing and over-protectiveness. As with cognitive impairments, brain damage or dysfunction may affect behaviour, either directly, for example disinhibition as a result of frontal lobe dysfunction or indirectly, with frustration at the loss of other cognitive functions such as memory or language. Finally, behavioural disturbances may result from causes that are completely independent of the epilepsy, as in any other child.

Children with epilepsy form a clinically heterogeneous group, differing along dimensions such as aetiology, seizure variables, electroencephalographic (EEG) activity, antiepileptic medication, age, sex and environment (Cull, 1988; Goldstein, 1991; Niemann, et al., 1985; Strauss, et al., 1995). In terms of aetiology, children with symptomatic epilepsy are more likely to have cognitive or behavioural impairments than those with idiopathic epilepsy (Cull, 1988). Seizure syndrome is a significant influence on the risk of impairment, with malignant syndromes of epilepsy often resulting in very high rates of impairment. For example, West's syndrome and Lennox-Gastaut syndrome may result in severe developmental impairments in 80-90% of children (Neville, 1997). The study of cognitive and behavioural comorbidity is further complicated by the multiplicity of other variables that may influence development in children with epilepsy and the fact that such children can be difficult to study reliably, showing fluctuating performance from one testing period to another (Metz-Lutz and Massa, 1999).

3.3.2 State dependent versus permanent disorders

Cognitive disorders associated with epilepsy fall into two categories: 'permanent' or 'state dependent'. State-dependent learning disorders describe potentially reversible or treatable cognitive impairments, as opposed to the permanent learning disorder resulting from brain damage or stable brain dysfunction (Cornaggia and Gobbi, 2001). Prolonged status epilepticus is the most well-known situation in which epilepsy may cause cognitive impairments through damage to the brain (Scott, et al., 1998). Nonconvulsive status epilepticus, classically accompanied by continuous generalised spike-wave discharges, is an example of ictal state-dependent cognitive impairment (Besag, 2002).

There is an emerging literature suggesting that there are children in whom epileptiform discharges may cause transitory cognitive impairments (TCIs) in the absence of clinical seizures (Aarts, et al., 1984; Binnie, 1993; Binnie, 2001), affecting alertness and memory (Aldenkamp, et al., 2001) and psychosocial functions (Marston, et al., 1993). For example, focal or generalised epileptiform discharges of less than one second duration to more than three seconds have been found to momentarily impair performance on intelligence tests (Kasteleijn-Nolst Trenite, et al., 1988; Siebelink, et al., 1988). Left-sided or dominant-hemisphere discharges have been shown to impair verbal tasks such as reading (Kasteleijn-Nolst Trenite, et al., 1990) whereas right-sided discharges affect visuo-spatial functioning (Aarts, et al., 1984).

Post-ictal state-dependent cognitive impairments may be persisting rather than transitory if the seizures experienced are so frequent as to induce an almost constant post-ictal state. It has been suggested that, if allowed to continue for a long time, state-dependent learning disorders may produce permanent learning disorders (Cornaggia and Gobbi, 2001). Evidence to support this from rare models of epilepsy, such as Landau-Kleffner syndrome (LKS), benign epilepsy with centrotemporal or Rolandic spikes (BECRS) and the syndrome of continuous spikes and waves during slow sleep (CSWS), will be discussed in the following section.

3.4 Childhood models of epilepsy, cognition and behaviour

3.4.1 Acquired aphasia with convulsive disorder: Landau-Kleffner syndrome

Language disorders are common in children with epilepsy. Robinson (1991) found that 21% of children with specific language impairments had a confirmed history of seizures and a further 11% had a possible seizure history. Post-ictal deficits are usually transitory and may affect isolated components of language. Recurrent seizures may result in persistent but fluctuating and reversible language disturbances (Deonna, et al., 1987; Deonna, et al., 1982). In many cases, the epilepsy and the language impairment have independent causes or are independent manifestations of one cerebral disorder but in some cases, a direct link exists between the epilepsy and the language problem (Deonna, 1991). One such example is the syndrome of acquired aphasia with convulsive disorder in children (Landau and Kleffner, 1957), otherwise known as LKS or acquired epileptiform aphasia.

LKS is a condition in which aphasia develops after a period of normal language development with no other signs of cerebral dysfunction apart from an abnormal EEG and convulsions in some cases. Most diagnosed cases have onset of language deficits between 3 and 7 years. The EEG typically demonstrates spikes, sharp waves or spike-and-wave discharges that are usually bilateral and occur predominantly over the centro-temporal regions.

In 1957, Landau and Kleffner suggested that the cause of LKS was "persistent discharges in brain tissue largely concerned with linguistic communication [resulting] in functional ablation of the areas of normal linguistic behaviour" (Landau and Kleffner, 1957 p529). The fact that the incidence of the disease is higher in males and reports of positive family histories and affected siblings have suggested a genetic component to its aetiology (Mouridsen, 1995). Others have proposed an encephalitic aetiology (Deonna, 1991), although CSF findings and other laboratory data are normal in most reported cases (Mouridsen, 1995). Several studies using positron emission tomography (PET) or single photon emission computed tomography (SPECT) have identified hypometabolic abnormalities in temporal, temporoparietal and frontotemporal regions (Maquet, et al., 1990; O'Regan, et al., 1998). O'Regan and colleagues (1998) suggest a metabolic basis for the epileptic encephalopathy: attempting to delimit the seizure discharge, the brain temporarily switches off metabolism to the surrounding area, thus interfering with the normal function of that area. It has also been suggested that almost continuous epileptic activity in cerebral language and corresponding contralateral areas at a critical period of life when environmental factors influence synaptogenesis maturation may sustain inappropriate axonal connections that would ordinarily have undergone apoptosis (Gordon, 1997) and prevent compensation by the contralateral hemisphere (Rossi, et al., 1999).

LKS has been described as the prototype of disorders with epileptiform regression, attracting more attention than its rarity would indicate because of its unusual pathophysiology, striking clinical features and variable prognosis. Robinson and colleagues (2001) describe the evolution of LKS as a three-stage syndrome. The first stage is defined by acute deterioration of receptive language and speech with preservation of non-verbal communication. Seizures are prominent in approximately half of affected children. The EEG picture is of centrotemporal disturbances when awake and electrical status epilepticus in sleep (ESES). Stage two is the chronic phase: the aphasia in severely affected children may progress to mutism and loss of understanding of environmental sounds, while seizures may not be fully controlled and behaviour and attention problems increase. Even in milder cases, in which the aphasia does not deteriorate beyond stage one, EEG abnormalities persist. Stage three marks a phase of spontaneous improvement with the gradual improvement or reacquisition of language skills and behaviour.

As mentioned above, LKS has a variable prognosis, although a review of the literature on the long-term outcome of the disorder indicates that the majority of children are left with language impairments of varying degrees of severity (Dugas, et al., 1995; Martins, et al., 1992). Recent studies have confirmed this finding. Robinson and colleagues (2001) found that only 16.7% of cases presented a complete language recovery following LKS: four (22%) had assessment scores at or below 50% of their chronological age at a mean follow-up of 67 months. Similarly, Rossi and colleagues (1999) reported that 18.2% of cases made a full recovery and one case (9%) still presented with aphasia after a mean follow-up of 9 years 8 months. Most children in both reports were left with moderate impairments in receptive and expressive language.

Bishop (1985) reviewed 45 cases presented in the literature, all of whom had been followed up for at least 12 years. Her results suggest that the prognosis of LKS is strongly related to age at onset, with a poor outcome for children with onset before the age of 5 years. This would suggest the language disorder is one of high-level auditory processing in which the normal route to language learning is obstructed, thereby affecting younger children more severely as they have had less opportunity to learn language previously. More recently, Klein and colleagues (2000) found that premorbid language and behaviour were more predictive of language recovery than the persistence of clinical seizures. In contrast, Robinson and colleagues (2001) found little evidence that onset at certain periods of development resulted in poorer outcome in either language or non-verbal IQ. They concluded that length of ESES was the strongest predictor of outcome in their cohort, with full language recovery confined to those in whom ESES had persisted for less than 3 years. Interaction with other variables such as aetiology or site and size of lesion may explain the fact that a systematic relationship has not been found between age at onset and recovery from ACA (Paquier and Van Dongen, 1998).

Disorders other than aphasia and seizures have been associated with LKS. Short-term auditory memory impairments (Robinson, et al., 2001) and significant behavioural problems such as attention-deficit hyperactivity disorder (ADHD), autistic spectrum disorders, sleep disorders, aggression and apathy have been described (Neville, et al., 2000). Neville and Boyd (1995) describe the case of a child with acquired aphasia and apraxia and propose a group of childhood epileptic disorders – including LKS – that affect a functionally combined bilateral motor/sensory level of the cerebral cortex. Eslava-Cobos and Mejia (1997) cite impairments in praxis, gnosis, affection, mood and sexuality and go so far as to propose that LKS is not a syndrome but a 'situation' involving epilepsy and the interruption of neuronal circuits responsible for higher cortical functions in various combinations. Adopting this proposition, aphasia would be considered only one of the possible expressions of the LKS 'situation'.

In conclusion, the relationship between language and convulsive disorders in LKS remains unclear. There is debate about whether the EEG represents an epiphenomenon of underlying structural brain pathology or whether the EEG discharges and metabolic changes involving the language cortices are vital in the pathophysiology of the disease process (Shinnar, et al., 2001b). There is still debate about what actually constitutes a case of the syndrome. Even in Landau and Kleffner's original study, there were other possible mechanisms of cerebral dysfunction, for instance minor head injury, suggesting that LKS may be a heterogeneous syndrome.

3.4.2 Benign focal epilepsies of childhood

Three clinical variants of benign focal epilepsies of childhood (BFEC) are recognised: benign epilepsy with centrotemporal or Rolandic spikes (BECRS), the most frequent form; childhood epilepsy with occipital paroxysms and benign psychomotor epilepsy (Metz-Lutz and Massa, 1999). This section will concentrate on BECRS, as the variant with the greatest potential relevance to language deficits associated with malaria. BECRS is the most common focal epilepsy of childhood, accounting for between 13 and 23% of all childhood epilepsies (Wirrell, 1998). Peak onset is between 7 and 8 years, although the syndrome may occur at any time between 3 and 13 years of age. The characteristic EEG manifestation is of blunt, high-voltage centrotemporal spikes, often followed by sleep-activated slow waves that tend to spread from side to side. Seizures classically occur during sleep and are often infrequent, with 13-21% of patients experiencing only a single seizure (Wirrell, 1998).

Several authors have considered BECRS to be a useful research model, overcoming many of the methodological problems confronted when investigating the complex interactions between cognitive function and epilepsy. Despite the focal nature of the seizures and EEG characteristics, there is no anatomical brain lesion and the prognosis is benign regardless of the antiepileptic drug therapy. Finally, most seizures occur at night and may not present as convulsions and the patient and his or her family and friends know the prognosis is benign, both of which may reduce the negative sociocultural consequences associated with a diagnosis of epilepsy (D'Alessandro, et al., 1990; Piccirilli, et al., 1994).

Although, as its name suggests, the syndrome is considered to be benign, it is not clear whether its 'benign nature' refers to seizure manifestations, normalisation of the EEG, normal psychomotor development or all three (Croona, et al., 1999). A number of studies have contested the 'benign' label attributed to BECRS, although the nature of the problems is variable. Poor performance on cognitive assessments measuring IQ (Weglage, et al., 1997; Yung, et al., 2000), aspects of memory (Croona, et al., 1999; Weglage, et al., 1997), executive functions (Croona, et al., 1999) and attention (Piccirilli, et al., 1994) have variously been reported. Impairments in speech production (Deonna, et al., 1993), fine motor performance (Weglage, et al., 1997) and behaviour (Yung, et al., 2000) have also been described.

More consistently, deficits in language functions have been identified (Deonna, et al., 2000; Staden, et al., 1998; Yung, et al., 2000), although Weglage and colleagues (1997) maintain that verbal functions were less affected than non-verbal functions in his patients. Deonna and colleagues (2000) describe three of their cohort of 22 children with 'developmental dysphasia' or delayed language development. Impairments were phonological and/or lexicosyntactic in character and improved over the three year follow-up period but did not resolve completely. Aphasic impairments have also been described by Yung and colleagues (2000), who report three children with an acquired epileptic aphasia in association with BECRS, one of whom had initially presented with a profile compatible with delayed language development. They interpret their findings as suggesting that the same epileptic process can interfere with language function at two different times in its evolution, causing a developmental language delay before the onset of spoken language and an acquired aphasia after the acquisition of language. Other studies have documented more isolated problems in semantics (D'Alessandro, et al., 1990; Deonna, et al., 2000), word finding, phonology, oromotor functions (Deonna, et al., 1993), reading and spelling (Deonna, et al., 2000). Staden and collegues (1998) administered a detailed battery of language assessments to 20 children with BECRS. Thirteen presented with a consistent pattern of mild to moderate language dysfunction, eight of whom had widespread deficits in up to eight of the 12 assessments. Impairments were concentrated in the areas of reading/spelling single words, auditory verbal learning, expressive grammar and auditory discrimination with background noise. The authors suggest that the deficits are indicative of a specific language impairment as IQ was assessed as normal in eight of the 13 children with language problems.

Other studies have found that although children with BECRS have more scholastic and neuropsychological problems as a group than controls, no single cognitive profile to characterise the group emerges (Deonna, et al., 2000). Some studies suggest that impairments identified would be unlikely to have any appreciable consequences in daily life, although they may adversely affect the more complex levels of information processing and result in behavioural problems and school adjustment (D'Alessandro, et al., 1990). Several authors have linked the cognitive problems with the intensity of paroxysmal activity (D'Alessandro, et al., 1990; Deonna, et al., 2000; Metz-Lutz and Massa, 1999). Baglietto and colleagues (2001) found that children with BECRS had poorer visuomotor coordination, non-verbal short term memory, sustained attention, picture naming and visual-perceptual ability compared to controls at interictal epileptic discharge (IED) activation during sleep. At spontaneous or treatment-induced IED remission, there were no differences between children with BECRS and controls.

The persisting question in BECRS is whether the EEG abnormalities play a direct role in causing developmental and neuropsychological problems or whether they are simply non-specific markers of an underlying encephalopathy. The disorder is considered to have a genetic component as there is an increased prevalence of various types of epilepsy in patients' families (Willmore and Ueda, 2002) and one third of siblings or first degree relatives have identical EEG abnormalities (Weglage, et al., 1997). A number of pathophysiological mechanisms are posited for the cognitive deficits seen in BECRS. Early and prolonged focal epileptic activity, even at a subclinical level, may affect neuronal networks in the process of specialisation and lead to the development of abnormal neuronal connections (Deonna, 2000) or neuronal degeneration (Wasterlain and Shirasaka, 1994). The findings of Deonna and colleagues' (2000) study suggest the epilepsy played a direct role in the cognitive impairments seen in their participants: in the three participants whose EEGs worsened, language and learning problems increased. However, the relationship between cognition and EEG discharges is a complex one: not only can epileptiform discharges affect cognitive performance but activities such as reading, playing music or nonspecific cognitive activity can affect discharge rates (Binnie, 2001).

The experience of BECRS suggests that paroxysmal activity alone may be sufficient to disrupt cognitive processes, even in the absence of organic brain damage, the negative effects of antiepileptic drug therapy and adverse sociocultural conditions (D'Alessandro, et al., 1990; Piccirilli, et al., 1994).

3.4.3 Epilepsy with continuous spikes and waves during slow-wave sleep

Electrical status epilepticus in sleep (ESES) or continuous spikes and waves during slow sleep (CSWS) is an EEG-defined syndrome in which epileptiform discharges are present during at least 85% of non-REM sleep. The syndrome was first presented by Patry and colleagues (1971) who described six children who had spike-and-slow-wave complexes almost continually during non-REM sleep but not during REM sleep or when awake. The aetiology can be identified in 35-40% of cases as a non-progressive encephalopathy (De Negri, 1997). CSWS usually occurs after a period of normal development: age of onset is typically between 6 and 14 years, with peak onset at about 8 years. Onset may be associated with epilepsy, regression of cognition and/or motor skills (Tassinari, et al., 2000) and behavioural impairment, the latter usually manifesting as increased aggressiveness, poor social contact, decreased attention span and hyperactivity (Tuchman, 1994). Language regression out of proportion to other abilities occurs in some cases (Ballaban-Gil and Tuchman, 2000). Cognitive and behavioural impairments often improve with the remission of epilepsy and EEG normalisation (Ballaban-Gil and Tuchman, 2000; Tassinari, et al., 1992), although most cases are left with persisting cognitive impairments (Roulet Perez, et al., 1993).

ESES may be part of a broad spectrum of childhood epileptic conditions but the three paradigmatic syndromes are CSWS, LKS and BECRS (De Negri, 1997). Several authors have emphasised the parallel courses of ESES and CSWS and LKS, suggesting that they may represent different manifestations of the same underlying mechanism (Ballaban-Gil and Tuchman, 2000; Gordon, 1997; Metz-Lutz and Massa, 1999; Roulet Perez, et al., 1993; Tuchman, 1994). A common origin seems to be substantiated by SPECT and PET studies (Rossi, et al., 1999). The nosological similarities between ESES, LKS and BECRS have also been underlined with the proposition that BECRS lies at the milder end of the same spectrum (Baglietto, et al., 2001; Deonna, 1991; Deonna, et al., 1993). The pathogenesis may be similar, although the syndromes of CSWS, LKS and BECRS differ in age, in the area of primary EEG focal activity and in their symptomatic, cryptogenetic or idiopathic character (De Negri, 1997).

3.5 Acquired childhood aphasia

In addition to being a feature of the childhood epilepsy syndromes described above, particularly LKS, language impairment of seizure-related origin may also be the result of status epilepticus, may occur as a post-ictal phenomenon or as a feature of minor epileptic status. Acquired language impairment in childhood may also occur following a variety of traumas: head injury, cerebrovascular lesions, cerebral tumours or infections of the CNS.

The classic descriptions of acquired childhood aphasia (ACA) were of a 'motoric' aphasia, irrespective of the location of the lesion (Lees, 1993b). This description, which was prevalent until the late 1970s, had as its main features: initial mutism or telegraphic speech; later anomia or poverty of lexical stock; articulatory disorders in the context of nonfluency; rare occurrence of phonemic paraphasias; absence of logorrhoea, semantic paraphasias or neologisms and a more favourable prognosis than that encountered in adult aphasia. As this description shows, the most salient feature was the lack of the common symptoms of adult posterior aphasia types. However, further studies have indicated a positive semeiology to ACA including both nonfluent and fluent aphasias, perseverations, verbal and phonemic paraphasias and neologisms (van Hout, 1991a).

Two main criteria for a diagnosis of ACA have consistently been identified throughout the evolution in understanding of the disorder: first, that the onset of the disorder is precipitated by a cerebral insult and secondly that it follows a period of normal language acquisition. The minimum age cited to follow a period of 'normal language acquisition' varies in the literature from 1 year, based on Woods and Carey's (1979) report that lesions incurred after this age are associated with more severe language deficits than those sustained earlier to 2 years, as this is the mean age of acquisition of first sentences (van Hout, 1997).

Characterisation of the linguistic deficits in ACA has been constrained by the methodological limitations inherent in many studies, usually stemming from the small number of participants available. For example, diverse aetiologies, cases of unilateral and bilateral damage and different age groups are often included in the same study. Despite this, impairments in most areas of language have been documented in the literature on ACA. Auditory comprehension deficits were not associated with ACA in initial reports. Of all aetiologies, LKS is most commonly associated with disorders in auditory comprehension, although subtle deficits have been described following other aetiologies and the evidence does not support the traditional proposition that deficits in auditory comprehension are rare and transitory (Ozanne and Murdoch, 1990). Deficits in grammatical production have been noted to be among the most common persisting deficits in children with ACA (Lees, 1997) and a variety of expressive semantic impairments including lexical retrieval problems, paraphasic and neologistic errors have been documented (Cooper and Flowers, 1987; van Dongen, et al., 1985; van Hout, et al., 1985). Pragmatic skills have received comparatively less attention, although Cooper and Flowers (1987) reported two children with symptoms indicative of pragmatic impairment: one rarely initiated conversation and the other used inappropriate or irrelevant language. Phonological disorders have been noted , particularly in children with left hemisphere lesions, usually in patterns suggestive of delay in later developing sounds rather than dysarthria, as cited in the traditional description of ACA (Ozanne and Murdoch, 1990).

Early hypotheses about prognostic factors suggested an inverse relationship between age of lesion and degree of language recovery (Woods and Carey, 1979), although a systematic relationship between these factors is not reported in the literature (Paquier and Van Dongen, 1998), possibly due to other prognostic variables such as the underlying aetiology and the size and site of the lesion. Infectious aetiologies have been reported to have a poorer prognosis than traumatic aetiologies (Loonen and van Dongen, 1991), although most of the studies reporting this have concerned Herpes Simplex virus, which has a particular tropism for the temporal lobes and a different mechanism to severe malaria. Lees and Neville (1990) suggested that the first 6 months was the crucial period for recovery because children in their study who did not reach the normal range of performance (defined as z-scores of –1 to +1) within this period never did so. The occurrence of persistent paraphasias is also considered to be an indication of poor prognosis (Lees, 1997; van Hout, et al., 1985).

The classic description of ACA stated a rapid and complete recovery of language skills. However, reports since the late 1970s have indicated that residual deficits occur, even after apparent recovery from the aphasia. Deficits have been noted in word retrieval, syntax/morphology and higher level functions such as verbal reasoning, the understanding of linguistically-based humour and sarcasm, monitoring discourse and understanding figurative language (Cooper and Flowers, 1987; Ozanne and Murdoch, 1990; Woods and Carey, 1979).

3.6 Malaria and seizures

3.6.1 CM and seizures

Infections of the brain are implicated in up to 7% of all cases of epilepsy (Adcock and Oxbury, 2000). As outlined in Chapter Two, previous research has shown that CNS infections may be associated with the development of epilepsy: bacterial meningitis and viral encephalitis carry a particularly increased risk.

Seizures, which are often multiple and prolonged, occur in up to 80% of cases of CM (Marsh, et al., 1995; Molyneux, et al., 1989) and status epilepticus occurs in up to one third of children admitted with this form of the disease (Crawley, et al., 1996).

Seizures occurring in CM, particularly those witnessed after hospital admission, are associated with death (Molyneux, et al., 1989). Multiple and prolonged seizures are associated with the development of neurological sequelae (Bondi, 1992; Brewster, et al., 1990; van Hensbroek, et al., 1997).

3.6.2 Seizures occurring during other forms of malaria

In addition to those occurring during CM, seizures are common in children with otherwise uncomplicated malaria in whom consciousness is rapidly regained after the seizure. There has been debate as to whether the origin of these seizures is febrile – related to malaria simply because it is the most common cause of fever in Africa – or whether falciparum malaria may be specifically epileptogenic. Akpede and colleagues (1993) found that 53% of seizures occurring in fully-conscious children with malaria had complicated features, indicating that malarial seizures are unlikely to be simple febrile convulsions. This proposition is supported by evidence from a Kenyan study, which showed that 84% of children with no other signs of neurological involvement had complicated seizures: 47% were partial and over 70% were repetitive (Waruiru, et al., 1996). Fifty-four percent of observed seizures in this study occurred at rectal temperatures below 38°C. These findings were replicated in a more recent study from Kenya, which found that 58% of seizures occurred below this temperature (Crawley, 2001). In addition, a Thai study found that even at similar peak temperatures, seizures were twice as likely to occur in children with falciparum malaria than vivax malaria, even when children with a diagnosis of CM were excluded (Wattanagoon, et al., 1994).

The evidence suggests that seizures associated with *P. falciparum* infection may represent a stage in the continuum of neurological involvement, with CM as the most severe form. CM and M/S are primarily differentiated by the difference in length and depth of impaired consciousness. The following sections present a discussion of the characteristics and consequences of simple and complicated febrile seizures arising in other situations.

3.6.3 Febrile seizures

Febrile seizures are defined as epileptic seizures occurring in children, usually between the ages of 6 months and 5 years, precipitated by fever arising from infection outside the nervous system in a child who is otherwise neurologically normal (RCP, 1991). They appear to be specifically related to an age group in whom increased susceptibility to seizures is induced by fever, although the detailed pathophysiology remains unclear (Shinnar and Glauser, 2002).

A febrile seizure may be classified as 'simple' or 'complex', a simple febrile seizure being isolated, brief and generalised. To maintain a clear distinction between complex febrile seizures and complex partial epilepsy, the following terminology will be used:

- A complex febrile seizure is focal (convulsive movements of one side of the body), repetitive (two or more in 24 hours) or prolonged (usually described as lasting more than 10 or 15 minutes but lasting more than 30 minutes in the current study). Although the terminology generally used is of a 'complex' seizure (Berg and Shinnar, 1996; Shinnar and Glauser, 2002), the terminology used in this thesis will be of a 'complicated' seizure. This is to avoid confusion between the seizure episodes occurring during malaria and the potential for partial epileptic seizures as a disorder subsequent to malaria.
- The terms 'complex partial epilepsy' or 'complex partial seizures' will be maintained, describing partial seizures associated with aura, automatisms and psychosensory, cognitive or emotional symptoms.

Most febrile seizures are simple and considered to be benign and self-limiting. The results of the UK Child Health and Education Survey indicated that 2.3% of the cohort experienced a febrile seizure within the first 5 years of life and that 18.8% of these had complicated features (Verity, et al., 1985a). In a prospective cohort study of 428 children with a first febrile seizure, Berg and Shinnar (1996) found that 35% had at least one complicated feature: 16% had focal features, 14% had repetitive seizures and 13% had prolonged seizures. Febrile status epilepticus, defined as a seizure lasting more than 30 minutes, occurred in 5% of the children.

Having a first or second-degree relative with a history of febrile seizures has consistently been identified as a risk factor for a first febrile seizure and also for recurrent febrile seizures, implying a genetic role. Other risk factors for recurrent febrile seizures include high peak temperatures, short duration of fever and age of less than 18 months (Shinnar and Glauser, 2002). Children with multiple risk factors have been found to have the highest risk of recurrence.

The morbidity of febrile seizures and febrile status epilepticus is low in most studies (Chang, et al., 2000; Lee, 1989; Shinnar, et al., 2001a), even after complicated febrile seizures (Verity, et al., 1985b; Verity, et al., 1998). The latter have been associated with neurological damage, particularly mesial temporal sclerosis (section 3.7.1) (Scott, et al., 1998). The effects of repeated seizures may be exacerbated by age, producing a recurrent cycle of neuronal loss in a critical area that results in a repeating pattern of lowered resistance to seizures and further seizure-induced injury, eventually leading to the epileptic state (Lado, et al., 2000).

There has been much debate about the risk of developing epilepsy subsequent to febrile seizures. The risk of epilepsy following a single, simple febrile seizure is similar to the risk in the general population (Annegers, et al., 1979; Annegers, et al., 1987; Verity and Golding, 1991). However, complicated febrile seizures have been associated with the development of epilepsy (Annegers, et al., 1979; Annegers, et al., 1987; Maher and McLachlan, 1995; Verity and Golding, 1991), particularly complex partial seizures with a temporal lobe focus. However, it is not clear whether febrile seizures are simply an age-specific marker of future seizure susceptibility; an indication of pre-existing brain damage, which is responsible for the later development of epilepsy or have a causal relationship with any subsequent epilepsy (Annegers, et al., 1987; Shinnar, 1998).

3.7 Temporal lobe epilepsy

TLE is a common cause of complex partial seizures (CPS): although the temporal lobe is the most common site of origin, seizures may arise in other lobes (Paradiso, et al., 1995) or regions outside the temporal lobes, for example the frontal pole, fronto-orbital cortex or cingulate gyrus (Elger, 2000) or elsewhere.

The ILAE classification describes temporal lobe seizures as originating from either hippocampal (mesiobasal limbic or primary rhinencephalic psychomotor) or lateral temporal areas. Many epileptologists adopt an aetiological approach and divide TLE into three types:

1) Mesial temporal epilepsy, associated with hippocampal sclerosis
2) Lesional temporal lobe epilepsy, defined by lesions other than hippocampal sclerosis in the temporal lobe
3) Cryptogenic temporal lobe epilepsy

(Wieser, et al., 2000)

Approximately one third of children with TLE have no underlying temporal lobe lesion, no associated psychological deficits and show seizure remission in later childhood (Harvey, 2000). Seizure signs and the course of seizure spread may be different in children compared to those in adults due to the nature of the developing brain and auras cannot be reported (Nordli, et al., 2001). The typical phenomena of TLE only occur in children above five or 6 years of age (Brockhaus and Elger, 1995; Elger, 2000).

3.7.1 Mesial temporal lobe epilepsy

Temporal lobe epilepsy associated with its most common pathological substrate, mesial temporal sclerosis, has resulted in the distinct epileptic syndrome of mesial temporal lobe epilepsy (MTLE) (Harvey, et al., 1995; Harvey, et al., 1997). This syndrome is of particular interest in the consideration of epilepsy and child development because the limbic system, which consists of the amygdalae, septum, cingulate gyrus and hippocampal formation (Crossman and Neary, 1995), is involved in memory, affect and behaviour.

The seizure semeiology of MTLE is often auras – typically epigastric sensations associated with olfactory, gustatory and psychic phenomena such as fear, *déjà vu* or *déjà entendu*) – evolving into CPS with ictal, postictal, *de novo* or reactive automatisms. Automatisms are commonly oroalimentary symptoms such as lip-smacking and swallowing and gestures such as picking clothes, fumbling or aimless movements. Wieser and colleagues (2000) classify such seizures into three groups. First, absence-like seizures; secondly, seizures characterised by automatisms and psychomotor symptoms and thirdly, seizures with psychosensory, cognitive or emotional symptoms characterised by visual, auditory, somesthetic or olfactory illusions or psychic symptoms.

The causative role of hippocampal sclerosis in MTLE is controversial. There is some debate as to the prevalence of mesial temporal sclerosis in TLE in childhood with some paediatric series suggesting that it is a rare cause (Wyllie, et al., 1993) while others suggest prevalence rates as high as 75% (Cross, et al., 1996; Mohamed, et al., 2001). One of the most contentious issues in epileptology is whether prolonged febrile seizures cause mesial temporal sclerosis. Many population-based and prospective studies have failed to find any association (Lado, et al., 2000; Shinnar and Glauser, 2002) and preventing febrile seizures does not result in a reduction in the incidence of subsequent epilepsy, which would be expected if a causal relationship existed (Shinnar, 1998). However, Maher and McLachlan (1995) found an association between febrile seizures over 90-100 minutes in length and TLE with mesial temporal sclerosis. Febrile seizures lasting more than 90 minutes occur in less than 1% of cases (Berg and Shinnar, 1996), although prolonged status epilepticus may be more common in a malaria-related context. Investigating children with CM, Crawley and colleagues found that 28% of children had an episode of status epilepticus, which was longer than 30 minutes in 83% of this group (median 150 minutes, range 40-390 minutes) (Crawley, et al., 2001; Dr J Crawley, personal communication). It has not been possible to exclude the possibility that the immediate cause of an early childhood seizure, such as an infectious or ischaemic insult, may also cause injury in the mesial temporal region, which may in itself prove to be epileptogenic (Lado, et al., 2000). In such a scenario, mesial temporal sclerosis occurs independently of seizures but is the immediate cause of epilepsy.

3.7.2 Developmental impairments associated with TLE

The neurobiology of TLE is more complex than the lesion model of focal brain damage that gave rise to classic neuropsychological paradigms: a diagnosis of TLE may indicate little about the child's cognitive and behavioural profile (Paradiso, et al., 1995; Shulman, 2000).

In their seminal study on the long-term effects of TLE, Ounsted and colleagues (1987) found that 30% of the 100 children they followed for 38 years had psychosocial problems and were completely dependent on others and 32% required special schooling. In a study using comprehensive neuropsychological assessments, Schoenfeld and colleagues (1999) found a pattern of generalised cognitive impairment in children with CPS and suggest that regions outside the epileptogenic focus were adversely affected. The pattern of impairments, although the result of epilepsy of much shorter duration, was similar to that found in adults with CPS (Hermann, et al., 1997), leading Schoenfeld and colleagues to propose that such generalised cognitive effects may be intrinsically associated with early-onset CPS. Studies on developmental level and IQ have indicated that IQ is lower in children with bilateral temporal lobe foci (Jambaque, et al., 1993). Gadian and colleagues (1996) found that left-sided temporal lobe pathology, as detected by magnetic resonance spectroscopy (MRS) is associated with a reduction in verbal IQ (VIQ) and right-sided pathology with a reduction in performance IQ (PIQ), although others have found no VIQ/PIQ discrepancy related to laterality of pathology (Jambaque, et al., 1993).

Language functions may be particularly affected in children with CPS, in both expressive and receptive domains (Schoenfeld, et al., 1999; Shulman, 2000). A PET study in adults with left TLE found the areas of greatest metabolic depression to be in left inferior frontal and superior temporal regions, which correlate to Broca's and Wernicke's areas respectively (Arnold, et al., 1996). No comparable study has been carried out in children. In addition to linguistic impairments, communication abilities may be adversely affected in TLE. Children assessed before temporal lobectomy and children with CPS have been found to have impairments in thought processing and discourse cohesion (Caplan, et al., 1993; Caplan, et al., 1994). More recently, Caplan and colleagues have found that children with CPS made more syntactic revisions than controls, making their speech sound stilted, artificial and detailed (Caplan, et al., 2001). The fact that these findings were particularly pronounced in participants with EEG evidence of a temporal lobe focus suggests that repair of basic linguistic functions involves the temporal lobe, in contrast to higher level linguistic planning, which appears to involve the frontal lobes. Anomia may be a particular feature of language impairment (Hamberger and Tamny, 1999) and may account for some of the verbal memory deficits associated with left TLE (Hermann, et al., 1988; Mayeux, et al., 1980). The results of a study by Billingsley and colleagues (2001) indicate greater participation of regions outside the left temporal lobe in language functions in adults with left TLE, leading them to suggest possible inter- and intra-hemispheric functional reorganisation of language representation.

The importance of medial temporal lobe structures in memory function is well-recognised. This has come largely from the study of memory in patients who have undergone temporal lobectomy for intractable epilepsy, emphasising the contributions of left and right temporal lobe systems for verbal and non-verbal material respectively (Paradiso, et al., 1995). Memory impairment is commonly found in TLE, particularly MTLE associated with hippocampal sclerosis (Rausch and Babb, 1993; Sass, et al., 1995). Studies suggest that episodic memory is dependent on the hippocampus (Vargha-Khadem, et al., 1997) and is particularly affected in the case of bilateral hippocampal pathology. There is some evidence for the effects of laterality on verbal and non-verbal memory (Helmstaedter, et al., 1994), although most studies have shown that children with both left and right TLE show deficits in both modalities of memory (Oxbury, 2000).

Behavioural impairments have also been linked to TLE: their heterogeneity is increasingly recognised as a consequence of the syndrome's complex neurobiology involving neuropathological factors and variable neurophysiological factors (Shulman, 2000), in addition to the psychosocial factors outlined in section 3.3.1. However, apart from later psychosis, which is commonly associated with TLE, children with this form of epilepsy do not seem to have more behaviour disturbances than children with other types of epilepsy (Caplan and Austin, 2000).

3.8 Epilepsy in resource-poor countries

Both the incidence and prevalence of epilepsy are often reported to be higher in resource-poor countries (Sander and Shorvon, 1996; Senanayake and Roman, 1993), although international comparisons can be problematic because of lack of uniformity in case definitions (Senanayake and Roman, 1992). Aetiological factors may be different in resource-poor countries: for example, birth injuries and infectious diseases may be more important factors than in richer countries (Jallon, 1997; Joshi, et al., 1977; Pal, 1999; Senanayake and Roman, 1991; Snow, et al., 1994).

Epilepsy has social as well as medical consequences, which are particularly related to the social perceptions and cultural beliefs about the disorder in the child's community (Dean and Lannon, 2000). Studies have provided conflicting evidence on the psychosocial consequences of epilepsy in resource-poor countries. Social stigma was reported by adults with epilepsy in Zambia (Birbeck, 2000) and Nigeria (Danesi, 1984), although little stigma was found to be associated with the disorder in Pakistan (Aziz, et al., 1997). In children, social stigma often manifests as teasing by peers and isolation from the wider family circle (Debruyn, 1990).

A variation in results is also seen in the effects on educational opportunities. A Tanzanian study found that onset of epilepsy before school age adversely affected a child's prospects of attending school, regardless of intellectual capacity (Rwiza, et al., 1993). Similarly, in India, only 50% of study children with epilepsy attended school compared to 95% of their peers (Pal, 1998) and in Zambia, children were removed from school after onset of epilepsy to prevent family embarrassment (Birbeck, 2000). On the other hand, only a marginal association between epilepsy and educational opportunities was found in Pakistan (Aziz, et al., 1997) and a study of Zimbabwean teachers found comparatively positive attitudes with 83% reporting that they would be happy to teach a child with epilepsy (Mielke, et al., 1997). In addition to the impact of stigma and reduced opportunities on employment and marriage prospects, there may be consequences on self-esteem and self-perception. Many adults interviewed in a Nigerian study rated their ability and potential as lower than that of people without epilepsy (Danesi, 1984), although urban Zimbabweans with epilepsy did not perceive themselves to have sufficient cognitive impairment to interfere with social functioning, work performance or relationships (Mielke, et al., 2000).

Knowledge, access and compliance with effective treatment are also particular issues in some resource-poor countries. Nicoletti and colleagues (1999) found that 90% of rural Bolivians with epilepsy had never taken antiepileptic drugs for more than a two-month period and a similar proportion of Zambian people were not receiving any treatment (Birbeck, 2000). Often, the first person consulted for treatment is the traditional healer (Butau and Piachaud, 1993; Nicoletti, et al., 1999,Rwiza, et al., 1992): a greater proportion of consultations regarding epilepsy have been found to occur relative to consultations for other physical disorders (Bondestam, et al., 1990). This may reflect that fact that in some areas, epilepsy is still thought to be caused by supernatural forces or it may be due to lack of awareness of effective pharmacological treatment and the fact that the traditional sector is more readily available, particularly in rural areas (Butau and Piachaud, 1993). Compliance with treatment may be adversely affected by the social and financial costs of hospital attendance (Pal, 1998). In a study in India, 54% of parents reported that their biggest expenditure was the cost of drugs and 36% said it was the cost of travel to hospital (Thomas and Bindu, 1999). However, lack of continued treatment may be due in part to poor availability rather than reluctance on the part of the patient (Rwiza, et al., 1992; Tekle-Haimanot, et al., 1997).

Mortality among people with epilepsy is greater than in those without epilepsy in both developed and resource-poor countries (Nashef, 2000; Nashef, et al., 1995; Shinnar and Pellock, 2002) and in children is associated with remote symptomatic aetiology (Sillanpaa, et al., 1998). Uncontrolled epilepsy may represent a particular risk to physical health in resource-poor countries: burn injuries from open fires or falls are reported in between 10% and 30% of people with epilepsy (Birbeck, 2000; Rwiza, et al., 1993; Tekle-Haimanot, et al., 1997). High seizure frequency and abnormality on neurological examination were both associated with excess mortality in an Indian study, although causes of death were not investigated (Thomas, et al., 2001). In 78% of deaths in rural Kenyans with epilepsy, the seizures were considered to be directly responsible for the death, mostly as a result of status epilepticus but in one case, following burns from a fire and in another, after falling from a coconut tree (Snow, et al., 1994).

3.8.1 Methodological issues

The elements of social stigma and embarrassment bring particular issues to the study of epilepsy in resource-poor countries. Medical and personal data may be difficult to ascertain because of the lack of medical records or the fact that diagnoses are not always adequately explained to patients on discharge from hospital (Pal, 1999). Poor recall and limited vernacular for specific diseases can hinder the investigation of aetiology (Snow, et al., 1994). Partial seizures, particularly complex partial seizures which have atypical epileptic manifestations, are often not recognised as forms of epilepsy by patients of their families in resource-poor countries (Senanayake and Roman, 1992). In consequence, interview techniques may fail to identify the true prevalence of such seizure types.

3.9 Summary: epilepsy as a syndrome

This chapter has examined the complex relationship between epilepsy and developmental impairments. Disorders such as LKS, CSWS and BECRS are important models for childhood epilepsy because they provide evidence that isolated and sometimes persistent neuropsychological disturbances, such as language impairments, can in themselves be epileptic manifestations (Deonna, 1991). Epilepsy affects the development of children in several domains and may best be viewed as a syndrome, one part of which is the seizure disorder (Besag, 2002; Neville, 1999). The view that epilepsy, particularly subclinical seizures, may cause developmental arrest or even regression is becoming more widely accepted (Scott and Neville, 1998). Indeed, subclinical seizure activity may be more important in the developing brain as high rates of such activity, for example during sleep, may disrupt the functioning of homologous language areas in the opposite hemisphere or areas adjacent to the seizure focus on the same side (Lees and Neville, 1996).

Evidence from studies of complicated febrile seizures suggests that epilepsy and developmental impairments may occur in the context of severe malaria with complicated seizures. Reports of impairments associated with complicated febrile seizures suggest temporal lobe damage or dysfunction, with manifestations including complex partial epilepsy and deficits in memory, language and behaviour. Thus, the central questions of this thesis are whether the prevalence of epilepsy is increased in children following severe forms of falciparum malaria and whether epilepsy is associated with impairments in language, memory, behaviour and other developmental functions.

Part Two: Assessment in Context

The process, purpose and justification for investigating neuro-cognitive processes in children whose development has been the subject of little previous investigation and who have limited access to rehabilitation services is the focus of this part of the thesis.

Chapter Four discusses issues pertaining to disability and rehabilitation in countries with few resources and services for affected children and presents contextual information on the Kilifi, the study site. The purpose of Chapter Five is to acknowledge the fact that many of the children in the study face multiple risks to normal development, of which malaria is only one potential contributor. This chapter discusses the literature on nutrition, other parasitic infections and socioeconomic conditions and describe how these factors were accounted for in the current study. As a large part of the work for the study was the development of suitable assessment tools, Chapter Six will discuss specific issues of cultural appropriateness, particularly in assessments of language and cognition. Finally, Chapter Seven will present an outline of the Kigiryama language, the mother tongue of the majority of study participants and the medium in which all of the assessments were conducted.

Chapter Four: Assessment and Rehabilitation in Resource-Poor Countries

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4.1 Introduction

Equitable access to appropriate services is an issue for people with disabilities in many countries but a particular issue in resource-poor countries, in which such services are often scarce. This chapter will discuss issues relating to the perception and remediation of disability in resource-poor countries and the purpose of the current study in a situation with little provision. The chapter will conclude with a description of the socioeconomic and cultural context of the study.

4.2 The Perception and remediation of disability

In the 1980s, the World Health Organisation (WHO) produced a classification to differentiate the concepts of impairment, disability and handicap (WHO, 1980). An impairment is described as a loss or abnormality of psychological, physiological or anatomical structure or function, which may result from a variety of aetiologies. A disability is a restriction or lack of ability to perform an activity in the manner or within the range considered normal. A handicap is a disadvantage for a particular individual that limits or prevents the fulfilment of a role that is normal for that individual. The prevalence of handicaps reflects the prevalence of disabilities but is also a reflection of the attitudes and barriers to rehabilitation and participation of people with disabilities in the community (Thorburn, 1990).

A new WHO classification has recently been published (International Classification of Functioning, Disability and Health, abbreviated to ICF), described as a 'components of health' rather than a 'consequences of disease' classification (WHO, 2001). The ICF domains are seen from the perspective of the body, the individual and society, reflecting the original concepts of impairment, disability and handicap but endeavouring to extend the scope of the 1980 classification to allow positive experiences to be described. This study is concerned with the prevalence of impairments associated with severe forms of malaria, rather than the investigation of disability. However, consideration of the concept of disability in resource-poor countries is important to the possible implications of the study in terms of disabilities associated with any identified impairments and the development of services for their remediation.

There have been few studies on the prevalence of disabilities in children in resource-poor countries, yet it has been estimated that 85% of the world's disabled children live in these regions (Helander, 1993). The causes of impairments in resource-poor countries are usually preventable, poverty-associated medical conditions. These include pre- and peri-natal insults, problems in the neonatal period, malnutrition and infectious diseases. They may also be the result of situational factors such as poorly-controlled toxic waste disposal, violence in the context of war or civil strife and iatrogenic effects as a consequence of uncontrolled private health clinics employing partly-qualified medical staff (Zinkin, 1995).

In the context of high mortality rates from common conditions, the focus of health services is on prevention and treatment of life-threatening conditions and little attention is usually paid to disability. Thorburn (1990) and Khan and Durkin (1995) hypothesise that although the risk of impairment is probably higher for children in resource-poor countries than other regions, the increased mortality of children with disabilities as a result of malnutrition and infectious disease may reduce the apparent rate of severe disabilities in such regions. Thorburn (1990) predicts that the effect of this will be a higher prevalence of moderate and mild disabilities.

Individuals in resource-poor countries usually have less choice and control over their health-related behaviour than those in resource-rich countries (Coreil, 1997). In addition, the perception of particular impairments resulting in disability is relative and may differ between resource-rich and resource-poor countries. Certain impairments such as mild learning disabilities or hearing impairments may be perceived as disabilities in resource-rich countries by virtue of their more stressful and demanding educational systems yet be little recognised in resource-poor countries (Thorburn, 1990). On the other hand, Fayyad and colleagues (2001) comment that in some countries, families may avoid taking a child with a mental health problem (including epilepsy) to a health clinic for fear of labelling or stigma, which may in itself result in disabilities in the social sphere.

McConachie and Zinkin (1995) argue that economics, culture and gender are the three main factors in the social and political context of disability. As for many people in resource-poor countries, poverty is often the overwhelming issue for people with disabilities, superseding issues such as lack of rehabilitative provision. Lack of financial resources may also preclude access to schooling or rehabilitation even if it is a priority for families of affected children because such services may require a fee or the purchase of equipment. Attitudes about causes of impairments and potential 'cures' prevalent in a particular culture may affect the self-image of children with disabilities, their families' morale and the efficacy of strategies espoused by agencies planning services. Finally, gender may impact upon access to schooling and rehabilitative services more than other factors such as severity of the impairment.

4.2.1 Prevention, rehabilitation and service provision

Effective services for prevention and rehabilitation of impairment rarely coexist in situations in which there are few health care resources. Child health and survival is considered to be the most important public health issue in resource-poor countries because of the large youth populations and because child mortality exceeds adult mortality. However, rehabilitation may be considered to be of equal importance to prevention because a reduction in the incidence of a disease only reduces the composition of disability in the short-term rather than the numbers of children affected (Thorburn, 1990). Mbise and Kysela (1990) describe the case of Tanzania, where preventive services in the forms of vaccinations and nutritional education were provided but were reduced in effectiveness due to lack of transportation, long travelling distances in rural areas, difficulties in communicating the benefits of vaccinations and prompt treatment, inadequate drug storage facilities and lack of trained personnel. In such situations, rehabilitative services will continue to be a particularly important component of the health care system.

Fayyad and colleagues (2001) describe service provision for children with developmental disorders, autism or learning disabilities in Lebanon. Despite the ample number of schools and centres with facilities for such children, the authors state that children with such disabilities still face three major obstacles. First, some families feel stigmatised or ashamed of their child and may keep him/her at home without access to rehabilitation services. Secondly, families may not be able to afford the fees levied for services or transport, although they want to make use of them. Finally, future integration into society is often difficult and children and adults with disabilities may remain on the fringes of society. These issues are similar to those faced by rural children on the Kenyan coast.

Rehabilitation services are scarce in Kilifi District. Physiotherapy and Occupational Therapy services are based at Kilifi District Hospital, although there are no Speech and Language Therapy or Psychology services. The Education and Assessment Resources Service recommends educational placements for children with special needs in a small number of local school with such provision.

The Western concept of rehabilitation is of a professionally-delivered service. Although there is a relationship between a country's GDP per capita and their ability to provide remedial services, the community-based rehabilitation (CBR) model, which integrates rehabilitation into community-level services, is an inexpensive and effective means of providing such a service. Thorburn (1990) estimates that 70-75% of the more simple rehabilitation problems can be effectively solved at the primary level in and by the community, although there is little data on the effectiveness of the methodology.

Thorburn (1990) comments that lack of information is one of the reasons for the lack of services for disabled children in resource-poor countries. She cites a report from Rehabilitation International on the status of disabled children in resource-poor countries, which lists the problems responsible for lack of services:

1. Lack of information about causes and prevalence of disabilities and consequent lack of efforts to prevent them
2. Persistent misconceptions and superstitions
3. Ignorance of what can be done to help a disabled child and the consequent fatalistic attitude to intervention
4. The misconception commonly held that cure of a disability is possible by medical or traditional treatments if only the right practitioner can be found
5. The belief that Western high technology is the only solution

6. The poor expectations for disabled people, resulting in their isolation and denial of opportunity, with consequent self-fulfilling prophecies of dependence and uselessness

Rehabilitation International Report to UNICEF, cited in Thorburn (1990)

This study aims to address the issue of lack of information as it pertains to the first point in this list. Data from the developmental assessments administered to children during the study will provide evidence on whether malaria is associated with persisting impairments, thus a potential cause of disability. Despite the lack of immediate rehabilitative provision for children with impairments participating in this study, the characterisation of developmental impairments associated with malaria will both allow governmental and other agencies to address the issues of schooling and rehabilitation services and facilitate the development of appropriate remedial measures.

4.3 Socioeconomic conditions in Kilifi district

Kilifi District, the site of the study, is in Coast Province bordering the Indian Ocean (figure 4.1). The nearest city is Mombasa, the second largest city in Kenya and its main sea port. The area is located 4° south of the Equator and has mean daily temperatures of between 22°C and 30°C, with relative humidity of approximately 70%. There are two main rainfall seasons per year: the long rains are between April and June and the short rains, between October and December. Malaria transmission follows the seasonal rainfall, with peak periods between June and August and December and January.

Figure 4. 1: Map of Kenya showing Kilifi, the study site

The population projection in the Kilifi District Development Plan for 1999, the year the study commenced, was 812, 684 (Government of Kenya, 1997). The projection for children in the 5-9 year age range was 136, 799. The population is skewed to the younger age ranges: children in the 0-14 age group account for 49% of the people in the district.

Agriculture is the most important economic activity in the area, engaging 70% of the labour force, mostly in the form of small-scale subsistence farms (Government of Kenya, 1997). There is a pattern of male migration to Mombasa for work: in consequence, women carry out most of the crop cultivation. The most important food crop is maize, followed by cassava; coconuts and cashewnuts are the most important cash crops. The rate of food self-sufficiency is low: 70% of households in Coast Province are unable to produce sufficient food crops to meet even half of the household energy requirements (Hoorweg, et al., 1995).

There are 323 primary schools in Kilifi District, with a pupil/teacher ratio of 35:1. The District has 40 secondary schools. The level of female enrolment in secondary schools is low at 38%. There is one school for children with hearing impairments and seven units for children with disabilities in various schools, one for children with visual impairments and six for children with learning disabilities (Government of Kenya, 1997).

The infant mortality rate in the district is 100/1000, which is higher than the Kenyan national figure of 66/1000. Chronic malnutrition is consistently high: 50% of pre-school children are classified as malnourished. Immunisation coverage is low due to traditional practices and beliefs (Government of Kenya, 1997). Formal health services are provided by Kilifi District Hospital, government dispensaries, private health clinics and community health workers, who are trained to supply subsidised drugs from home and to assess patients for referral to other facilities when necessary. However, over 60% of rural households are located more than 2 kilometres from the nearest health facility and 50% live a similar distance from a community health worker (Molyneux, 1999). In consequence, the majority of people rely on the informal sector – local shops stocking antipyretics and antimalarials and *waganga*, or traditional healers – for first-line healthcare.

The research unit, the coastal branch of the Kenya Medical Research Institute (KEMRI) is a collaborative programme with The Wellcome Trust, UK. An area comprising a 40km stretch of coastline north of Kilifi town, extending 30km inland has been under demographic and epidemiological surveillance since the early 1990s (Snow, et al., 1993b). The study area consists of rural and peri-urban communities with most of the population originating from the Mijikenda ethnic group. The languages spoken by this group and used as the medium of assessment in this study will be described in Chapter Seven. The research unit is attached to Kilifi District Hospital, the main referral hospital, used by more than 80% of a population of 80 000 in the study area. The clinical arm of the research unit comprises a 40-bed paediatric ward, staffed by two to three nurses and receiving 5000 admissions per year (12 per day). There is also a high dependency unit with seven beds, two nurses and a dedicated clinical laboratory. Thirty-seven percent of admissions and 10% of deaths in 1999/2000 were due to malaria (Dr C Newton, personal communication).

4.4 Summary

Estimates suggest that the proportion of children with disabilities may be higher in resource-poor countries than in their richer counterparts. Areas such as Kilifi have few rehabilitative services for such children. The characterisation of developmental impairments associated with severe forms of malaria may assist in the future development of appropriate service provision.

Chapter Five: Influences on Child Development in Resource-Poor Countries

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5.1 Introduction

The United Nations Convention on the Rights of the Child states that all children have the right to 'the enjoyment of the highest attainable standard of health': however, many children, particularly those in resource-poor regions of the world, live in conditions of economic deprivation, receive inadequate nourishment and face chronic illness. Chapter Four described the prevailing subsistence economy in Kilifi District and the high infant mortality rate, high level of chronic malnutrition, low rate of food self-sufficiency and low level of female secondary education in the area. These factors may act as confounders in the current study because of their hypothesised impact on developmental outcomes and may comprise a complex of economic, social and educational elements – one of which may be the effect of severe malaria – influencing the development of children in Kilifi. This chapter outlines factors relevant to the Kilifi context: protein energy malnutrition, iron deficiency anaemia, parasitic infections other than malaria, socioeconomic conditions and HIV-related encephalopathy. The chapter discusses the evidence for their deleterious effects on child development and describes how each factor was accounted for in the current study.

5.2 Nutritional status

Protein energy malnutrition (PEM) includes severe clinical malnutrition – with a distinction traditionally made between marasmus, kwashiorkor and mixed forms – and less severe forms of growth delay, usually referred to as mild or moderate forms of malnutrition. Marasmus is a form of emaciation resulting from an overall deficiency of calories and nutrients, usually affecting young infants who have severely undernourished mothers who cannot produce adequate breast milk. Kwashiorkor usually occurs in young children who have been weaned and are consuming a diet high in carbohydrates but deficient in protein (Morgan and Gibson, 1988). This distinction is now regarded as an oversimplification of the dietary aetiology of malnutrition and many practitioners describe only different degrees of PEM (Richter and Griesel, 1994).

In resource-poor countries, 5-10% of children exhibit severe clinical malnutrition: Martorell (1999) comments that this represents the extreme end or 'tip of the iceberg' of nutritional problems with the invisible proportion of the iceberg comprising stunted children without clinical signs. PEM is diagnosed by comparing anthropometric measurements to reference values for age and sex, although mild PEM cannot always be detected by anthropometry (Sigman, 1995). *Stunting* is measured by comparing height with age and reflects linear growth achieved pre- and postnatally, primarily before 2 to 3 years of age. Stunting is indicative of prolonged, cumulative deficiencies in health and/or nutrition (Frongillo Jr., 1999). *Low weight* is measured by comparing weight with age and reflects both short-term weight accumulation and long-term weight gain pre- and postnatally. *Wasting* is measured by comparing weight with height and has the advantage of not requiring knowledge of age, which can be difficult to ascertain in some communities. Wasting is usually a severe and often, recent process, such as disease, acute starvation or chronic dietary deficits, that has led to significant weight loss. The prevalence of stunting, low weight and wasting in East African children under 5 years of age was 48%, 33% and 7% respectively in 1995 (Frongillo Jr., 1999).

Malnutrition potentiates the effects of infection and contributes to more than half of all deaths in children under 5 years of age in resource-poor countries (Frongillo Jr., 1999). Most of these deaths occur in children with mild to moderate malnutrition. Infections adversely affect nutritional status while nutritional status affects vulnerability to and the severity of infections. The nature of the relationship between malaria and malnutrition is unclear with debate concerning a possible protective effect of malnutrition and iron deficiency (Greenwood, et al., 1991). Two recent studies from South-East Asia indicate that the debate continues. Nacher and colleagues (2002) found a significant protective effect of malnutrition from cerebral malaria in Thai patients, whereas Takakura and colleagues (2001) found that falciparum malaria was associated with acute malnutrition in children and adolescents from Laos. While the relationship between malaria and nutritional status remains uncertain, the evidence clearly suggests that dietary deficiencies may inhibit recovery from infection, resulting in impaired growth and increased vulnerability to subsequent infections (Richter and Griesel, 1994).

Several studies have suggested an association between severe PEM in early childhood and poor cognitive and behavioural development (Grantham-McGregor and Cumper, 1992). A causal relationship cannot be unequivocally inferred because of complexities in study design, namely the difficulty of separating the effects of nutrition from those of poverty in observational studies. Malnutrition has been linked to poor nutritional intake of macro- and micro-nutrients, infection, caregiver-child interactions, intergenerational effects (for example, a stunted mother giving birth to a low-birth-weight daughter and subsequent stunting in the daughter) and ecological factors, all conditions that are also associated with poverty (Frongillo Jr., 1999; Richter and Griesel, 1994; Sigman, 1995). In addition, it is often difficult to find comparison groups who have not themselves suffered some degree of undernutrition.

Mild and moderate malnutrition has also been associated with medium- and long-term deficits in cognition and behaviour. Pollitt (1996) describes a longitudinal study from rural Guatemala, which investigated the impact of pre- and postnatal nutritional status on long-term cognitive outcome. The trial measured the effects of supplementary feeding on later cognitive development, following children up for 11 years after the termination of the trial. Data were collected on body size and composition, skeletal maturation, intellectual performance, school attendance history and socioeconomic status (SES). Participants at the lower end of the SES scale who had received high-protein supplementation in utero and early in life had better motor abilities at 2 years and better perceptual organisation and verbal skills at 4 and 5 years, compared to participants who had received a low-energy, no-protein drink. This group also exhibited an enhanced performance on cognitive assessments at 18 years of age, even though the intervention had been discontinued years earlier. The benefits were of lesser magnitude in participants who had received nutritional supplements later in life, suggesting that the first 2 years of life are particularly sensitive to the effects of nutrition. The benefits of supplementation were enhanced in participants who had attended school, indicating that nutritional status and its augmentation is only part of a complex of economic and educational factors related to cognitive development.

Sigman and colleagues have carried out studies of the effects of nutrition on cognitive abilities in young Kenyan children (Sigman, et al., 1991; Sigman, et al., 1989a). They followed a group of children from 18 months to 5 years of age, measuring nutritional level and cognitive abilities, using standardised assessments adapted to the cultural situation. Diet quantity, defined as adequacy of protein-energy intake was related to physical development and symbolic play skills but not to a Bayley Mental Scale score at 30 months (Sigman, et al., 1989a). There was a stronger association between quality of the diet, defined mostly by the availability of animal products, and the development of cognitive abilities, evidenced by more symbolic play at 30 months and higher scores on the assessments at 5 years compared to children with lower intakes of animal products (Sigman, et al., 1991). Diet quality was also related to more advanced cognitive performance in comparative studies carried out in Mexico and Egypt (Sigman, 1995).

Similarly, in Kenyan and Egyptian studies, the combination of nutritional status and adequacy of the social and educational environment was found to be the best predictor of cognitive abilities (Sigman, 1995; Sigman, et al., 1989b). Studies of middle-class children with organic illnesses that result in undernutrition, such as cystic fibrosis, do not show poor developmental outcomes compared to these malnourished children from poor communities, emphasising the importance of social factors in the impact of malnutrition on child development (Richter and Griesel, 1994). However, studies such as those carried out in Guatemala and Barbados (described above) controlled for SES and social deprivation, yet still found that cognitive functioning was affected.

Intrauterine growth retardation (IUGR) has also been associated with greater postnatal risk for poor growth and development. In resource-poor countries, approximately 23% of neonates have low birth weight (defined as less than 2500g), principally due to the frequency of IUGR (Martorell, 1999). Gorman and Pollitt (1992) assessed the developmental risk associated with IUGR and body symmetry at birth to investigate whether intrauterine malnutrition at critical periods of brain growth has later functional effects and whether a combination of pre- and postnatal malnutrition increased the risk of developmental delay. They found that IUGR was independently associated with poor verbal abilities at 36 months. At 36 and 48 months, IUGR and growth during the first year of life were associated with poor short-term memory skills.

The mechanism by which PEM is associated with poor cognitive development is unclear. The 'main effects' model proposes that malnutrition involves a biochemical insult to the brain, implying a linear cause-and-effect relationship between risk and outcome. Timing is crucial for most of the proposed mechanisms that link malnutrition to poor cognition, which are thought to depend on the phase of anatomical and biochemical maturity at the time of the deficit. Damage to the brain is likely to occur during the rapid phases of growth in the prenatal period and infancy (Martorell, 1999). Morgan and Gibson (1988) postulate that intrauterine malnutrition during the second trimester of pregnancy is likely to result in a reduction in neuronal numbers, whereas in the last trimester or early neonatal life it will affect the numbers of glial cells and the maturation of neurons. The main effects model has been criticised as being reductionist, ignoring the social context in which malnutrition occurs. Thus, theories postulating a direct causal relationship between early malnutrition and later cognitive performance have been replaced by analyses of the interactions between nutritional and social experiences, for example altered caregiver-child relations or the effect of 'functional isolation', where a malnourished infant becomes apathetic and withdrawn from social and learning activities (Richter and Griesel, 1994).

Grantham-McGregor and colleagues conducted two studies in Jamaica to investigate the hypothesis that PEM results in reduced levels of activity and exploration and in consequence, delayed acquisition of cognitive skills (Grantham-McGregor and Cumper, 1992). The group found that severely malnourished children, observed while in the acute stage in hospital, were significantly less active, used fewer types of exploratory behaviours and were more apathetic than adequately nourished children who were hospitalised with other diseases. A second study investigating stunted children found that their activity levels, as measured on home observations, were reduced in comparison to those of non-stunted children, although activity level was not predictive of future development. Although these studies indicated that severely malnourished or stunted children have reduced levels of activity, neither study confirmed a causal link between reduced activity and delayed development.

Chavez and colleagues (1995), investigating the effects of nutritional supplementation on cognition and behaviour from the prenatal period to 10 years of age, found that differences between supplemented and non-supplemented children were apparent at 18 months of age and persisted, although to a lesser degree, to 18 years of age. Their data generated several hypotheses about the impact of moderate malnutrition on cognitive and behavioural performance. First, intrauterine malnutrition may affect later performance in the child. Second, as discussed above, physical activity may be decreased, thus reducing the amount of stimulation received. Third, malnutrition may cause personality changes, causing children to become insecure and shy. Finally, community and family culture may be affected, thus impairing social interaction and education. Chavez and colleagues conclude that a combination of all four factors is likely to be responsible for the cognitive and behavioural effects associated with malnutrition.

Much of the international debate on malnutrition has concentrated on appropriate measures and standards of normal growth. In the South African context, several authors have contended that North American growth standards inflate estimates of malnutrition and that local standards for growth should be developed, although such standards should not be seen as an implication of differences between groups in terms of growth potential (Richter and Griesel, 1994). Other South African professionals in the field of child health have concluded that North American standards should be used, justifying their decision on the basis of '...the equal growth potential of all children, regardless of the extent to which that potential may be thwarted in any particular circumstance.' (Richter and Griesel, 1994 p73). They advocated growth potential as the ideal standard against which the growth of individual children across the world should be assessed. In addition, Kenyan children from wealthy urban and rural families have been found to be at or above American National Centre for Health Statistics (ANCHS) median values (Stephenson et.al., 1983, cited in Sigman, et al., 1998).

The evidence reviewed above suggests that malnutrition, as part of a complex of factors associated with deprivation and poverty, is associated with poor cognitive and behavioural development and ultimately with reduced educational achievement.

Therefore, anthropometric measurements of weight and height were taken in the current study. Classifications of stunting, wasting or low weight were based on attained height or weight that falls more than two standard deviations below that expected on the basis of international growth references for a child's age and sex (Frongillo Jr., 1999). Weight for age, height for age and weight for height z-scores were calculated using reference data from the ANCHS using NutStat on EpiInfo 2000 (CDC, Atlanta, USA). Due to the fact that most children in Kilifi District are born at home, a measure of birth weight was not possible.

5.3 Anaemia

Iron deficiency is the most common cause of anaemia worldwide, with a prevalence of 50% among African children between five and 12 years (Watkins and Pollitt, 1998). Seventy-six percent of 559 children surveyed in Kilifi District were diagnosed as anaemic (haemoglobin (Hb) ≤110g/l in children under 7 years or ≤120g/l in children 7 years or older) (Newton, et al., 1997), a proportion replicated in a more recent study in the area, which reported a prevalence of 76.3% (Brooker, et al., 1999). Children infected with malaria parasites in Newton and colleagues' study had significantly lower Hb concentrations than those without parasitaemia and in 50.4% of those admitted to hospital with malaria, clinical and laboratory investigations suggested that malaria was the primary cause of severe anaemia (Hb ≤50g/l). These findings suggest that falciparum malaria is an important cause of anaemia in Kilifi District, although iron deficiency is also common: 33% of a random subgroup of community controls in whom iron and transferrin were measured, had a plasma iron concentration <4 μmol/l (Newton, et al., 1997).

Iron deficiency anaemia in young children has been associated with poor cognitive performance and developmental outcomes in later childhood. Stoltzfus (2001) carried out a double blind, placebo controlled, randomised multifactorial trial of iron supplementation and antihelminthic treatment with Zanzibari infants. Five hundred and thirty-eight children between the ages of 1 and 4 years received either a placebo or a supplement of ferrous sulphate (20mg/ml) and antihelminthic treatment consisting of 500mg mebendazole tri-monthly. Children identified as severely anaemic at baseline were treated with oral iron and included in subsequent analyses on an intention to treat basis. Following a baseline assessment of language and motor functions and 12 months of treatment or placebo, children were reassessed. The results indicated that antihelminthic treatment had a positive but non-significant effect on developmental scores. Iron supplementation was associated with significant improvements in language scores across the range of supplemented children and significant increases in motor scores in children with low baseline Hb concentrations.

Improvements in short-term cognitive performance were investigated in a Zairian study administering iron supplementation and treatment for intestinal parasites (Boivin and Giordani, 1993). A battery of cognitive assessments was administered to 47 primary school children who, following medical evaluation, were randomly assigned to antihelminthic treatment, iron supplementation or both. A placebo treatment was not used in the case of iron supplements. Reassessment after four weeks showed significant improvements on global cognitive performance indicators in children who had received both treatments, compared to those who had received a single treatment or neither treatment, making it difficult to separate the relative effects of anaemia and parasitisation. The authors of this study concluded that their interventions had a limited effect on the cognitive abilities of the children involved '...because the extent of anaemia and its amelioration with the sample is only a partial expression of the complex of factors that constitute the overall favourability of the children's developmental milieu' (Boivin and Giordani, 1993 p263).

Iron deficiency anaemia in infancy is also associated with poor cognitive performance in later childhood. Lozoff and colleagues (1991) followed up 163 Costa Rican children whose iron status had been documented in infancy and who had received treatment for anaemia from 12 to 23 months of age. When assessed using a battery of neuropsychological assessments at the age of 5 years, children who had suffered moderate to severe iron deficiency anaemia (≤100g/l) as infants had significantly lower test scores than controls, despite having normal current haematologic status. Children with anaemia in infancy were from homes of low SES, although the significant differences in assessment scores remained even after adjustment for these factors.

Iron deficiency is associated with poverty and low levels of parental education, both of which are independently associated with poor cognitive outcome (Watkins and Pollitt, 1998). As discussed in the context of PEM, it is difficult to separate the effects of nutrition from those of poverty in observational studies, yet ethical considerations preclude the withholding of treatment from anaemic children, making experimental studies, such as that conducted by Stoltzfus and colleagues (2001), rare. In addition, the studies described encountered similar challenges in the selection of appropriate outcome measures as faced in the current study (discussed further in Chapter Six). Stoltzfus and colleagues (2001) used parental reports of gross motor and language milestones as outcome measures, which may not have detected more subtle impairments, possibly underestimating both the pre-treatment level of impairment and the effects of supplementation. Boivin and Giordani (1993) used the Kaufman Assessment Battery for Children, translated into the mother tongue of the participants. Although employing a more detailed measure of cognitive ability, no information on adaptations to the tool or investigation of its reliability and validity in the cultural context of the study were described. Lozoff and colleagues (1991) administered several measures of cognitive function, which had been standardised on US populations, to the Costa Rican children in their study, although they claimed that their tools were culturally-appropriate because control scores were comparable to US norms.

Several mechanisms have been posited to explain the possible effects of iron deficiency anaemia on child development and cognition. One potential factor is the role of iron as a structural component of enzymes and molecules involved in the development and functioning of the nervous system (Watkins and Pollitt, 1998), which may affect development due to the fact that iron deficiency is most prevalent in 6 to 24 month old infants, who are at a fundamental stage in the development of cognitive and motor processes (Lozoff, 1998). A second effect of iron deficiency anaemia is the reduced ability to transport oxygen around the body, which may be expected to affect all cellular mechanisms (Watkins and Pollitt, 1998). The confounding factors described above may represent a third factor: a context of environmental disadvantage, responsible for both the anaemia and poor assessment performance, in the absence of a direct connection between the two (Lozoff, 1998). Finally, the concept of 'functional isolation', which originated from malnutrition research, may constitute another possible mechanism for poor developmental outcomes. Lozoff (1998) describes children with iron deficiency anaemia maintaining close contact with the mother during play and displaying altered affect, increased hesitance and fearfulness.

In summary, the studies reviewed suggest that iron deficiency anaemia may be associated with reduced levels of performance that persist after the period of deficiency, although interpretation of the findings in studies of anaemia is often hindered by limitations in study design and the context of socioeconomic deprivation. A decision was made at the beginning of the current study to avoid any invasive procedures that may jeopardise the execution of the assessments, therefore iron status was not measured. Many children from the source population were unfamiliar with the formats and procedures of cognitive assessment, not having attended school and participated in formal, educational activities (section 6.5) or had access to such materials at home. The success of the assessment procedures depended on the interest, ease and composure of the children involved. Studies conducted in this area have indicated that the prevalence of anaemia in the Kilifi community is similar to that of children admitted to hospital with malaria (Brooker, et al., 1999; Newton, et al., 1997), therefore the potential impact of iron deficiency anaemia on development would be expected to be similar across the exposure groups.

5.4 Other parasitic infections

Helminthic infections such as roundworm, hookworm, whipworm and tapeworm, are common in resource-poor countries, particularly in communities lacking adequate sewage disposal (Kvalsvig and Connolly, 1994). An estimated 1.05 billion people carry intestinal hookworms; 1.47 billion carry roundworms (*Ascaris lumbricoides*) and 1.3 billion, whipworms (*Trichuris trichiura*), with the highest prevalence and intensity occurring in children of school-going age (Watkins and Pollitt, 1997). Protozoan infections such as *Giardia lamblia* and *Entamoeba histolytica* are also common in deprived areas whereas water-transmitted infections such as schistosomiasis and bilharzia are particularly common in warm, low-lying areas (Kvalsvig and Connolly, 1994). In Kilifi District, between 24.1% (Newton, et al., 1997) and 28.7% (Brooker, et al., 1999) of children are infected with hookworm, 20.2% with *Ascaris lumbricoides* and 15% with *Trichuris trichiura* (Brooker, et al., 1999).

The debilitating effects of macroparasitic infections have been documented since the early 20th century when American scientist C.W. Stiles described the impact of hookworm on the population of the southern United States (Watkins and Pollitt, 1997). However, the literature on the cognitive impact of such infections is contradictory, with some studies reporting deleterious effects and others giving accounts of positive outcomes. Some of these inconsistencies may be explained by methodological weaknesses, for example lack of control or adjustment for SES. This is a potential confounder in studies of parasitic infections because macroparasitic infections are common wherever there is poor sanitation and tropical and sub-tropical climates are also more favourable for transmission. The background of poverty often found in affected populations usually implies accompanying undernutrition, lack of educational facilities and stimulation in the home. In addition, populations resident in such areas are at greater risk of multiple infections, and it is not known whether the effects of polyparasitism are additive or synergistic (Watkins and Pollitt, 1997).

The negative impact of parasitisation is implied by the positive effects of antihelminthic treatment observed in a number of experimental studies. Nokes and colleagues (1992) randomly assigned Jamaican schoolchildren with moderate to heavy infestations of *Trichuris trichiura* to receive an antihelminthic drug or a placebo. A baseline cognitive assessment was administered to the participants before the intervention and potential confounding variables, including nutritional status, iron status, school attendance, IQ and SES, were controlled for statistically. At follow-up after two months, children who had received treatment demonstrated improvements in assessments of auditory short-term memory and word retrieval compared to the non-treated children. These results were not replicated in another Jamaican study in which otherwise healthy schoolchildren with light to moderate *Trichuris trichiura* infections were randomly assigned to treatment or placebo groups and tested 3 months later using a battery of cognitive and language assessments (Gardner, et al., 1996). The results showed no significant improvement with treatment in any of the tests. The authors concluded that light to moderate *Trichuris trichiura* infection has little effect on cognitive functioning in adequately nourished children.

In an experimental study in rural Guatemala, 226 children between the ages of 7 and 12 years with moderate to heavy infestations of roundworm, some of whom also had mild whipworm infections, were randomly assigned to a deworming treatment group (Watkins and Pollitt, 1997). Six months after treatment, children who had had heavy burdens of roundworm demonstrated improved working memory and reaction time. However, some of the children with lighter infections showed poorer performances following treatment, suggesting that a low level of parasitisation conferred improved performance in these functions. The results did not indicate any association between treatment and measures of reading, vocabulary or school attendance.

Several mechanisms have been suggested by which infection may affect cognition. Hypothesised mechanisms may be divided into direct and indirect factors. Evidence for direct effects is only at the level of speculation with the current evidence: possible factors include neurological effects resulting from the physical presence of egg deposits in the case of schistosomiasis, or toxicity effects from the substances secreted by the parasites, leading to biochemical changes in the nervous system (Watkins and Pollitt, 1997). Physiological factors have also been proposed, such as physical discomfort and disturbed sleep, which may lead to reduced levels of attention or behavioural change (Holding and Snow, 2001). There is more evidence for an indirect effect on the host's nutritional status, particularly in the form of iron deficiency, and susceptibility to infection, although the relationship between the parasite, the putative mediating factor and cognitive outcome has not been fully established (Watkins and Pollitt, 1997).

The evidence for cognitive effects resulting from parasitic infections is contradictory. Watkins and Pollitt (1997) conclude that, in the case of geohelminthic infections, only high levels of infestation are likely to impair cognition and only as part of the malnutrition-deprivation complex described in section 5.2. In the context of this study, this level of evidence was not considered sufficient to justify the specific investigation of parasites. In addition, there is evidence to suggest that the effects of parasites on cognition are mediated through nutritional status, which was measured by the protocol described in section 5.2.

5.5 Socioeconomic status

The importance of the child's environment and background on his/her development is illustrated by the fact that maternal education is the best single predictor of child health in resource-poor countries (Coreil, 1997; Kvalsvig and Connolly, 1994). Low socioeconomic conditions have been associated with greater risks to child health in utero, at birth and during childhood (Bradley and Corwyn, 2002), which are, in turn, associated with more complications and developmental consequences (Parker, et al., 1988). Nutritional variables also covary with socioeconomic and environmental variables such as inadequate housing, maternal educational level and caregiver-child relations (Wachs and McCabe, 1998).

Measures of socioeconomic status (SES) such as quality of housing, crowding, residency in a rural area (Koram, et al., 1995), level of maternal education, language comprehension and ownership of audio-visual equipment (Carme, et al., 1994) have been associated with the risk of developing malaria. However, in a study of environmental and entomological risk factors for malaria, Snow and colleagues (1998) concluded that the impact of household features on risk is mediated by vector density and the level of acquired immunity in the population.

SES has also been associated with cognitive development and academic attainment. In the USA, reduced school achievement and IQ later in childhood have been associated with conditions of poverty (Duncan, et al., 1994) and low parental education (Alexander, et al., 1993). In the UK, more than half of 240 children from low SES homes (defined as children receiving free school meals) studied at nursery-entry, were classified as having moderate or severe language delays (Locke, et al., 2002). Similar results have been found in resource-poor countries. For example, a study in rural Guatemala found a correlation between measures of maternal education and house quality and earlier school entry, grades passed and maximum grade attained (Gorman and Pollitt, 1993).

As low SES frequently co-occurs with other poverty-related conditions that may affect child health, it is difficult to ascertain the mechanisms by which SES influences child development. One of the most commonly cited factors relating SES to children's development is access to resources. Poor nutrition, inadequate prenatal and childhood health care, dilapidated and crowded housing, lack of access to cognitively stimulating materials and experiences, lower parental expectations, less parent-child interaction and teacher attitudes have all been proposed as mechanisms mediating the effects of SES on child development (Bradley and Corwyn, 2002). Other proposed mechanisms are stress reactions (in the child and parents, that in the latter leading to negative parenting) and lifestyle behaviours. However, conditions of low SES, poverty or deprivation have not been invariably associated with negative outcomes for child development: variations in social cohesion, family stability and the personal resources of the parents, in addition to the child's personal characteristics, may act as moderators of the effects of SES (Richter, 1994).

Indicators of SES are only one method by which to measure the complex, multifaceted system of environmental influences on child development. Wachs and McCabe (1998) describe the work of Bronfenbrenner, who defined four levels of environmental influence. The specific physical and social characteristics of the child's surroundings comprise the 'microsystem' and the 'mesosystem' refers to the connections between two microsystems (for example, home and school). The 'exosystem' encompasses links between settings, one of which may exert influence on but is not directly encountered by the child (for example, the parent's workplace). The highest level is the 'macrosystem', which describes cultural values systems, beliefs and lifestyles.

Most definitions of SES include reference to parental occupation, income, educational level and/or residential location. Both theory and empirical findings indicate that there is likely to be a disparity in the performance of SES indicators across cultural groups (Durkin, et al., 1994). For example, Bradley and Corwyn (2002) comment that the presence of larger numbers of siblings results in less allocation of parental time and attention to a child, indicating low SES. However, a study in the Kilifi community found that larger numbers of siblings resulted in better performance on cognitive assessments (Holding, et al., 1999), although this finding requires replication to verify its validity. This may be related to the fact that siblings play a greater caretaking role in many rural African communities than in North American and European communities and that children are more often in polyadic social situations with age-mates than in a mother-child dyad (Mbise and Kysela, 1990).

Measures of SES commonly applied in Europe and North America may have limited ability in many African societies, which are more homogenous in nature, to separate communities out into discrete and meaningful groups.

In this area, there is little existing data on which socioeconomic indicators are predictive of child development and achievement. Measures used in a previous study of malaria and cognitive performance in this area (Holding, et al., 1999) were selected because there was information relating them to the development of severe malaria (Marsh, et al., 1995). Other studies in resource-poor areas have used education, land ownership, household income and household expenditure as SES indicators and found significant associations with child health and development (Najman, et al., 1992; Victora, et al., 1992; Zurayk, et al., 1987). In an investigation of appropriate SES indicators of child health in Pakistan and Bangladesh, Durkin and colleagues (1994) concluded that the use of multiple measures is necessary for the reliable measurement of mediating SES factors. They found that a combination of parental occupation and education, ownership of land and household possessions and floor material was significantly associated with poor child health and mortality.

Hauser (1994) presents guidelines for the measurement of SES in studies of child development, advocating the selection of items for their brevity; ease of administration; the willingness and ability of respondents to answer; the costs of editing, processing and recoding of responses; whether responses will be reliable and valid and whether the items measured will adequately capture relevant circumstances of the child's social environment. Following these guidelines, indicators of SES for this study were selected for their potential capacity to stratify families into different groups and on the basis of whether they were realistically possible to collect. Wachs and McCabe (1998) state that investigations of the child's environment and background are incomplete without consideration of all environmental levels but investigation of all of these factors would require detailed questioning, probing, observation and possibly intrusive techniques, such as inspection of household interiors. In the context of the current assessment-based study, whose success depended on the maintenance of children's interest and ease and the goodwill of parents, giving up their time to escort the children and participate in questionnaires, this was not felt to be appropriate. The following indicators were selected because they were found to correlate with development and performance in a previous study in the area (Holding, et al., 1999) or in other studies in resource-poor countries:

- Mother's level of education

  A standard variable associated with child health and development in resource-poor and industrialised countries.
- Mother's ability to speak English

  A mother's ability to speak English reflects her level of education and experience outside of the home: breadth of experience may be reflected in different parenting skills. Although few mothers were expected to be able to speak English, this variable was found to correlate with performance on several cognitive assessments in a previous study in this area (Holding, et al., 1999).
- Father's (or main breadwinner's) occupation

  As an indication of income level, information on the father's occupation may be easier to ascertain than actual income and has been found to strongly link with salary level in this context (Hoorweg, et al., 1995).
- Number of siblings

  This variable was associated with cognitive performance in Holding and colleagues' (1999) study.
- Land ownership

  This variable was found to be associated with child health in a study in Pakistan and Bangladesh (Durkin, et al., 1994).

Other indicators were selected from suggestions made by members of the local community of variables that may indicate levels of SES:

- Number of meals eaten by the child per day

  This variable was suggested as a possible indicator of the child's dietary intake and access to the family's economic resources. Family income level does not necessarily equate with disposable income available for child care and nutrition and adequacy of available food does not solely determine the child's food intake (Wachs and McCabe, 1998).
- Type of flour milling

  Hoorweg and colleagues (1995) found that the rate of food self-sufficiency in

Kilifi District was low. Families who grow their own maize (the staple food of the region) grind it at home or at a mill. Members of the local community suggested that this was seen as an indication of wealth (as it may suggest land ownership and a smaller family), good home organisation and management, in comparison to buying maize flour at a shop.

- Listens to a radio

  This variable was suggested by community members in preference to ownership of a radio on the basis that some people, despite not owning one, regularly listen to radio broadcasts, a factor considered to represent a level of educational achievement and societal awareness.

The final questionnaire contained eight measures of SES. The results are presented in Chapter Twelve, where an evaluation is made of the extent to which each of these variables are able to stratify the group to select the most appropriate variables to include in the analysis.

5.6 HIV-related encephalopathy

At the end of 2001, an estimated 220,000 children in Kenya were living with HIV (WHO, 2002). A recent study in Kilifi found that 4.2% of children discharged alive from Kilifi District Hospital had HIV infection (Berkley, et al., in press). Neurological complications are, in general, due to direct infection of the nervous system through migration of infected macrophages, originating outside the CNS, through the blood brain barrier and into the brain; the involvement of microglia and multinucleated giant cells and neurotoxic factors, such as cytokine damage to myelin (Pontrelli, et al., 1999). As with malaria, malnutrition, concomitant infections and conditions of economic deprivation may potentiate the effects of the virus. In the first decade of paediatric AIDS, it was estimated that up to 90% of children may develop HIV-related encephalopathy (Belman, et al., 1988), although more recent estimates from Europe and North America are lower, possibly due to earlier diagnosis and interventions with anti-retroviral regimens (Brouwers, et al., 1998). The prevalence in rural Kenya may be more accurately represented by earlier estimates because there is little infrastructure for the early diagnosis and treatment of children with HIV.

Encephalopathy associated with HIV occurs in either a progressive or static form and involves a complex of cognitive, motor and behavioural abnormalities of varying severities. Children with HIV encephalopathy have been found to have deficits in psychomotor development (Knight, et al., 2000), behaviour (Moss, et al., 1996) and language skills (Wolters, et al., 1995). Progressive encephalopathy may involve the loss of previously-acquired developmental milestones and the development of symmetrical motor deficits such as paresis, gait disturbance, abnormal tone or abnormal reflexes (Ojukwu and Epstein, 1998; Pressman, 1992). HIV-1 can affect cognitive, motor, language and neurological functioning as early as 6 months in vertically-infected children (Wachtel, et al., 1993), although a confounding factor in many European and North American studies is that children may have had prenatal drug exposure. Developmental impairments have also been found in HIV-infected children who have normal neurological examinations, although their performance is usually better than those with evidence of CNS disease (Condini, et al., 1991; Knight, et al., 2000; Moss, et al., 1996; Msellati, et al., 1993).

HIV-related encephalopathy is unlikely to have been a confounding factor in this study because the target population was between 6 and 9 years of age. North American studies conducted in the 1980s, before the advent of anti-retroviral treatment and programs for early diagnosis and therefore more comparable to the Kilifi situation, suggest that mortality under these conditions is high and occurs early. Only six of 51 children with HIV-related encephalopathy reported by Hittelman (1990) survived beyond the age of 5 years. Death occurred between one to 23 months after onset of neurological deterioration in children in Belman and colleagues' (1988) study, whose median age was 16 months. Therefore, children were not assessed for HIV or HIV-related neurological complications in the current study.

5.7 Summary

A recurring theme in the studies reviewed in this chapter is the complex interaction between factors associated with the economically-deprived conditions found in an area such as Kilifi District. This highlights the fact that the examination of single determinants in isolation does not adequately reflect the multifactorial manner in which human development is determined (Wachs and McCabe, 1998). On the other hand, in a study of this size, the investigation of variables beyond the domain of interest must be partly determined by practical considerations, such as the impact on the participants, time and cost. Evidence of effects on child health and development, weighed against the ramifications of their measurement on other facets of the study indicates that, of the five factors reviewed in this chapter, nutritional status and socioeconomic status should be included as covariates in the analysis of the developmental assessments. The methods of measuring these factors will be presented in Chapter Eight and the selection of specific covariates for analysis will be described in Chapter Twelve.

Chapter Six: Culturally Valid Assessment

6.1 Introduction

Culture may be defined as the set of values, beliefs, perceptions, institutions, technologies, survival systems and codes of conduct held by members of a particular group of people (Payne and Taylor, 2002). One framework within which the link between culture and child development can be discussed is the 'developmental niche' (Super and Harkness, 1986). This framework identifies components of the child's environment that are shaped by features of the wider sociocultural setting. Three principal groups of factors are described, which operate together as a system. First, the physical and social settings of everyday life: where, with whom and in what activities children spend their time. Second, culturally regulated customs of childcare, specifically the caretakers' repertoire of normative approaches to childrearing, such as length of breastfeeding and traditional methods of discipline. Third, the psychology of the caretakers: parental theories and beliefs about children's behaviour and development, for example the locus of authority and the economic value of children. The nature of the developmental niche differs among individuals and varies at different points during the developmental process. The degree to which test components reflect the cognitive goals that are set for individuals in the target culture defines the 'ecological validity' of the assessment tool (Mishra, 1996).

Taylor and Payne (1983) state that culturally valid assessment is "...a data collection process wherein testing, measurement and evaluation are conducted using instruments and procedures that discriminate only in those areas for which they were designed (i.e. normal versus pathological behaviour) and do not discriminate unfairly either for or against a client for cultural reasons..." (p.11). In comparison to the number of published assessments in the UK, there are very few available assessments designed for the rural Kenyan context, therefore novel instruments had to be designed for some elements of the current study. This chapter outlines the factors germane to this process, beginning with a description of the historical background to cross-cultural assessment and evidence for the influence of culture on development and performance. Aspects of Giryama culture and the experience of Giryama children that may have particular relevance to the assessment procedure are discussed, with their implications for the current study. The chapter concludes with a description of the specific measures employed in the study to construct culturally-valid assessment tools.

6.2 Background to cross-cultural assessment

Assessments designed for cross-cultural situations were first produced in the early twentieth century. The hypothesis underlying many of the first assessment tools was that behaviour was independent of the surrounding culture and was merely superimposed by a cultural veneer that could be penetrated by what were termed 'culture-free' tests. The later adoption of 'culture-common' or 'culture-fair' tests demonstrated the realisation that culture permeates all aspects of behaviour but reflected the new hypothesis that assessments could target only those experiences and expressions of behaviour common to different cultures. Anastasi and Urbina (1997) reflecting more recent opinion, comment that a single test cannot be universally applicable to all cultures but can only aim to reduce cultural differentials in test performance. They conclude that a child's behaviour is influenced by the cultural milieu in which he or she is raised and as many developmental assessments are measures of a behaviour sample, that the influence of culture will and should be detectable. Boivin (1991) found that Zairian children performed significantly below the age-related norms of American children on a number of tests that have been widely regarded to be non-verbal, culture-fair measures of various facets of cognitive abilities: the Matrix Analogies Test (Naglieri, 1985), the tactual performance task of the Halstead-Reitan Neuropsychological Assessment Battery (Reitan and Wolfson, 1985) and the simultaneous and sequential reasoning subsections of the Kaufman Assessment Battery for Children (Kaufman and Kaufman, 1983). He concluded that despite the 'culture-fair' label, due to the fact that all of the tests originated within the context of Western psychological research and theory, any validity in the cross-cultural situations in which they have been sometimes used is coincidental.

6.3 The Influence of culture on performance

The experiences available in the child's immediate physical environment have a direct effect on his or her development and as a consequence, on the range of appropriate materials with which to measure that development. An example of specificity of development is the apparent precocity of early gross motor development in rural African children noted in a number of studies (Cintas, 1988; Freedman and DeBoer, 1979; Super, 1976). This has been linked to both environmental influences (dirt floors motivate the child to walk rather than crawl) and specific child-care customs (parents actively encouraging those skills). Studies examining other skills have found similar effects. For example, Australian Aboriginal children were found to have significantly better visual-spatial memory abilities than white children, perhaps because their environment constrained them to develop an aptitude for direction finding (Kearins, 1981).

Cross-cultural researchers disagree as to whether such differences represent maturational lag in certain cultures in what is otherwise a universal sequence in the development of cognitive processes or whether there are qualitatively different end points in development (Bates, 1997; Dasen, 1988). However, what such findings suggest is that the familiarity of materials and the content and structure of a task will influence whether the child's performance is a true representation of his or her ability. This was exemplified in a study by Serpell (1979), who observed real life activities in children from various cultures to determine which materials were most familiar to different groups of children. He found that Zambian children preferred to copy shapes with wire, whereas British children preferred pencil and paper. Their level of performance on the respective tasks matched their level of familiarity with each task. Serpell also found that familiarity with a particular material also influenced motivational levels: British children were found to be reticent to even attempt the wire-modelling task presented to them.

Miller and colleagues (1984) describe a scenario in which the use of materials inappropriate to a cultural situation disrupted the test procedure. In their study, the Denver Developmental Screening Test was administered to Hmong (Laotian) children, whose families had been living in the USA for between 1 and 18 months. Most children refused to pick up a raisin (testing fine motor skills) because it looked like a common medicine they had traditionally been told to avoid.

6.4 Familiarity with the testing situation

The social rules of language interaction – who may speak to whom, in which situations – are culturally-bound. In many resource-poor countries, children have no freedom to engage in prolonged dyadic play with adults (Mbise and Kysela, 1990) and spend much of their time in polyadic situations with siblings or other children (Lieven, 1994). For Kenyan children, it is unusual to sit and converse with an adult, especially a strange adult, so the expectation of most language and cognitive assessments – for a child and adult to interact – is an unfamiliar activity. Lack of familiarity with aspects of the testing situation in some children from rural or non-white homes has been cited in other studies as a possible reason for low performance levels (Brislin, et al., 1973; Miller-Jones, 1989). This hypothesis is supported by that fact that practice and prompts enhance performance levels in African children previously unfamiliar with standardised testing situations (Brislin, et al., 1973; Mwamwenda, 1992).

6.5 Formal education

Formal education may affect the child's understanding and experience of the assessment situation: the schooling child may be more familiar with test strategies, thus less likely to make errors due to misunderstanding task demands. In investigations among the Kpelle people of West Africa, unschooled children performed poorly compared to their schooling counterparts on unstructured memory tasks such as the free recall of word lists (Cole and Scribner, 1974). Their performance level improved when cues were used in the unstructured tasks or when naturalistic story tasks were used. Schooling of poor quality may not diminish all of the positive effects on cognitive performance. Das (1992) found that schooling of comparatively poor quality in remote areas of India enhanced children's performance on tasks of simultaneous and successive processing and planning. Conversely, differences in tests of recall have been found between Indian children attending 'good' schools (characterised by sufficient space for staff and children, transportation, trained teachers, library and recreational facilities and the use of new teaching technology) and those attending 'ordinary' schools (characterised by a relative lack of these facilities) (Mishra, 1996). Mwamwenda and Mwamwenda (1991) assessed performance on Piagetian tasks in Batswana children attending English-medium and Setswana-medium schools. They hypothesised that the fee-paying English-medium schools would deliver superior quality education than the government-funded schools working in Setswana, which generally employ teachers with less or no training and have fewer educational resources. The results of the study showed a significantly better performance in children from English-speaking schools than those from Setswana-speaking schools on two of the three tasks (class inclusion and conservation). However, socioeconomic status was not taken into account in the study and may have influenced the performance of the respective groups.

There is disagreement as to whether it is the effect of formal schooling itself or the impact of literacy that has the most profound effect on cognitive processes (Mishra, 1996). Literacy in itself is hypothesised to promote the development of different conceptual frameworks. Mishra (1996) describes two effects of literacy at the individual level proposed by Scribner and Cole in 1981. First, the assimilation of knowledge and information transmitted by written texts promotes growth of the mind and second, influences the content of thought and the processes of thinking. According to Olson (1976), the oral relay of information via proverbs, stories and other mnemonic tools is most commonly encountered in predominantly illiterate societies. The content of information in such societies focuses on the functional description of concrete objects. By contrast, in literate societies, communication is relayed by written prose and content is more often related to relationships between more abstract concepts.

For rural Giryama children who are not schooling, it is unusual to sit for prolonged periods engaged in conversation or completing educational-like tasks. However, the response requirement of most language and cognitive assessments is for the child to exhibit their best behaviour to a stranger (the assessor) in a structured, unfamiliar environment (Baine, 1990).

6.6 Language issues

Language use is social and embedded in culture (Miller, 1984). Many studies conducted in countries in which assessments have not been standardised on the population have used translated versions of UK or US assessments (Howard and De Salazar, 1984). However, it is important to consider the language environment of the host country, as a translated question may not elicit the same response as originally intended. In addition, syntactic differences may be found between cultures using the same language, as reported by Baddeley and colleagues (1995), who attempted to use the Test for the Reception of Grammar (TROG) (Bishop, 1983) with children speaking Jamaican patois. Adaptation and revision are usually required in addition to translation because item content and test format may be more familiar in one culture than another (Anastasi and Urbina, 1997).

These issues are illustrated in a study in which a translated version of the Denver Developmental Screening Test was administered to Vietnamese children (Miller, et al., 1984). One task required the children to select coloured blocks in response to a particular colour being named by the examiner. The Vietnamese children seemed to consistently confuse the colours blue and green: it later became apparent that the names for these two colours were from the same overall colour group in their language, thus indistinguishable without a qualifying description. This example highlights the importance of having someone familiar with the language of the area involved at every stage of test construction and administration.

Howard and De Salazar (1984) described their adaptation of the Denver Developmental Screening Test for Costa Rican children. Although they translated the test into Spanish, piloting highlighted further changes to the content needed for valid administration. For example, the instruction 'draw a man' did not elicit the desired response, nor did the replacement of 'man' with 'boy', 'girl', 'mother' or 'father'. However, there was an almost unanimously positive response to the instruction 'draw a doll'.

Pahl and Kara (1992) assessed the applicability of the Renfrew Word Finding Scale to the South African context, administering the test to 60 white or Indian children from English-speaking homes. They found that only six children obtained scores equal to or above their chronological age levels using British norms and that 39 performed at a level suggestive of expressive vocabulary problems, despite the fact that their teachers considered their language abilities to be normal. Specific items on the test were consistently named incorrectly: for example, none of the Indian children were able to name 'spire/steeple', suggesting that cultural reasons were responsible for the errors.

6.7 Picture recognition

The majority of assessments of language and cognition use picture stimuli. As with language, picture recognition involves symbolic representation. Children begin to recognise pictures of objects as early as 5 months of age (De Loache, et al., 1979). Reynell (1980) described the development of symbolic understanding as beginning with the recognition of real objects, progressing to that of miniature objects then the understanding of more arbitrary symbols such as the recognition of photographs of an object. Finally, the child learns to recognise stylised drawings of objects. A picture is not an exact replica of an object, merely a two-dimensional representation that presents certain cues, which as a result of previous experience, trigger the perception of the object (Anastasi and Urbina, 1997).

Some cross-cultural studies have suggested that the ability to recognise and interpret pictures is culture-specific. Serpell and Deregowski (1980) consider picture recognition to be a "culturally-restricted perceptual skill": Western children learn to perceive pictures in the functional contexts of learning to speak and listening to stories with the help of picture books, activities unavailable to most rural African children. However, other studies have found that lack of previous exposure to pictures does not negatively affect recognition (Deregowski, 1968) and that advanced age, schooling or an especially high level of intelligence are not essential for successful picture recognition (Kennedy, 1974).

6.8 Implications for the current study

The development of new assessments in a situation such as Kilifi necessitates ethnographically-based research on the language and culture, with the aim of generating a developmental model for the intended study population, which is both resource- and time-consuming (Pakendorf and Alant, 1997). Therefore, an alternative approach was decided upon in which assessments were derived from validated instruments in common use in the UK, when a Kenyan alternative was not available, or used assessment methods routinely in use in the UK, with revisions and modifications made to make them appropriate for the study population. The adaptation or reformulation of standardised assessments, as undertaken by Mbise and Kysela (1990) in Tanzania, offers the chance to create culturally and linguisticallyvalid test materials yet follow an established framework. In this way, 'imported' assessments can be adapted or new assessments developed from the principles of standardised tools, using methods and materials derived from the local culture.

Pakendorf and Alant (1997) comment that when test items are translated, omitted or altered in content; pictorial stimuli are adapted for suitability to the culture and the sequence of presentation of test items is reordered, it is debatable how many of the original test characteristics are retained. Thus, it is important to have a group unexposed to the condition of interest, drawn from the same population as those exposed. Sbordone (1996) discusses the ecological validity of the normative – or unexposed – group, stating that if the exposed group does not 'fit' the unexposed group in attributes such as age, sex, cultural and linguistic background, any comparisons between the groups or judgements about the presence of impairments will be spurious. This is particularly pertinent in the situation of transferring assessments across cultures. For example, Anderson (2001) found that the use of imported normative data resulted in an unacceptably high diagnostic rate of neuropsychological impairment in healthy South African adults and emphasised the importance of establishing norms and assessment criteria in the local population. In addition, it is essential that assessors are blind to the group status of the participants to prevent bias in scoring decisions. Both of these conditions were met in the current study.

The processes outlined below were implemented in an attempt to create 'culturally-valid' tools and assessment procedures for the current study. The tools and procedures are described in more detail in Chapters Eight to Eleven.

- Developing all tools in conjunction with mother tongue Kigiryama speakers brought up in the local area and consulting a local teacher when necessary.
- Assessing children in their own homes or in rooms away from the hospital setting, when possible, to minimise the unfamiliar aspects of the assessment situation.
- Training mother tongue Kigiryama speakers from the local area to carry out assessment procedures. The focus of cross-cultural testing has recently shifted from the assessment itself to the assessor's behaviour in the testing situation, which needs to be adapted to the needs of the test-taker (Anastasi and Urbina,

1997). Assessors from the test-takers' ethnic group and language background would be assumed to make such adaptations most effectively.

- Using materials familiar to children in the local area.
- Piloting all tools on schooling and non-schooling children.
- Piloting all pictures for level of recognition before inclusion in assessments. Any pictures consistently named incorrectly (i.e. more than 80%) were redrawn or discarded.
- Using practice items and prompts, where appropriate, to reduce the chance of errors due to misunderstanding of task requirements.

6.9 Summary

This chapter has highlighted the importance of culturally-valid assessment tools and procedures in the current context as a means by which study participants can fairly demonstrate their skills. There are several factors in Giryama culture and experience that require consideration in the process of designing culturally-valid assessment procedures. First, many Giryama children are not used to adult-child dyadic situations, such as occur during most cognitive and language assessments. Second, many children in this community do not attend school: formal education is hypothesised to affect assessment performance, possibly mediated by the effects of literacy or familiarity with educational-like tasks and strategies for completing such tasks. Third, previous studies have demonstrated the inappropriateness of using translated versions of UK- or US-based assessment tools, without adaptations to the content and stimulus materials. Finally, there is evidence that lack of previous exposure to picture stimuli may reduce a child's ability to process symbolic representations. The current study employed adapted or revised versions of UK assessments, where Kenyan tools were unavailable, and recruited a comparison group drawn from the same population as the groups exposed to severe malaria. Other procedures to increase the cultural validity of the tools were implemented during protocol and assessment development, which are described in more detail in Chapters Eight to Eleven.

Chapter Seven: The Language Base of the Study

7.1 Introduction

This chapter presents an outline of Kigiryama, the language spoken by the majority of participants in the study and the medium of assessment. The aim of this brief overview is to provide a context in which to present the development of the speech and language battery (Chapters Nine to Eleven) and more specifically, to elucidate alterations described in those chapters to the grammatical content of assessments originating in the UK. A description of the diversity of languages spoken on the Kenyan coast will precede an outline of the basic structure of Kigiryama, followed by a summary of the implications of this language context for the study.

7.2 The study of Bantu languages

The Bantu languages are Africa's largest language family, characterised by a common noun class and morphosyntactic agreement system (Suzman, 1996). Kiswahili is estimated to have the greatest number of speakers, mainly in Kenya, Tanzania, Congo and Uganda. In comparison to other major world language groupings, there has been little work on the acquisition of Bantu languages: most developmental work has been carried out in the Bantu languages of Southern Africa, for example, Sesotho, Setswana, Chichewa and Zulu of Lesotho, Botswana, Malawi and South Africa respectively (Demuth, 1992; Suzman, 1996).

7.3 Languages of coastal Kenya

There are 61 languages spoken in Kenya, representing each of its major ethnic groups and other emigrant groups (Grimes, 2000). Kiswahili, a language resulting from the mixing of African Bantu languages and the Arabic of sea-traders, is the lingua franca of the country. English is the official language of the country but is often the third language of many of its speakers.

Kigiryama, the mother tongue of the Giryama people, is the largest of the Mijikenda group of central Bantu languages, with approximately 623,000 speakers (Grimes, 2000). The 'ki-' (sometimes 'chi-') prefix denotes 'the language of' a particular group and will be used in reference to the languages throughout this thesis. 'Mijikenda' paraphrases as 'nine settlements' or 'nine communities' and refers to nine distinguishable tribal and language groups of the coastal strip. The Mijikenda cluster can be subdivided into a northern (including Kigiryama) and a southern subgroup, the geographic boundary between the two being Mombasa. All of the Mijikenda languages are closely related and are, to a large extent, mutually understandable. Exposure to Mijikenda languages other than the child's mother tongue usually occurs early in life, thus most older children and adults attain a level of understanding and fluency of other languages spoken in the geographical area (Mr E Mungai, Bible Translation and Literacy linguistics consultant, personal communication). Van Otterloo and Van Otterloo (1980) found that the percentage of cognate words between Kigiryama and certain of the other languages of the northern subgroup (those of the Kambe, Jibana, Chonyi, Kauma peoples) was between 86% and 89%. Kigiryama is also closely related to Kiswahili with 73% of words shared between the two languages.

Printed literature was produced in Kigiryama early in the 20th century but is now obsolete and out of print. A revised orthography has been developed by the Giryama Language Project (GLP) and is currently in the process of being approved by the Kenyan government. The GLP has published over 30 titles including literacy materials; traditional proverbs, stories and songs; leaflets on health and development; Bible stories and a triglot (English/Kiswahili/Kigiryama) word list. In addition, more than 500 people have been transitioned to read Kigiryama from Kiswahili (Mr S Iha, GLP leader, personal communication). In current practice, however, the language remains predominantly unwritten. In addition, the level of literacy among the Giryama, defined by GLP as reading/writing fluency in Kiswahili and English (the literacy skills taught at school), is low at approximately 40%.

7.3.1 The structure of Kigiryama

There are few published Kigiryama language resources and those available are at a comparatively basic level, therefore the following is an entry level description of the language, concentrating on aspects of the language relevant to elements of the thesis.

As a Bantu language, Kigiryama is agglutinative in verb phrase construction (verbs are constructed by attaching several morphemes together). Prefixes are attached to a root verb to specify the subject and object of the verb, tense/aspect, negation and can also be used to mark a relative clause. One word ('a-') is used to indicate the third person pronouns, 'he' and 'she'. Suffixes operate independently of the tense/aspect system and can be used to specify a passive, reciprocal, causative, stative or applicative phrase. Post-final suffixes may also be used to mark locative state or questions (how, where, what, why). Some affixes are obligatory whereas others are optional (for example, a relative clause can be marked by the attachment of a prefix to the verb or by the addition of a separate word in the sentence) and rules govern the possible combinations of prefixes and suffixes (BTL, 1993). Three examples are given overleaf: the first line of each example is the text; the second line displays the text split into its constituent morphemes; the third line (italicised) gives the English gloss for each morpheme and the final line is a free English translation.

- 'Fundakwenda dukani machero'

  Fu/ nda/ kw/ enda duka/ ni machero

  We (future) (inf) go shop (locative) tomorrow

  'We will go to the shop tomorrow'

- 'Ninamumanya ye chifu'

  Ni/ na/ mu/ manya ye chifu

  I (continuous) him know the chief

  'I know the chief'

- 'Kagita wari mudzo zhomu'

  K/ a/ gita wari mudzo zhomu

  (neg) He/she cook ugali good very

  'He/she is not cooking very good ugali (maizemeal)'

NB: The '-a' suffix to the verb root may be considered to be a separate morpheme, included to ensure that the verb has an open vowel structure (BTL, 1993). In the examples presented above, it was described as part of the verb root to simplify the analysis of the examples.

The distinction in languages between tense, aspect and mood is often unclear. Many Bantu languages use aspect more than tense, especially languages which often use the verbal suffix. Kigiryama uses the verbal prefix to mark tense and aspect: in such languages, tense typically plays an important role (Dr S Nicolle, BTL linguistics consultant, personal communication). A brief overview of the tense/aspect/mood system is that the major absolute tenses are future, today's past tense and the distant past tense. A relative tense, employing the consecutive past prefix 'ki-', is also used for narration. The continuous aspect is indicative of present time reference unless there is a tense marker or contextual clue to indicate otherwise. The habitual aspect describes events that take place usually, habitually, normally or always. There are four moods: indicative (making statements), imperative (giving commands), interrogative (asking questions) and subjunctive (expressing wishes, indirect commands and prohibitions) (BTL, 1993).

Kigiryama has 19 noun classes, labelled 1-18 and 22, which are essential for the correct construction of the noun phrase (BTL, 1993). The classes are summarised in table 7.1.

Class number	Noun prefix singular/plural	Types of word	Example
1/2	mu-/a-	people	musichana/asichana (girl/s)
3/4	mu-/mi-	trees, objects associated with the ground	muhi/mihi (tree/s)
5/6	-/ma-	fruits, objects associated with tradition and magic	chungwa/machungwa (orange/s)
7/8	ki-/vi-; ch-/zh-	man-made objects	kihi/vihi (chair/s)
9/10	N-/N-	miscellaneous, animals, birds, borrowed words	nyumba/nyumba (house/s)
11	lu-	long, wavy, oscillating	lugwe (rope)
12/13	ka-/u-	diminutive class	kahoho/uhoho (small child/ren)
14	u-	abstract nouns	usafi (cleanliness)
15	ku-	verbal nouns, infinitives	kushoma (reading)
16/17/18	ha-; ku-; mu-	specific; general; inside location	hatu; kutu; mutu (place: specific/general/inside)
22	ri-	big or bad things	rikumba (big fish)

Table 7. 1: Kigiryama noun classes

A defining mark of Bantu languages is that a number of constituents of the noun phrase must agree with the noun: demonstratives, adjectives, numerals, subject and object prefixes, the relative prefix and the associative marker 'of'.

There is no information on the size of Kigiryama vocabulary but recent work on another Kenyan language, Kitharaka, if pertinent to languages in the Mijikenda group, estimated a vocabulary of 15,000 words (Dr S Nicolle, BTL linguistics consultant, personal communication). All words in Kigiryama end with a vowel due to the open syllable structure of the language. There are 44 consonant phonemes, including semi-vowels, five vowel phonemes and two basic levels of tone for grammatical distinctions: high and low (BTL, 1993). Unlike many Bantu languages, Kigiryama does not use tone for lexical distinctions.

7.4 Summary: implications for the study

This chapter has presented a brief outline of the structure of Kigiryama, with the aim of elucidating alterations to the grammatical content of speech and language assessments originating in the UK (Chapters Nine to Eleven). There are several implications of the structure and context of the language for the design of study assessments and procedures. First, in adaptations of English-language assessments, alterations will be necessary to ensure the weighting of test items reflects key aspects of Kigiryama grammar. A cautious approach is required, as little is known about the acquisition or developmental progression of the language. Second, the assistance of mother tongue Kigiryama speakers or schoolteachers will be beneficial, as they may be able to advise on developmentally-appropriate content. Third, most children in the target population are from the Giryama ethnic group but if children occasionally express a preference for assessment in one of the other Mijikenda languages, the level of mutual comprehension between groups will facilitate the transition of assessment content into the chosen language. Several of the assessors and fieldworkers (described further in section 8.4) originate from Mijikenda groups other than the Giryama and will thus be fluent speakers of those languages.

Part Three: Methodology and Assessment Development

The assessment battery used in this study included tests designed to measure performance across the range of developmental domains. Assessments of epilepsy, motor skills, hearing and vision were based on international standardised techniques whilst cognitive and behavioural assessments were based on tests established in Kilifi. Speech and language assessments were developed by the candidate. The design and methodology of the study and the development of culturally-appropriate, reliable and valid speech and language assessments is the focus of this part of the thesis.

Chapter Eight presents the rationale and aims of the study, describing the assessment tools and assessors involved in their administration and the procedure followed. Chapters Nine to Eleven concentrate on the development of the speech and language assessment battery, beginning with the theoretical background to the assessments and the presentation of a framework to account for the hypothesised effects of brain insults on speech and language and the limitations presented by the context of the study in Chapter Nine. Chapter Ten describes the initial development of the assessment tools and presents details on the pilot study while Chapter Eleven discusses alterations and refinements made to the battery in the light of the pilot study findings.

Chapter Eight: Study Design and Methodology

8.1 Study rationale

CM is a diffuse encephalopathy: alterations in level of consciousness, ranging from drowsiness to deep coma, are often precipitated by seizures, which are reported in the histories of 50-80% of children (Molyneux, et al., 1989; Schmutzhard and Gerstenbrand, 1984). Most survivors of severe falciparum malaria are reported to make a full neurological recovery, although persisting neuro-cognitive deficits have been reported in between 4.4% and 13.8% of survivors of CM (section 2.5). An estimated 30,000 African children under the age of ten have been left with residual disabling effects in the past decade (Snow, et al., 1999). However, few studies have carried out long-term follow-up of survivors of CM or attempted to describe the nature and severity of persisting deficits. Both prolonged coma and seizures, which are multiple or prolonged, are associated with neurological impairment following CM (Bondi, 1992; Brewster, et al., 1990; van Hensbroek, et al., 1997).

Other neurological manifestations of falciparum malaria such as multiple, prolonged or focal seizures with rapid recovery of consciousness after the seizure are more common than CM (Waruiru, et al., 1996). However, the prevalence and characteristics of acquired neurological impairment following such manifestations are not known. In the context of febrile seizures, complicated seizures are associated with neurological damage, particularly to the temporal lobe (Annegers, et al., 1987; Maher and McLachlan, 1995) and the subsequent development of epilepsy (Verity and Golding, 1991), particularly complex partial seizures. In countries with limited resources, such seizures are often not recognised as forms of epilepsy (Senanayake and Roman, 1992), but can be identified clinically and clarified by EEG and are potentially amenable to treatment. Studies using invasive EEG monitoring of temporal lobe seizures have indicated that they are predominantly mesial temporal/hippocampal in origin (Hermann, et al., 1992): damage in this area incurs a risk of deficits in memory, particularly episodic memory (Vargha-Khadem, et al., 1997). Language disorders are common in children with epilepsy (Robinson, 1991), often as an apparently independent manifestation of the cerebral disorder but sometimes as the result of a direct link with the seizure disorder, as in Landau-Kleffner syndrome (Deonna, 1991).

8.2 Objectives and hypotheses

The objectives of the study are:

1. To assess whether the prevalence of epilepsies, in particular partial epilepsy, is increased in children with a history of severe malaria, with specific reference to malaria and complicated seizures.
2. To determine if epilepsy is accompanied by developmental impairments, particularly in language, memory and behaviour.

The null hypotheses are:

1. The prevalence of epilepsy is not increased following severe forms of malaria.
2. There is no association between epilepsy and impairments of language, memory and behaviour.

8.3 Development of the assessment protocol

The assessment battery used in this study included assessments designed to measure performance across the range of developmental domains, while concentrating on temporal lobe aspects. Assessments of epilepsy, cognition, motor skills, hearing and vision were based on standardised techniques or tests established in Kilifi and are described below. Speech and language assessments were developed by the candidate and will be described in Chapters Nine to Eleven.

8.3.1 Epilepsy questionnaire

The epilepsy questionnaire was based on routine clinical practice and other questionnaires that have been used to carry out surveys in resource-poor countries (Feksi, et al., 1991; Pal, et al., 1998; Placencia, et al., 1992). The epilepsy history consists of a three-part questionnaire to the parent about the child's seizure history (Appendix 1). The first section aims to ascertain whether the child has experienced seizures before and includes direct questions (such as 'has the child ever had episodes when s/he loses consciousness?') and indirect questions (such as 'has the child ever had episodes when s/he smells an odd smell?'). The latter were particularly designed to detect complex partial seizures, that may have occurred without the parent or child realising it was a seizure (Senanayake and Roman, 1992).

If the parent reported seizure episodes, the assessor progressed to a series of questions to define the characteristics of the seizure/s. These are divided into characteristics occurring before the seizure, for example aura or abnormal behaviour; characteristics of the seizure itself, for example, convulsive movements, minor motor manifestations, automatisms and hallucinations and events occurring after the seizure episode, for example drowsiness, abnormal behaviour and aphasic symptoms. In addition, the parent was asked about the frequency of seizures, precipitants of seizures (for example, fever), at what age they started and the date of the last episode. The pattern of responses was used to classify the seizure type and duration and to establish whether seizures were provoked.

Children reported to have experienced two or more seizures (unrelated to fever in those aged 6 years), with at least one in the previous 12 months, were designated to an 'active epilepsy' group. A further group of children, who had experienced two or more seizures (unrelated to fever in those at or below 6 years of age) but none within the past 12 months, were classified as having 'inactive epilepsy'. These definitions accord with the guidelines used for initiating treatment by the Government of Kenya and the Kenya Association for the Welfare of Epileptics (KAWE). Seizure type was determined according to the ILAE classification (section 3.2).

8.3.2 Cognitive assessment

The specific aims of this assessment battery were to analyse the effects of malaria and seizures on temporal lobe and hippocampal functions and to obtain a measure of non-verbal function.

8.3.2.1 Memory assessment

The Kilifi Creek Behavioural Memory Test (KCBMT; Appendix 2) was based on the Rivermead Behavioural Memory Test for Children (RBMTC) aged 5 to 10 years (Wilson, et al., 1991) and is designed to detect impairment of everyday memory functioning, differing from most objective memory tests in that the material is not experimental. Wilson and colleagues (1993) describe the adaptation of the adult version of the test for use with children between the ages of 5 and 10. The test was piloted on 36 children with severe epilepsy and memory difficulties, who were attending a residential school. The ecological validity of the RBMTC was established from a 10-item houseparent rating scale of the children's everyday memory performance, which required houseparents to respond to questions such as 'how often does the child forget details of his/her daily routine?' (rated as 'very often', 'quite often', 'occasionally', 'rarely' or 'never'). There was a significant correlation between ratings and performance on the test (Spearman rank correlation = 0.71, $p < 0.001$). The adult version of the RBMTC has been found to have similar discriminative abilities as the Wechsler Memory Scale-III (Wechsler, 1997) in groups with memory problems and temporal lobe epilepsy (Perez and Godoy, 1998).

The RBMTC comprises 12 components, each of which is an analogue of an everyday task:

- Remembering a short story (immediate and delayed recall):
  The child is asked to listen to a short prose passage and remember as much as possible. After free recall, the child is prompted using ten questions. Later in the assessment, the child is asked to recall the story again, with the use of prompt questions when necessary. The story is divided into 31 units of detail: one point is awarded for each detail recalled correctly in free recall or in response to a prompt question and half a point is awarded for an approximate synonym or partially correct recall or response.
- Picture recognition:
  The child is shown and required to name ten pictures of familiar objects, which he/she is told he/she will be shown later in the assessment, mixed with novel pictures, and asked to identify. After a filled delay (during which other subtests are administered, thus the length of the delay is determined by the speed at which

the child completes the other subtests), the child is shown 20 pictures: the ten previously seen pictures must be discriminated from the ten distractors. The score is calculated by deducting the number of false positive from the number identified correctly.

- Remembering a short route (immediate and delayed recall):
  The assessor traces out a short path comprising five stages between a series of specified locations – the chair, door, window and table – in the room. The child is required to retrace the same path immediately and again later in the assessment. One point is awarded for each stage on the route followed in the correct order, with a maximum of five points.
- Delivering a message (immediate and delayed):
  During the previous task, the assessor leaves an envelope at a specified location. The child is required to pick it up and leave it in the correct place on both the immediate and delayed routes. Two points are awarded if the child spontaneously remembers the envelope; one point is given if it is collected after a reminder and one point is awarded if the envelope is delivered to the correct location. The maximum score is three points.
- Face recognition:
  This task is the same as picture recognition, except that the stimuli are photographic portraits. When the photographs are initially presented, the child is asked to identify whether the person is a man or woman and whether they are young, middle-aged or old.
- Orientation questions:
  The child asked eleven questions measuring orientation to time, place and date: (1) Name?; (2) Age?; (3) Birthdate?; (4) Year of birth?; (5) What day is it?; (6) What month is it?; (7) What year is it?; (8) Teacher's name?; (9) Which class at school?; (10) Name of headmaster/mistress?; (11) Name of school? One point is awarded for each correct answer.
- Remembering an appointment:
  The child is shown an alarm (including a demonstration of the ringing), which is set to go off after 20 minutes. The child is instructed and has an opportunity to practise asking the assessor a question ('Are you going to see me again?') when the alarm rings Scores are awarded according to whether the child requires prompting, with a maximum score of two.

- Remembering a first and last name:

  A photographic portrait is shown to the child and the assessor tells him/her the first and last name of the person portrayed, asking the child to repeat it. Later in the assessment, the child is shown the photograph again and asked the person's name. Scores are awarded for each name the child remembers and according to whether prompting is necessary. The maximum score is four.
- Remembering a hidden object:

  A packet of gold stars is shown to the child then hidden. The child is required to remind the assessor about the stars and tell or show him/her where they are hidden at the end of the assessment session. Scores are awarded for remembering the item and its location and the need for prompting, with a maximum of four points.

Modifications to the RBMTC were made by an educational psychologist based at KEMRI with previous experience of conducting psychological assessments in the area, and two members of the assessment team (see section 8.4.2). Objects familiar to Giryama children were selected to replace those in the RBMTC picture recognition test and drawn by a local artist. Similarly, photographs of Giryama people were taken for use in the face recognition and remembering a name tasks. The 'hidden object' (a sweet replaced the stars) was altered to be more representative of an item Giryama children would be familiar with. The content of the story was also changed, as there is evidence for better recall of stories consistent with a person's cultural knowledge (Mishra, 1996). Finally, the content of the orientation questions was altered to reflect the experience of Giryama children. Piloting of these questions suggested that many of the RBMTC questions may be inappropriate in this community. For example, Giryama children do not usually know their date of birth, months and years and not all children were attending school, making the schooling questions inappropriate for a proportion of the participants. Therefore, 18 questions were included in the KCBMT to provide enough scope to discard the seven least appropriate after analysis to leave 11. Due to the particular challenges of establishing the test-retest reliability of a measure of memory, reliability testing was not conducted with the KCBMT but will be addressed in a future study.

8.3.2.2 Non-verbal functioning assessment

There is some structural information that may be relevant to non-verbal functioning following severe malaria. In a study of 65 Kenyan children with CM, the most common EEG discharge site was the posterior parieto-temporal region (Crawley, et al., 1996). CT findings 1 month after discharge in children with neurological impairments indicated that five out of seven children had atrophy in the parieto-temporal region: the atrophy was unilateral in three children and generalised in two. This region is associated with the co-ordination of complex cognitive tasks, and lesions here may result in impairments on constructional tasks (for example, copying shapes using drawings, blocks or sticks).

For these reasons and as a measure of non-verbal functioning, a construction task (Appendix 2) used in a previous study in the same area (Holding, et al., 1999) was included in the battery. The format for the task was based on an assessment reported by Rutter and colleagues (1970) and comprised a series of 18 line-drawings of shapes of increasing complexity that the child was required to construct using a set of wooden sticks. The task had been extended from the original test format and developed into a learning task (a teach-test format), in which the child received prompts and verbal feedback for each item. In addition, stick drawings replaced the stick templates used in the original study. The task measures visual-spatial perception, visual-motor co-ordination, simultaneous processing and reasoning.

To begin the task, the child and assessor construct the shape together, the assessor guiding the child to examine the picture, select the correct number of sticks, choose a point at which to start the construction and re-check the drawing at regular intervals. On subsequent items, the assessor continues to provide guidance on placement and orientation of sticks and reminders to check the drawing. Each item receives a possible score of two: one mark for shape (use of the correct number of sticks, presented in the same manner as the drawing with no stick more than 1cm out of place) and one for orientation (no rotation of more than 45°). The 18 items are divided into six sections: each child is required to complete sections one and two. Thereafter, a discontinuation rule of one whole section of '0' scores or two consecutive sections in which all scores are less than '2' is applied. The child receives a score of '1' for each section in which he/she attains any score above '0' to make a possible total score of 6 for the task. The shape produced for each item was drawn by the assessor and the final score was decided in consultation with the second assessor.

The method of measuring test-retest reliability suggested by Bland and Altman (1986) was adopted in the current study and is described in detail in section 11.4.1. Using this method, the mean difference between the two administrations is calculated as an estimate of the overall bias and the 95% limits of agreement as an indication of the range of variability in individual scores. Clinical judgement is required to decide whether this is an acceptable level of agreement. Reliability testing of this and other cognitive assessments described in this chapter was carried out with 20 children under the conditions described in section 11.4. The mean difference in scores between the first and second administrations of the non-verbal functioning assessment (0.33, SD=0.97) indicates a high level of repeatability. The 95% limits of agreement (-1.57 – 2.23) suggest some variability in individual scores, possibly suggestive of a practice effect.

8.3.2.3 Attention test

Attention was reported to be impaired in two of the four published studies on cognitive deficits associated with severe malaria (Boivin, in press; Holding, et al., 1999). In addition, attention is a common source of impaired performance in childhood epilepsy syndromes such as benign epilepsy with centrotemporal or Rolandic spikes (BECRS) (Baglietto, et al., 2001; D'Alessandro, et al., 1990; Piccirilli, et al., 1994), Landau Kleffner syndrome (LKS) (Neville, et al., 2000; Robinson, et al., 2001) and continuous spikes and waves during slow sleep (CSWS) (Tuchman, 1994).

An attention test was incorporated into the cognitive assessment comprising a visual search task (Appendix 2) designed to measure speed of information processing, spatial processing, planning, impulsivity and sustained and selective attention, which had been developed in a previous study in this area (Holding, et al., 1999). This task was based on a similar task used in Jamaica to assess the sequelae of another parasitic infection, *Trichuris trichiura* (Baddeley, et al., 1995). The task comprised series of silhouette drawings of objects presented in rows on five sheets of A4 paper. The drawings were piloted for recognition. The child is required to identify and mark a target object (a ball), which appears randomly, once or twice in each row. The assessor begins by demonstrating the task to the child, who is then presented with a practice sheet: during the practice session, the assessor corrects any mistakes made by the child and emphasises the importance of speed in the task. The number of errors of omission (measuring sustained attention) and commission (measuring impulsivity) and the time taken to complete the task (in minutes and seconds) are used to score the test.

The mean difference on time taken to complete the task between the first and second administrations of the visual search was 0.74 (SD=0.81), suggesting an acceptable level of repeatability. The 95% limits of agreement (-0.85 – 2.33) are indicative of levels of individual variability comparable with a previous administration of the task (Holding, et al., 1999).

8.3.3 Behaviour assessment

The review presented in Chapter Two indicated that behaviour problems are commonly associated with CNS infections. Behaviour problems may develop after hospital discharge in children with CM (Newton and Krishna, 1998) and have previously been reported in children recovered from severe malaria with impaired consciousness in Kilifi (Holding, et al., 1999). As discussed in Chapter Three, the most epileptogenic parts of the brain – the limbic system, temporal lobes and frontal lobes – are the substrates of behaviour (O'Regan, et al., 1998) and problems in this domain are often reported in children with epilepsy. The US National Health Interview Survey found that children with epilepsy were 4.7 times more likely to present with inappropriate behaviours (McDermott, et al., 1995). Problematic behaviours have been reported by parents within six weeks of a first non-febrile seizure (Dunn, et al., 1997) and have been associated with childhood epilepsy syndromes such as BECRS (Yung, et al., 2000), LKS (Neville, et al., 2000) and CSWS (Tuchman, 1994). Behaviour problems are often associated particularly with temporal lobe epilepsy (TLE), although some authors state that TLE is not responsible for any more problems than other epilepsy syndromes (Caplan and Austin, 2000).

The importance of the caregiving environment in the development or amelioration of behavioural problems was emphasised by Campbell (1995) in a review of research on behaviour problems in preschool children. She found that negative or inconsistent parental behaviour and significant family adversity were associated with the development and persistence of behaviour problems. Family- and relationship-level variables have been found to predict behaviour problems in a US context, independent of disease-related factors, including epilepsy (Pianta and Lothman, 1994). The home or wider cultural environment may also influence the perception of developmental progress and the definition of problematic behaviour. For example, a marker of development and socialisation in the Luhya ethnic group of Kenya is the ability to assist others and give and receive social support, whereas parents in the UK or USA regard literacy skills and verbal facility as an indication of developmental progress (Weisner, 1989 cited in Serpell, 1993).

Behaviour is most commonly measured via observation or checklists completed by parents or teachers. Observations are limited to the assessment of behaviour in a particular context (unless repeated in different contexts) and may be biased by the presence of the observer. Behaviour checklists, although liable to bias from respondent attitudes and understanding of the questions and the technique of the interviewer, may produce a more representative measure of the child's normal behaviour patterns and in a cross-cultural situation, a greater indication of whether certain behaviours are considered to be problematic. In consequence, the measure of behaviour used in the current study was a parental questionnaire, which has been successfully employed in a previous study in this population (Holding, et al., 1999) and aimed to provide information about the child's behaviour in his/her normal daily surroundings (Appendix 3). The initial pool of 50 items was drawn from the Vineland Adaptive Behaviour Scales (Sparrow, et al., 1984), the Behaviour Screening Questionnaire (BSQ) (Richman, et al., 1982) and the Kenya Institute Of Special Education Screening Schedule (KISE). These items were piloted with local parents and questions that were culturally-inappropriate or difficult to understand were removed. A conversational format using prompts and explanations was developed: the interviewer records parental comments on the response form, which are later quantified according to a three-point scale (0 = never exhibits the behaviour; 1 = sometimes; 2 = often).

The questionnaire requires the parent to describe the child's development in six areas - social cognition; self-help skills and independence; tolerance of change; attention and concentration; anti-social behaviour and emotional lability – through a series of 15 questions. Using the data from Holding and colleagues' pilot and main studies, a detailed set of coding guidelines was employed in this study to increase the consistency of scoring. In addition, two people – the interviewer and candidate – scored each questionnaire independently, discussing any discrepancies until a consensus was reached. Holding and colleagues based their classification of behaviour problems on the system suggested by Richman and colleagues (1982), whereby the scores are divided into thirds, reflecting the three-point item-level scale, the top third indicating 'impaired behaviour', the middle third, 'borderline behaviour' and the bottom third, 'normal behaviour'.

Test-retest reliability measurements suggested that the level of repeatability was acceptable, with a mean difference of –0.26 (SD=2.05) between the first and second administrations of the questionnaire. The 95% limits of agreement indicated some variability in individual scores (-4.28 – 3.76) but not to a level that would alter the final categorisation of scores, as described above.

8.3.4 Neurological assessment

This neurological assessment (Appendix 1) comprised an assessment of cranial nerve and motor functions based on an assessment described by Palisano and colleagues (1997). These are standard neurological examinations that take between 20 and 40 minutes to perform. They are aimed at detecting gross motor neurological deficits, including differences between the sides of the body. Other tests, for example the Fogg test, were added to detect mild neurological signs.

8.3.5 Electroencephalogram

Each child had one 16-channel EEG using 21 scalp electrodes with standard 10-20 system electrode placement (Jasper, 1958). Recording was carried out for 20 minutes and included activation procedures with hyperventilation for three minutes and photic stimulation. The child was asked to repeatedly blow a windmill during the hyperventilation session.

Visual analysis of the EEGs was carried out according to standard clinical criteria (Binnie, et al., 1982) by an experienced neurophysiologist (Dr S White), with the rater aware of the age of each child but blind to the group status. Particular note was made of epileptiform activity (spikes, sharp waves, spike and wave complexes) and any focal features (epileptiform or non-specific slow wave abnormalities) (Appendix 4).

8.3.6 Visual screening

Vision screening was performed using the Sonksen-Silver Visual Acuity Test (Salt, et al., 1995), a system specifically developed for children(Salt, et al., 1995). The test requires the child to match letter shapes on the assessor's card to the corresponding letter shapes on his/her card by pointing, making it suitable for children who are illiterate. Visual acuity was measured at six metres, first with both eyes open, followed by the left eye then the right eye (Appendix 5). The candidate performed the task and an assessor stood behind the child and covered his/her eye when appropriate.

8.3.7 Hearing screening

Screening audiometry was conducted out using a Kamplex KS16 screening audiometer (P.C. Werth, UK) (Appendix 6). The machine was provided with a response button, which the child held and pressed in response to each tone. The audiometer was kept in an air-conditioned room to minimise problems related to the high humidity on the coast. Air conduction at 500, 1000, 2000 and 4000dB in each ear was carried out according to the recommendations of the British Society of Audiology (BSA, 1988). Audiometric descriptors have been altered from the BSA recommendations because the testing facilities employed in the study do not meet their standards. A soundproofed room is not available at the unit, so a quiet office was used for each test, although there was usually a degree of ambient noise from outside or surrounding offices. Therefore, a diagnosis of hearing impairment was based on a level in the better ear of:

Mild – 30-50dB

Moderate – 51-80dB

Severe – 81-105dB

Profound – 106+dB

8.3.8 Socioeconomic status questionnaire

Measures representing socioeconomic status were collected via a parental questionnaire (Appendix 7). Measures of socioeconomic status included father's (or main breadwinner's) occupation, mother's level of education, mother's ability to speak English and number of siblings. The details of these questions were presented in Chapter Five.

8.3.9 General health assessment

Measures of nutritional status were included as the prevalence of malnutrition has been found to be higher in the coastal provinces of Kenya than most other provinces (Ngare and Muttunga, 1999). Poor nutritional status, reviewed in detail in Chapter Five, has been linked to deficits in behaviour (Galler and Ramsey, 1989) and cognition (Sigman, et al., 1989). Measures of height and weight were taken at the time of the neurological assessment.

An obstetric and perinatal questionnaire was also administered to detect complications during the pregnancy and birth (Appendix 1). However, with no medical records available in most cases, it was difficult to reliably establish the prevalence of, for example, premature births in the study children.

8.4 Training of personnel

The candidate designed the study protocol and managed and co-ordinated a team of assessors and fieldworkers. This approach was adopted for several reasons. First, the number and diversity of assessment procedures required a team approach. Secondly, the candidate is not of Kenyan extraction: if an assessor's competency in the language of the participant is inadequate, the validity of assessment administration and interpretation becomes problematic (MacNeill Horton Jr., et al., 2001). Thirdly, locally-based assessors were able to provide input on the language and the cultural aspects of assessment development. Finally, as described in section 6.8, to increase the chance of assessment results that are representative of the child's actual abilities, it is necessary reduce the number of unfamiliar aspects of the assessment situation, which includes recruiting team members from the same ethnic group as the target population. The involvement of carefully selected assessors reduces the possibility of sources of conflict in cultural assumptions and communicative norms prior to the assessment procedure (Pakendorf and Alant, 1997). The roles and training of the assessment team are detailed below.

8.4.1 Speech and language assessments

Two assessors and three fieldworkers, all from the Mijikenda ethnic group, were responsible for collecting speech and language data. The assessors carried out the comprehension, syntax, higher level language and word finding assessments and recorded the spontaneous language sample and word finding test. One of the fieldworkers was responsible for the phonetic transcription of the word finding sample for use in the phonological assessment and the orthographic transcription of the spontaneous language sample. The latter was profiled by the assessor who had collected the sample for the lexical semantics assessment.

The other two fieldworkers were responsible for conducting the parental pragmatics questionnaire in addition to the parental behaviour questionnaire and collecting socioeconomic data.

Assessors and fieldworkers were trained by the candidate before data collection began. One of the assessors was trained before the pilot study (section 10.4). The other assessor had previously worked at the Education and Assessment Resources Service and had some experience of paediatric speech and language testing, thus required a shorter period of training. Training was divided into three stages. First, teaching sessions were held on language acquisition, the facets of speech and language forming the theoretical framework of the study (described in Chapter Nine), speech and language pathology and assessment techniques, emphasising the particular principles of assessment in the context of research methodology. Secondly, the assessors contributed to aspects of the design and refinement of the assessment battery. Finally, practice assessment sessions, observed by the candidate, were carried out with children from the target population. Feedback and discussion took place after each session.

The fieldworker responsible for transcription was already familiar with the International Phonetic Alphabet so his training comprised a 'refresher' course on phonetic transcription and practical work on transcription methods. The fieldworkers responsible for conducting parental questionnaires underwent training in interview techniques, recording and scoring responses. Practice interviews, observed by the candidate, were held with mothers recruited from the out-patient department of Kilifi District Hospital (KDH). Discussion and feedback took place after each interview.

The candidate designed instruction manuals for the speech and language assessments (Appendix 8). They were inserted at the beginning of each assessment booklet so they were available for reference at any time during the course of the study.

8.4.2 Cognitive assessment

Two assessors were responsible for carrying out the cognitive assessment. One assessor was of Mijikenda origin and the other was from another ethnic group but had lived in the area for many years and could speak Kigiryama. Both assessors had previous experience of conducting cognitive assessments and were involved in the development and adaptation of the assessments. Specific training in the tasks employed in the current study was carried out by an educational psychologist based at KEMRI (Dr P Holding). An instruction manual for the cognitive assessment was available for reference during the study.

8.4.3 Behaviour questionnaire

The behaviour questionnaire was administered to parents by the two fieldworkers also responsible for carrying out the pragmatics questionnaire. Their general training is described in the speech and language assessment section (section 8.4.1). Additional training on the specifics of the behaviour questionnaire was carried out by an educational psychologist based at the KEMRI unit (Dr P Holding), with assistance from the candidate. The fieldworkers did not have direct contact with the children to ensure that all assessors were blind to the group status of the study participants.

8.4.4 Neurological assessment/epilepsy questionnaire

The neurological assessment and parental questionnaire on epilepsy were conducted in the same session by one of two unit physicians. Both underwent training in neurological examination from an experienced Paediatric Neurologist (Dr C Newton) and were observed performing the examination in several practice sessions.

8.4.5 Electroencephalogram

The EEG was carried out by a trained unit technician and was independently read by an experienced Paediatric Neurophysiologist (Dr S White) visiting from Great Ormond Street Hospital in London, UK. The unit technician was a Clinical Officer who had received six weeks of training in neurophysiology at Kenyatta Hospital, Nairobi, Kenya and a further four weeks at the Neurophysiology Department of Great Ormond Street Hospital, London, UK. He received on-site supervision from a Paediatric Neurologist and the visiting Paediatric Neurophysiologist.

8.4.6 Vision and hearing tests

The candidate carried out the majority of the hearing and vision tests. However, one of the fieldworkers from the language team was trained by the candidate in the techniques of audiometry and visual screening, in order that two assessors were available. The training involved theoretical sessions on assessment techniques for children, the background to the tests chosen for the study and specific training on recording audiometric results. Observed practical sessions were carried out with children from the target population with opportunity for discussion and feedback after each session.

8.4.7 Recruitment of participants

A demographer identified all participants from unit databases. Children were recruited by a fieldworker who had received training in locating rural-based children using maps produced in a previous census study. The fieldworker also collected demographic data on each participant. Both the demographer and fieldworker remained separate from the assessment process to preserve the integrity of the 'blinding' of the assessors to the group status of each participant.

8.4.8 Quality assessment

A system of cross-checking was instigated whereby pairs of assessors would check each other's assessment forms for accuracy, missing scores and inconsistencies. The candidate would carry out a final cross-check when collating each child's file. Weekly trouble-shooting meetings were held throughout the course of data collection, during which the candidate updated the team on the progress of the study and each team member was given the opportunity to raise issues and problems for discussion.

'Assessment refresher days' for the cognitive and language assessors were organised periodically by the candidate to ensure the standard of assessment practice was maintained and to give the team an opportunity to reflect on their own and each other's performances. Each day was divided into three sessions: first, observation of assessments (with each assessor performing and observing at least one assessment), second, discussion of general assessment principles and techniques and finally, presentation of case studies and problem solving. In addition, the candidate carried out regular observations of the assessors to supplement this process.

8.5 Sample size determination

Based upon a 4.5% cumulative risk up to age 10 of developing epilepsy following complicated febrile seizures (Annegers, et al., 1979), the prevalence of epilepsy following malaria with complicated seizures is assumed to be approximately 4.5%. In order to detect an increase in epilepsy from 0.5% in children who haven't had seizures or CNS infection (Hauser and Kurland, 1975) to 4.5% with 80% power at the 5% significance level, approximately 290 children would need to be recruited to each group. To detect an increase in the prevalence of epilepsy following cerebral malaria compared to 0.5%, approximately 110 children would be needed per group, based upon a 10% risk of developing epilepsy following CNS infection (Annegers, et al., 1988). On the basis of these calculations, the recruitment aim was a maximum of 300 children in each group.

8.6 Study site and population

Children were recruited from a demarcated study area on the coast of Kenya comprising a 40km stretch of coastline, extending 30km inland (section 4.3). All assessments, with the exception of the speech and language, were carried out at KDH. The speech and language assessment was performed at the child's home as this has been found to be more conducive to spontaneous speech production.

Three groups of children were recruited to the study. The children were between 6 and 9 years of age at assessment, as cognition and speech and language can be assessed more reliably at this age than in younger children. Children exposed to severe malaria were identified from databases of admissions to KDH. A random sample of children unexposed to severe malaria was drawn from a surveillance database of children living in the study area. All children spoke a Mijikenda language as their first language and fulfilled the inclusion criteria for one of the three study groups:

1. Children who had previously been admitted to hospital with cerebral malaria, defined as a deep level of unconsciousness with inability to localise a painful stimulus (Blantyre coma score of ≤ 2 for 4 or more hours); a peripheral asexual parasitaemia and exclusion of other causes of encephalopathy (Newton, et al., 2000). This group will henceforth be referred to as the 'CM group'.

2. Children who had previously been admitted with a primary diagnosis of malaria and complicated seizures (>2 per 24 hours, focal or prolonged > 30 minutes). This group will henceforth be referred to as the 'M/S group'.
3. Children who had not previously been admitted to KDH with either complication of severe falciparum malaria. This group will henceforth be referred to as the 'unexposed group'.

Children were excluded if their parents refused to give informed consent or withdrew it at any point during the assessment process.

8.7 Ethical issues and informed consent

Ethical permission for the study was obtained in Kenya (Kenya Medical Research Institute) and the UK (Great Ormond Street Hospital; Institute of Child Health). Informed consent was obtained from each child's parent before the start of the assessment procedure. The development of the informed consent form (Appendix 9) began with the production of a draft by the assessment team, which was discussed with other unit members and a local schoolteacher. Two further drafts were produced and piloted with ten parents in the outpatient department of KDH through a question and answer session. The final draft was produced through discussion with team members and again piloted with parents through a question and answer session. The procedure for gaining informed consent involved discussion of the form with the parent followed by a briefing session to advise the parent on how to explain the study to the child.

Any children diagnosed with severe impairments during the study were referred to the following services:
Cognition / Speech and language: Education and Assessment Resources Service
Epilepsy: Neurology Clinic
Motor: Physiotherapy / Occupational therapy
Hearing: Children were provided with a hearing aid if appropriate
Vision: Children were provided with glasses if appropriate; blind children were referred to Occupational therapy

8.8 Procedure

The procedure for each child was spread over a three-day period. Recruitment was carried out in two-week blocks, thus day two occurred a maximum of two weeks after day one. Days two and three were consecutive.

Day One

A fieldworker visited the child's home to recruit the child. The study was explained to the parent and informed consent obtained. The fieldworker arranged an appointment with the parent for the next visit.

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Day Two

The speech and language assessment team visited the child's home for the speech and language assessment. This was carried out in a quiet area on the compound of the house, most often under a tree for shade and comfort. While the child was being assessed, a fieldworker carried out the parental questionnaires. After the assessment, the parent and child were invited to hospital the following day.

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Day Three

The parent and child came into the hospital for the day. The cognitive assessment was administered in the morning. After lunch, the vision and hearing screening, EEG and neurological assessment were carried out.

After the recruitment and informed consent procedure on day one, the parent was asked whether they considered their child to have any deficits in hearing or vision. Any children whose parents gave affirmative responses underwent hearing and vision screening before the other assessments to ensure that any impairments present did not prejudice their performance on other tasks.

The field session on day two began with formal introductions and greetings, an important precursor to conversation in Kenya and a play session involving all children at the child's homestead, which aimed to create a relaxed environment for testing. A small table and two chairs, specifically manufactured for the study, were transported to each session and set in a shaded, quiet area of the compound (figure 8.1). Each assessor carried their own portable equipment box with copies of each assessment, the necessary materials and forms. When the assessor considered the child to be ready to begin, he/she invited the child to join him/her in the assessment area, obtained the child's consent and explained the format of the tasks.

Figure 8. 1: Typical setting for the speech and language assessment

At this point, it was emphasised that the session would consist of 'learning tasks' only because many children in the study area associate KEMRI personnel with injections and the taking of blood samples. The dictaphone used to record the spontaneous language sample and the phonological assessment, which would be unfamiliar to the majority of participants, was then introduced to the child: he/she was invited to record his/her voice and play it back. If the child was reluctant or uncooperative, other children would be invited to join in the initial session or the mother would be asked to sit with the child, although requested not to give any prompts. The aim of each assessment was outlined and the response format expected from the child explained and modelled before the start of each assessment. Assessments were administered in the following order unless the child was unco-operative, in which case the session began with whichever task he/she was willing to perform: spontaneous language session, receptive language assessment, higher level language assessment, syntax assessment and word finding assessment. Each child was given one break of 10 minutes. Including the break, the average session time was 50 minutes. During the assessment, a fieldworker would administer the pragmatics, behavioural and socioeconomic questionnaires to the mother (or another relative on rare occasions when the mother was absent). At the end of the session, the parent was given the fare for transport to the hospital for day three.

On arrival at KDH on day three, the child and parent were greeted by the cognitive assessors and offered milky tea and bread for breakfast. As three children were assessed per day and siblings often accompanied them, there were invariably other children available for play. A box of toys was available for their use. Following the play session, the cognitive tasks were explained to the child and the assessments began once the assessor was confident that the child was relaxed and ready to participate. Each cognitive assessment session was held in a large tent or classroom (two assessments often occurred simultaneously) situated away from the main hospital site. Each contained a table and two chairs similar to those used on day two and the assessor's equipment box. The assessor explained the aim of each task and modelled the response format expected from the child before the start of each assessment. A standard assessment order was used – orientation questions from the KCBMT; construction task; remainder of KCBMT; receptive vocabulary assessment; visual search (attention test) – unless the child was uncooperative, as above. A 10-minute break was given during administration of the battery, resulting in an average test time of 1 hour and 30 minutes.

After lunch, which was provided for each family, the three children were rotated between the vision and hearing screening, neurological assessment and EEG. Where possible, the EEG was performed last because it was the most unfamiliar and potentially unsettling procedure of the day. The visual screening was performed in a shady area adjacent to the cognitive assessment tent to allow for the six metre distance required for testing. The child sat on a chair with the letter card on a table in front of him/her and the assessor stood opposite on a spot marking the six metre distance. The hearing screening was carried out in a quiet office. Before the screening, the audiometer was introduced to the child and he/she was given the opportunity to practise responding to different tones until the assessor was confident that he/she understood the response format. During the testing procedure, the child was asked to sit with his/her back to the audiometer so it was not possible to follow the visual cues of the assessor pressing the button for each tone. The neurological assessment and EEG were performed on the hospital site for easy access to equipment used during these procedures that was also in routine clinical use. Each item of equipment employed in these procedures was introduced and explained to the child before use. Fares for transport home were provided for each family at the end of the day and children received a reward for participation in each assessment on days two and three.

All assessors were blinded to the group status of each child. Before data collection commenced, the procedure was piloted on ten children from the target population and found to proceed efficiently.

8.9 Statistical analysis

8.9.1 Data management

Database formats and codings were designed by the candidate in conjunction with the manager of the Computer Department at KEMRI. Dedicated entry formats were used on FoxPro version 2.1 for each assessment, including pre-set limits on the possible range of entries (for example, if the possible answers to an item were '0' and '1', the item would be set to only receive one of these entries, reducing the risk of erroneous data). All data were double-entered by different data entry clerks, one of whom compared the final datasets for discrepancies. Any discrepancies were reconciled by referral back to the original assessment forms retained in each child's file.

8.9.2 Data analysis

Analysis was carried out using STATA version 6. Logistic regression was used to compare the proportion of children with epilepsy in the exposure groups. The difference was estimated between exposed and unexposed group scores and between epilepsy and non-epilepsy group scores using multiple regression for normally-distributed outcomes. Very skewed outcomes were categorised into binary variables after examination of the histograms and analysed using logistic regression. An *a priori* decision was made to adjust all estimates for age, sex, nutritional status and socio-economic status and language, cognitive and behavioural scores also for schooling status, as there is evidence that each would influence performance on these assessments.

Univariate analyses on background data (Chapter 12) and assessment subtests were performed using the chi-squared test. Test-retest and inter-rater reliabilities were calculated using the mean difference between the two measures as an estimate of the overall bias and the 95% limits of agreement as an indication of the range of variability in individual scores (Bland and Altman, 1986). Data analysis was performed in conjunction with a statistician.

Chapter Nine: Theoretical Framework of the Speech and Language Battery

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9.1 Introduction

"A normal procedure in scientific investigation, especially when dealing with a new or unformed field of study, is to attempt to impose some organisation upon it by constructing a 'model' of the field" (Crystal and Varley, 1998 p62). Models proffer a representation of a theory, generate hypotheses and provide insights about a field of study. Wirz (1993), describing assessment techniques in the UK, comments that advances in the assessment of children with language disorders have been based on the accumulation of a knowledge base of clinical linguistic theory and normal language acquisition. Such a knowledge base does not yet exist in the coastal Kenyan situation (Chapters Four and Seven). There has been no research into the developmental sequence of Kigiryama acquisition and little information exists on the structure of the language. Speech and language impairments are common after CNS infections and several studies have provided evidence of the occurrence of such impairments after CM (section 2.3.3). In consequence, it was necessary to adopt a broad approach in developing a theoretical framework that would take into account potential neurological damage and its hypothesised effects on language, while accommodating the constraints set by the context.

The aims of this chapter are twofold: first, to review models that may be useful in the construction of a theoretical framework for the speech and language assessments in this study and second, to review evidence from previous studies within these contexts, to provide an indication of potential areas of language dysfunction. The assessment battery constructed for the current study tested spoken language only. Written language was not included for the following reasons: first, Kigiryama is predominantly an unwritten language with an orthography currently under development (section 7.3); second, impairments in spoken language would be potentially more disabling in a community with an oral tradition and third, many of the study participants had never attended school and would be unlikely to know how to read and write.

9.2 Acquired language disorders in childhood: models and mechanisms

9.2.1 Outcome after early brain injury

A continuing controversy in the study of early brain lesions is the degree of brain specialisation for language present in infants and the relative plasticity of intact regions of the immature brain, which may provide some functional compensation for damaged regions.

Lenneberg (1967, cited in Bates, 1997) was an early proponent of the hemispheric equipotentiality hypothesis, which states that the two cerebral hemispheres have the same developmental potential at birth. However, a number of studies have suggested that there may be early hemispheric specialisation for language in the left hemisphere. Aram and colleagues have conducted a series of cross-sectional studies since 1981 on the language development of children with early unilateral brain lesions. Reviewing this work, Aram (1992) concludes that children with left-hemisphere lesions have mild yet persistent deficits in expressive and receptive syntax, naming and lexical retrieval, relative to children with intact left hemispheres. These findings are suggestive of early hemispheric specialisation for certain facets of language and also imply recovery and presumed reorganisation of language abilities compared to adults with similar lesions (Aram, 1992). Vargha-Khadem and colleagues (1985) assessed language performance in three groups of children with congenital, 'early acquired' (2 months to 5 years) and 'late acquired' (5 to 14 years) unilateral lesions. In children with left-hemisphere lesions, increasing age at injury was associated with poorer performance in naming and comprehension, relative to controls or children with right-hemisphere lesions. Again, these results are suggestive of early and progressively increasing specialisation of the left hemisphere for language and also of the deleterious effects of lesions sustained after the age of 5 years.

The findings of later reports have led to renewed interest in a moderated form of the equipotentiality hypothesis. Vargha-Khadem and colleagues (1992) assessed children with congenital lesions, categorising participants by the presence or history of seizures: they found that the seizure group displayed poorer performance on measures of verbal and non-verbal IQ and memory compared to controls or children with lesions but no seizures. Unilateral brain damage resulted in few and mild deficits, provided there was no concomitant seizure activity or severe EEG abnormality. Vargha-Khadem and colleagues interpreted these findings as support for the equipotentiality of hemispheric functions subserving language. Bates and colleagues (1997) carried out a series of prospective studies with children who incurred unilateral brain lesions before the age of 6 months, finding few significant differences in lexical skills as a function of lesion side. In the early stages of language development, they found that the prevalence of delays in comprehension was greater in children with right-hemisphere lesions, although from 10 to 60 months of age, children with left temporal lobe lesions displayed significantly greater delays in expressive vocabulary and grammar. These findings suggest an element of left hemisphere specialisation for language. Investigation of older children (5-7 years) with the same early-onset aetiology indicated that although there were significant differences in language performance between children with left-hemisphere lesions and matched controls, the former group were performing within the normal range, indicating some reorganisation of function (Reilly, et al., 1998).

A recent case study, using functional magnetic resonance imaging (fMRI) suggests that the brain is capable of plasticity and developmental reorganisation to a later age (Hertz-Pannier, et al., 2002). The authors administered pre- and post-operative fMRI tasks to a child who, following a period of normal language acquisition, developed intractable epilepsy related to Rasmussen's syndrome of the left hemisphere at 5 years 6 months and underwent hemispherectomy at 9 years of age. The child experienced marked recovery of language skills after initial post-operative aphasia. Pre-operative imaging (6 years 10 months) showed left lateralisation of language functions during a word fluency task. Post-operative fMRI tasks (10 years 6 months) showed activation in the right hemisphere during expressive and receptive language tasks, predominantly in regions that could not be detected pre-operatively but that mirrored regions activated before hemispherectomy in the left hemisphere (inferior frontal, temporal and parietal cortices).

Vicari and colleagues (2000) discuss a middle ground to the debate: "...that equipotentiality and early hemispheric specialisation are not in opposition but should be viewed as two poles of a continuum, with several reasonable intermediate positions" (pp32-3). They found delays in expressive vocabulary in children with congenital brain lesions between the ages of 13 and 46 months. In the early stages of language development, delays were significantly greater in children with left-hemisphere injury relative to those with right-hemisphere lesions. This discrepancy was not apparent in children at the sentence-stage of language development. Vicari and colleagues conclude that their findings support the continuum view. Lexical deficits in younger children support an element of advantage for language learning in the left hemisphere, whereas findings in older children imply that initial specialisation can be overcome, possibly through the influence of developmental plasticity.

9.2.2 Developmental versus acquired disorders

Developmental language disorders often result from a degree of learning difficulty, hearing loss or structural abnormalities of the articulators, although there exists a group of children with problems in language acquisition, whose diagnosis is usually one of exclusion (no sensory-perceptual deficit, no motor disorder, no evidence of global learning difficulties, no socioemotional disorder and no sociodemographic condition) (Crystal and Varley, 1998). Such disorders have been referred to variously as 'developmental aphasia', 'developmental dysphasia', 'delayed language', 'specific developmental language disorder' and 'specific language impairment' (SLI), the latter term currently in common usage (Bishop, 1997). Children with SLI display linguistic difficulties – the most obvious occurring in aspects of language form, particularly syntax and phonology (Bishop, 2000) – in the context of otherwise normal development, although they may experience social and educational problems, whether as a cause or a consequence of the linguistic deficit (Crystal and Varley, 1998).

A distinction between acquired and developmental disorders, differentiated by the loss of already acquired knowledge versus difficulties in acquiring this knowledge, is pervasive throughout linguistic research and clinical practice (Crystal and Varley, 1998). Acquired language disorders in children are less common than those of developmental origin. The distinction is not always straightforward, however, particularly in retrospective studies. For example, in his study of causes of severe and persistent speech and language disorders, Robinson (1991) was unable to classify six children because it was unclear from their history whether there had been normal language development or not. He classified the nature of onset in these children as 'uncertain'. Two criteria have consistently been identified in the diagnosis of acquired language disorders: first, that their onset is precipitated by a cerebral insult of some kind and second, that the disorder follows a period of normal language acquisition (Ozanne and Murdoch, 1990). The cause of the neurological deficits witnessed in CM (section 2.3.3) is presumed to be a cerebral insult, although there is no corresponding evidence for the case of M/S. In addition, the largest proportion of cases of severe forms of malaria occurs between the ages of 1 and 4 years (Newton and Krishna, 1998). Thus, the evidence suggests that language impairments associated with malaria are more likely to constitute an acquired disorder. In consequence, this review of models of speech and language impairments will begin with the classification of acquired language disorders in children.

9.2.3 The central language mechanism

Several hypothetical models of the central language mechanism have been proposed. Love and Webb (2001) describe a model based on Carl Wernicke's conception of the central language mechanism, the components of which have been supported through neurodiagnostic and neuroimaging procedures.

This model proposes the major components of the central language mechanism: fibre pathways, gyri and subcortical areas crossing three lobes of the cerebrum, which together form the perisylvian area of the dominant hemisphere. Broca's and Wernicke's areas are the major components of this model and are responsible for the expressive aspects of motor speech and the reception of language respectively. Wernicke's area consists of the superior and middle temporal gyri and permits verbal comprehension and the formulation of internal linguistic concepts. Broca's area is situated in the frontal lobe and functions as a centre for the motor programming of the speech articulation movement. According to the model, motor plans are projected from Broca's area to the adjacent premotor cortex and the lower portion of the motor cortex then articulatory mechanisms are activated via signals sent down the corticobulbar tracts and cranial nerves.

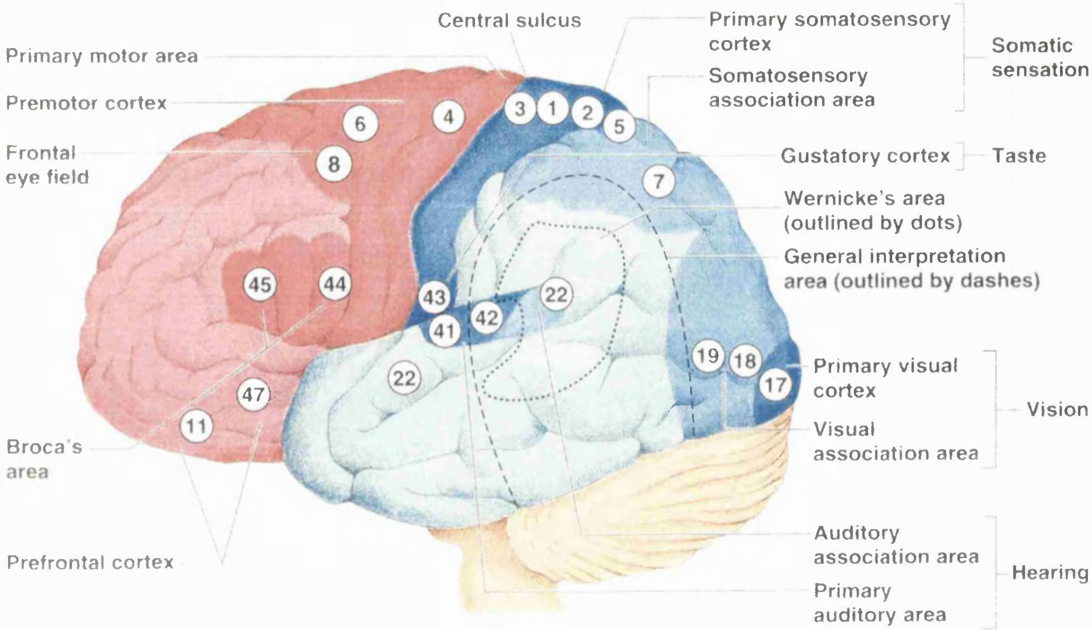

Figure 9. 1: Areas of the left cerebral hemisphere, from Marieb (1995)

The arcuate fasciculus is the bundle of connective fibres transmitting linguistic information between Broca's and Wernicke's areas. From the temporal lobe, the fibres arch around the supramarginal gyrus, pass through the parietal operculum, then join the superior longitudinal fasciculus before terminating in the frontal lobe. The corpus callosum, the mass of white matter connecting the two hemispheres transmits information between the hemispheres.

The angular gyrus is located in the left parietal lobe and integrates visual, auditory and tactile information. This region is also responsible for symbolic integration for reading and lesions to this site are posited to be involved in the development of alexia. The supramarginal gyrus lies anterior to the angular gyrus around the posterior end of the Sylvian fissure and is responsible for symbolic integration for writing. Lesions are associated with agraphia. The angular gyrus and supramarginal gyrus are together known as the inferior parietal lobule.

Subcortical language mechanisms are poorly understood in comparison to cortical mechanisms. However, lesions in the thalamus, internal capsule, striatum and globus pallidus may result in speech and language disturbances and lesions of the basal ganglia have been associated with dysarthric and dysphonic symptoms.

Cortical areas outside the perisylvian zone are involved in secondary cortical language mechanisms. The transcortical vascular border zone lies between the territory of the middle cerebral artery and that of the anterior and posterior cerebral arteries. This is the region in which reductions in cerebral perfusion seen in cerebral malaria initially manifest (Dr C Newton, personal communication). Lesions in these areas have been associated with aphasias without repetition disturbance, referred to in some models as the transcortical aphasias (see table 9.1).

The advantage of this model is the predictability of symptoms associated with specific lesion sites. Love and Webb (2001) outline the limitations of the model acknowledged by one of its main proponents, the neurologist Norman Geschwind. First, some features of aphasic syndromes are not easily explained using this model. Second, cases of aphasia occur that are not predicted by the model and finally, there are occasions when the expected symptoms do not occur despite the presence of a lesion.

In recent years, models such as this have been challenged by research in cognitive neuropsychology, which advocates investigations of individuals rather than grouping people into categories on the basis of common co-occurrences of symptoms. Tasks are fractionated into their component processes, as opposed to the approach of mapping broad cognitive functions, such as comprehension, onto brain structures. These studies have generated models of the processes involved in the understanding and production of single words, which enable the construction of a profile of an individual's strengths and weaknesses, which can be used as a basis for therapy (Stackhouse and Wells, 1993). A simple information-processing model will be discussed further in section 9.5.2.

9.2.4 Models of acquired childhood aphasia

Models of acquired language disorders in children have traditionally been based upon adult aphasia models. One of the major adult aphasia classifications, a lesion-based model developed by (Goodglass and Kaplan, 1972) (table 9.1), is the mainstay of classificatory models in acquired childhood aphasia (ACA) (Lees, 1993a).

Syndrome	Characteristics
Broca's aphasia	Nonfluent production, decreased verbal output, restricted grammar and vocabulary. Auditory comprehension better than production of language.
Wernicke's aphasia	Fluent production, characterised by impaired auditory verbal comprehension, use of paraphasias and anomia.
Anomic aphasia	Severe word-finding difficulties with fluent production and circumlocution. Limited receptive or expressive difficulties.
Global aphasia	Severe impairment of receptive and expressive language. Limited production with stereotyped utterances.
Conduction aphasia	Fluent production and intact comprehension, characterised by selective impairment in repetition.
Transcortical aphasias	Transcortical motor aphasia is similar to Broca's aphasia but marked by more dysfluency. Transcortical sensory aphasia consists of a severe deficits in auditory comprehension and naming. In both types, repetition is intact.
Auditory verbal agnosia or Pure word deafness	Severe deficit in auditory verbal comprehension
Mixed non-fluent aphasia	Some expressive language with non-fluencies. Moderate auditory verbal comprehension problems.

Table 9. 1: Major aphasia categories described by Goodglass and Kaplan (1972)

Lees (1993a) applied two classificatory models – the Goodglass/Kaplan model and a model of developmental language disorders (Rapin and Allen, 1987) (table 9.2) to 34 children with ACA resulting from a range of aetiologies. She aimed to assess the relevance and use of the two models in classifying the subtypes of language disorders seen in ACA. The Goodglass/Kaplan model provided an adequate framework for the classification of only 47% of the children in the study. Of the 53% who could not be classified, four children presented with fluctuating aphasias with episodes of word deafness, anomia and Wernicke's-type aphasia; eight had reduced speed of auditory verbal processing and lexical recall following closed-head injuries and five had brief periods of paraphasias followed by mild word-finding problems.

Similarly, 59% of children could not be allocated to one of Rapin and Allen's subtypes. The four children with fluctuating aphasias experienced periods of verbal auditory agnosia, semantic-pragmatic deficit and severe word-finding difficulties. Thirteen children with a history of head injury showed a broad range of comprehension and word finding difficulties and two children had brief aphasic episodes with deficits in comprehension and word finding. One child with Landau-Kleffner syndrome fulfilled criteria for three of the subtypes over the course of assessment: verbal auditory agnosia, semantic-pragmatic deficit and lexical-syntactic deficit.

Disorder Subtype	Characteristics
Verbal auditory agnosia	Also known as word deafness. Severe receptive language disorder, considered to have a poor prognosis.
Phonological-syntactic deficit	Severe deficits in expressive language with dysfluent production and errors in morphological and phonological contrasts.
Verbal dyspraxia	Dysfluency and severe phonological deficit resulting in unintelligible speech.
Phonological programming deficit	Reduced phonological contrasts and speech intelligibility.
Lexical-syntactic deficit	Severe deficits in word retrieval and sentence formulation. Difficulties in understanding complex grammar and use of paraphasias.
Semantic-pragmatic deficit	Difficulties in the use of language and word meaning. Fluent speech, which may include stereotypes, perseveration and circumlocution. Comprehension is often literal.

Table 9. 2: Developmental language disorder subtypes described by Rapin and Allen (1987)

Lees (1993a) concluded that although the deficits seen in ACA are related to adult aphasic syndromes and developmental language disorders, reliance on models designed to classify other phenomena is inappropriate. Bishop and Rosenbloom (1987) stress the inadequacy of models based on research with adult neurological patients for explaining childhood language disorders: adult anatomical, physiological and clinical studies correlate poorly with what is seen in paediatric practice. Also, early damage may be said to modify the development of cerebral organisation of function or be compensated by greater plasticity in the younger brain (Oxbury, 2000).

Lees (1993a) advocates the use of a consistent assessment battery to produce comparable profiles of different children, which could be used to develop a classificatory model that takes account of fluctuating aphasias and changes in presentation over the course of recovery. Bishop and Rosenbloom (1987) also recognise the shortcomings of developmental language disorder categories but emphasise their importance as a means of scientific communication between professionals. The description of each child on an individual basis in preference to the use of classificatory models will not aid the accumulation of knowledge about syndromes and disorders, which is particularly important in this study where the body of existing knowledge is very small. Therefore, the following sections will investigate other models and consider their use in this study.

9.3 Medical and behavioural models

9.3.1 The medical model

The medical and behavioural approaches are the main models in paediatric speech and language pathology. The medical model is derived from the principles and practice of the medical sciences, focussing on the causes of disease and how to eliminate them. The categorisation of speech and language disorders is primarily based on the supposed aetiology or underlying mechanism of the impairment (Donaldson, 1995), the advantage of the model being that it gives prognostic information. In their taxonomy of childhood language disorders, Bishop and Rosenbloom (1987) describe seven broad categories based on aetiological and functional criteria (table 9.3).

	Category
1	Pure speech disorders (dysphonia, dysfluency, dysarthria)
2	Language disorder secondary to hearing loss
3	Language disorder associated with more general intellectual impairment and secondary to brain damage or disorder
4	Dysphasia arising from brain lesions acquired after language has developed
5	Language disorder associated with behavioural or psychiatric disorder
6	Language disorder as a consequence of environmental deprivation
7	Language disorder not attributable to any of the above (SLI)

Table 9. 3: Classification of childhood language disorders according to the medical model, modified from Bishop and Rosenbloom (1987)

In their critique of this model, Bishop and Rosenbloom (1987) state that it provides a satisfactory framework only for category one of the list cited in table 9.3. Disorders in this category tend to be the result of specific diseases affecting the speech apparatus (for example, cleft palate or upper motor neuron lesions) and produce distinctive patterns of abnormality depending on the nature and location of the physical disorder. For the other disorders, there is no direct correspondence between the aetiology and the nature and prognosis of the child's language deficits. As there is so little existing information on language disorders associated with severe malaria, any of these categories could, theoretically, be relevant to the current situation but impairments may be hypothesised to fall into categories three or four. In consequence, the medical model, as used in its traditional sense, would not provide the necessary information to construct a valid theoretical framework for the speech and language assessments.

9.3.2 The behavioural model

The behavioural model originates in the linguistic and psychological sciences. A simple linguistic model of language disorders makes a primary distinction between language structure and language use and is useful when patients have particular difficulties with a single aspect of language structure. Language structure is divided into three main components: phonology, grammar and semantics (figure 9.2). Phonology is divided into segmental and non-segmental aspects, the former relating to the particular phonemes (or segments) of a language and the latter describing vocal tone, pitch, loudness, timbre and speed. Grammar is divided into the structure of words (morphology) and the structure of sentences (syntax). Semantics describes word meanings and meaning relationships between words, such as antonyms and synonyms. Semantics also relates to aspects of meaning such as double meanings. Pragmatics spans both language structure and use, reflecting the fact that the choice of language structure is mediated by the context and the use to which it will be put. Figure 9.2 shows a schematised representation of the main branches of linguistic analysis.

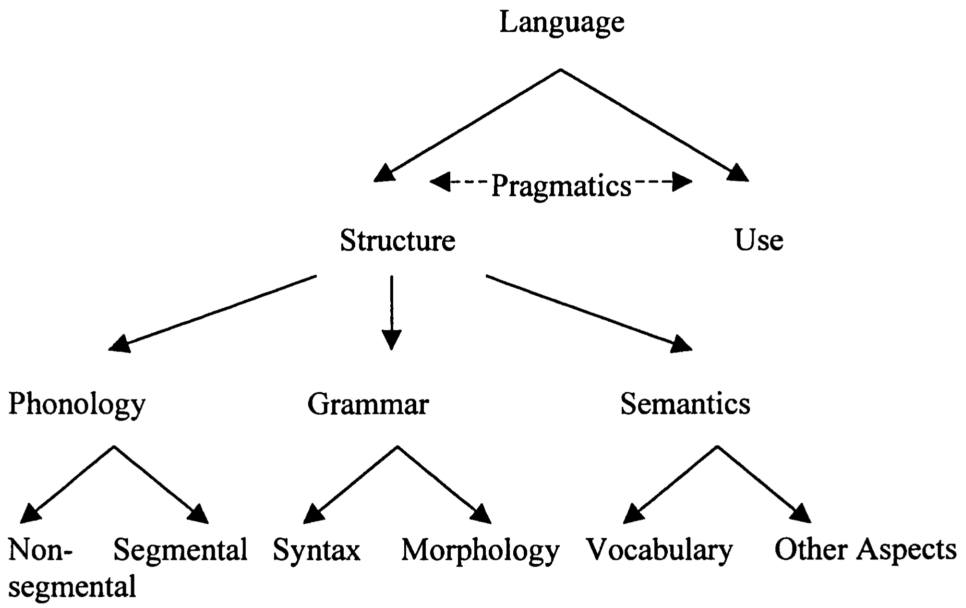

Figure 9. 2: The main branches of linguistic analysis, adapted from Crystal and Varley (1998)

A detailed version of the behavioural or linguistic model based on observations of normal language development was proposed by Bloom and Lahey (1978) and is described in the following section.

9.4 Content, form and use model

This model was first developed by Bloom and Lahey (1978) and further described by Lahey (1988). The Content, Form and Use (C/F/U) model is primarily a language production approach based on the study of normal language development in North American children. Language is seen as involving interactions between its meaning (content), shape (form) and function (use): the C/F/U plan is a hypothesis about the sequence in which these interactions can best be learned through intervention.

The content or semantics of language comprises topics and content. Content – the general categories that children talk about, for example animals – remains constant across cultures. Topics, however, vary across cultures and age – an urban English child may talk about hamsters whereas a rural Kenyan child may talk about chickens – so that vocabularies are different. Lahey (1988) discusses three categories of content: objects, relations between objects and relations between events. In the category of objects, there are particular objects and classes of objects. Relations between objects may reflect the relation of the object with itself (for example, existence) or with other objects (for example, attributes such as relative size) or the way that objects from different classes interrelate (for example, possession). Similarly, relations between events may reflect relations within a single event (for example, when the event occurred) or relations between events (for example, causal relations). The model is schematised in figure 9.3.

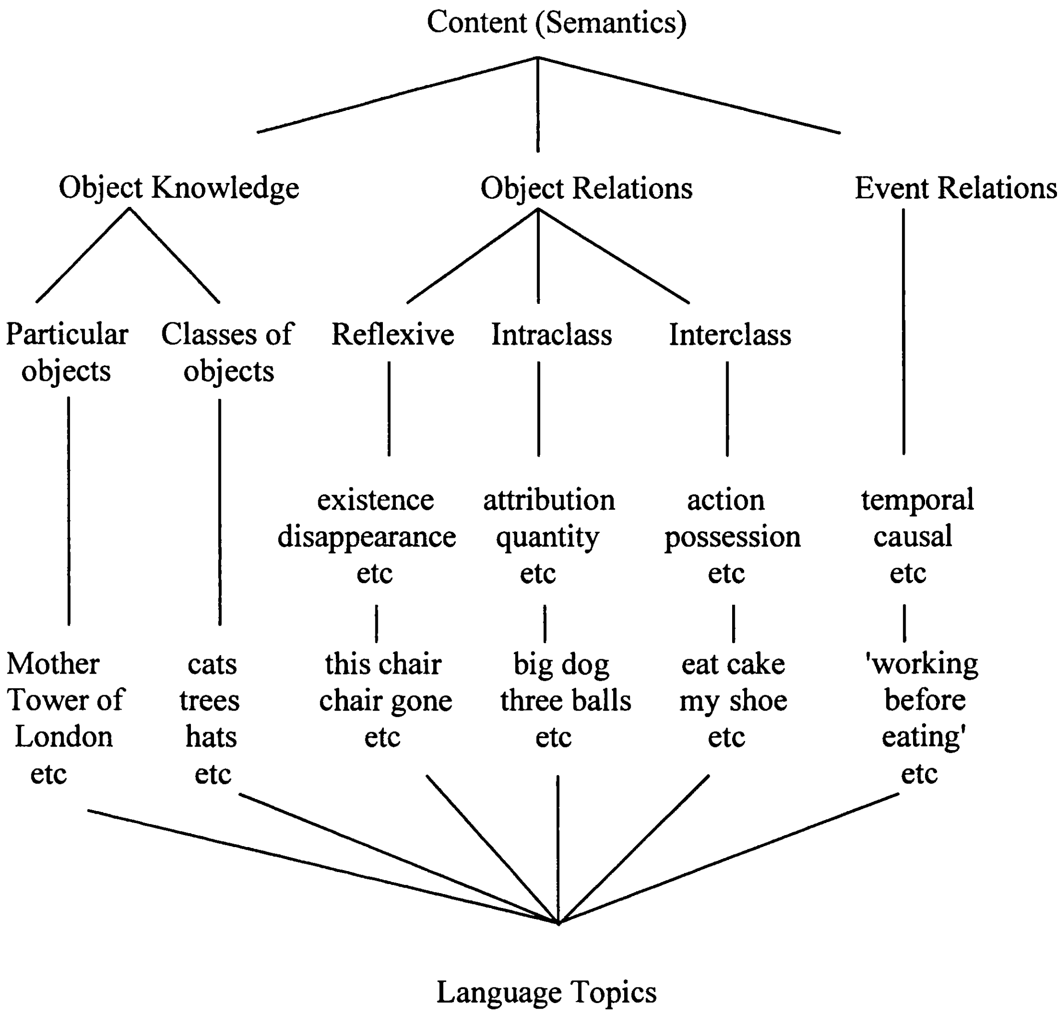

Figure 9. 3: Language content and topics, adapted from Lahey (1988)

Language form is divided into three broad categories: phonology, morphology and syntax, each of which contribute to the grammar, or underlying rule system of a language, and which represent a categorisation of the superficial forms of (spoken) language. As in the behavioural model, phonology is divided into segmental and non-segmental, referred to here as suprasegmental, aspects. The C/F/U model elaborates the category of morphology to divide words into 'content words', the nouns, verbs, adjectives and adverbs that carry meaning, and 'function words', the prepositions, articles, conjunctions and pronouns that link the content words. Content words can be further classified as substantive words, or objects, and relational words, verbs and adjectives. In English, morphological inflections are bound to content words: for instance, the morpheme '-s' indicates plurality, possession or habitual actions. Syntax, the arrangement of words in a sentence according to the meaning relations among them, can be described in terms of linear relations or hierarchical relations. A linear structural relationship reflects an arrangement in which the addition of new words does not alter the meaning of the sentence. In contrast, a hierarchical structural relationship results in a superordinate meaning in comparison to the individual meanings of the separate words. For instance, when the noun 'ball' is combined with the noun 'mother' to produce 'mother's ball', the superordinate meaning is possession, which is separate from the meaning of the individual words. Syntax is dependent on both function words and morphological inflections. The aspects of language form are schematised in figure 9.4:

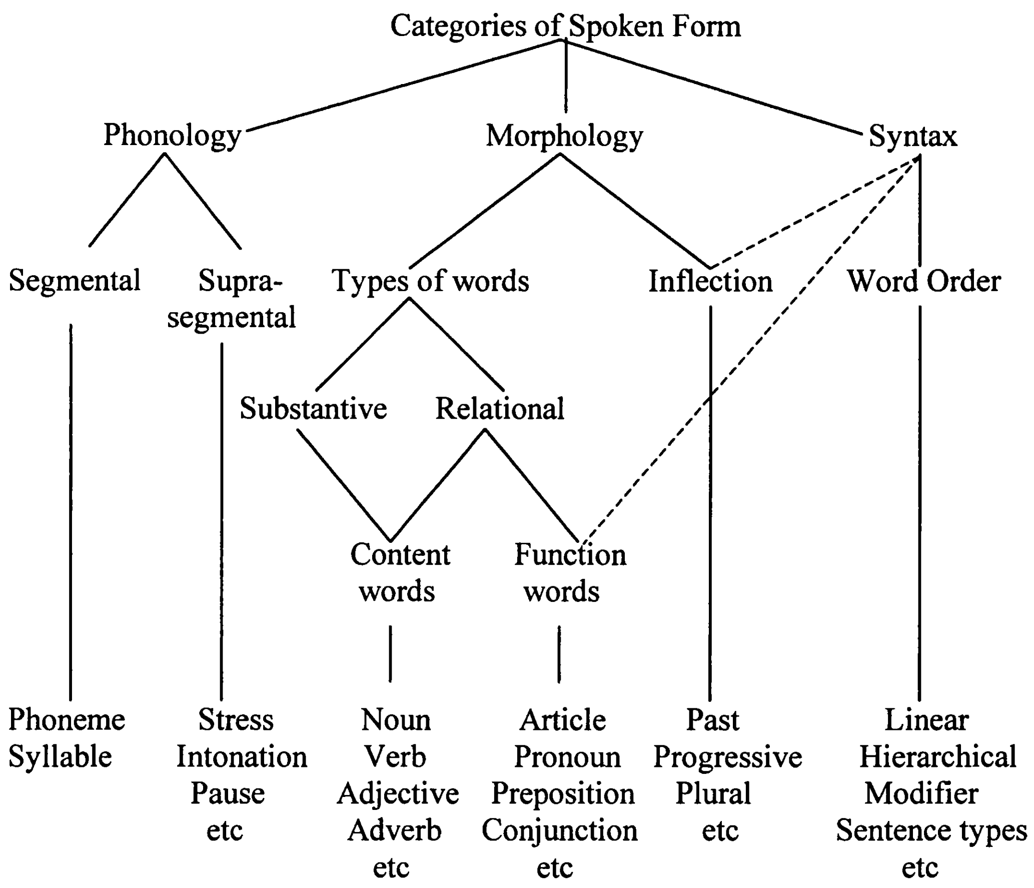

Figure 9. 4: Categories of spoken language form, adapted from Lahey (1988)

Language use or pragmatics can be separated into language functions and language contexts. The functions of language can be described in reference to personal and social goals. Personal goals, also called intrapersonal or mathetic functions, denote the use of language to achieve goals not involving other people, for example solving a problem or making a comment to oneself. Social goals, also called interpersonal or pragmatic functions, refer to language use to achieve socially-mediated objectives such as obtaining information or gaining another person's attention. The second aspect of language use describes the contexts and rules a speaker uses to decide which form of the message will best serve its function. This involves non-linguistic and linguistic contexts, the former referring to situational cues, the skills of adapting to the needs of the listener and various conversational devices and the latter describing the relationship of the message to what has been said before. Non-contingent messages introduce a new topic of conversation whereas contingent messages relate to prior utterances, creating a sequence on the same topic. Aspects of language use are schematised in figure 9.5.

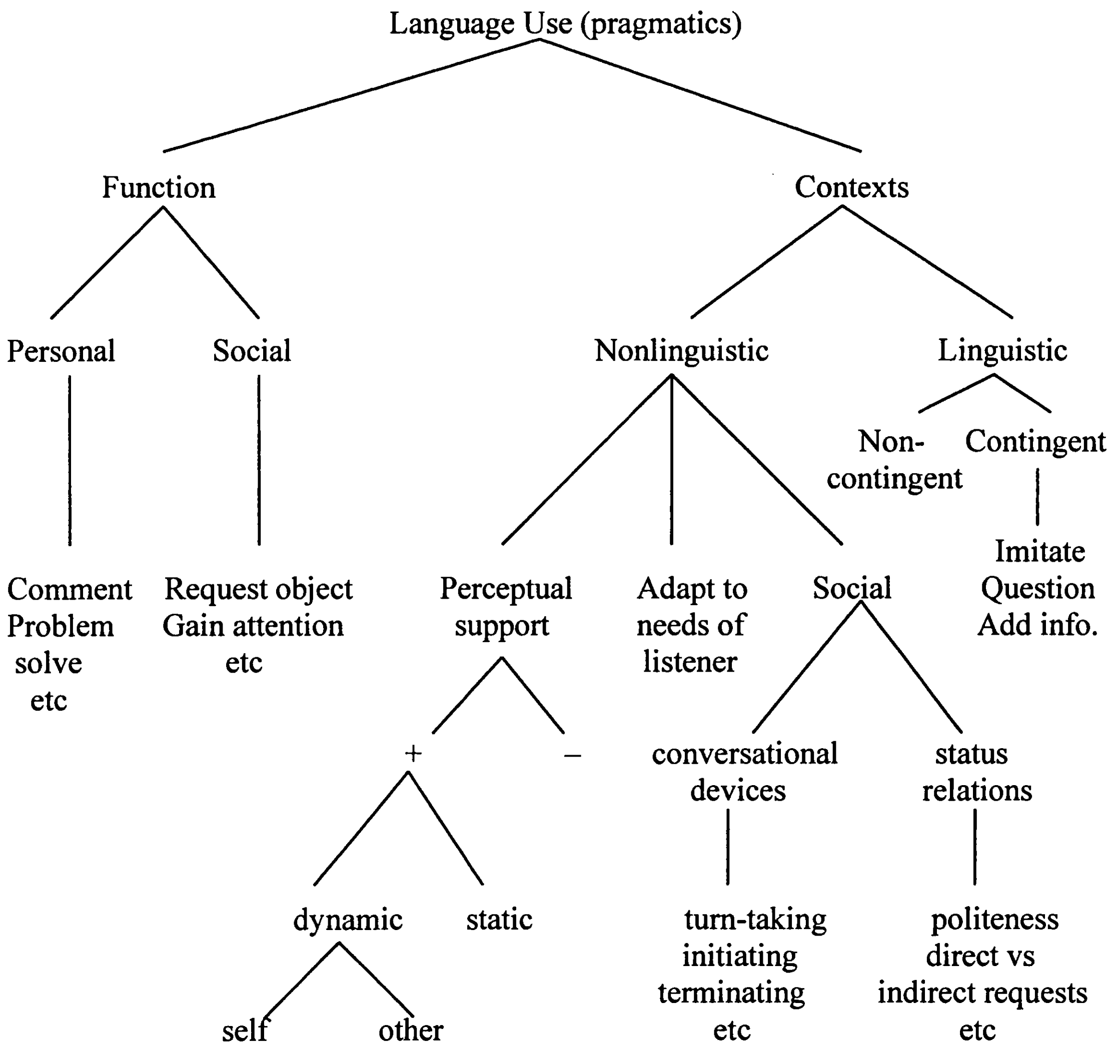

Figure 9. 5: Language Use, adapted from Lahey (1988)

9.5 Correlating medical and behavioural models

9.5.1 Bishop/Rosenbloom model

Bishop and Rosenbloom (1987) consider the medical and behavioural approaches to classification to be complementary and describe a two-way classification of language disorders (table 9.4). The combination of the two approaches is particularly pertinent to the current context: although there is little information on the linguistic background to potential speech and language disorders associated with malaria, some information exists on the integrity of the neuroanatomical system supporting speech and language.

Malaria often occurs after the child has started to develop spoken language, thus may fall under the medical category of brain damage or dysfunction acquired in childhood. Cerebral malaria is a diffuse encephalopathy, which may hypothetically result in bilateral lesions to the language areas, resulting in impairments to receptive and expressive language according to this model. The involvement of the brain in other severe forms of malaria such as malaria with complicated seizures is less clear, although evidence from the effects of similar seizures in other situations (section 3.6.3) suggests that the potential damage is more localised. A lesion in the left hemisphere may have age-dependent consequences due to the plasticity of functional organisation in the developing brain (section 9.2.1). Children acquiring lesions later in childhood are less likely to recover if they develop aphasic symptoms (Woods and Carey, 1979). In infants, such damage may depress general intelligence rather than causing specific impairments in language (Bishop and Rosenbloom, 1987), although more recent evidence suggests that language impairments may occur, even in children who acquired lesions before 6 months of age (Bates, et al., 1997).

In the only previous study to have reported speech and language findings following severe malaria in some detail, Holding and colleagues (1999) found particular deficits in syntax and articulation. Their category of 'articulation' problems is likely to refer to phonological deficits, as there is no evidence cited of structural abnormalities or physiological inco-ordination of the articulators. This combination of deficits corresponds to the category of specific problems with syntax and phonology, which is linked to left hemisphere lesions.

Medical / **Behavioural**	**Structural or sensorimotor defect of speech apparatus**	**Hearing loss**	**Brain damage or dysfunction acquired pre/ perinatally**	**Brain damage or dysfunction acquired in childhood**	**Emotional/ behavioural disorders**	**Environmental deprivation**	**Aetiology unclear**
Speech limited in quality and/ or quantity but other language skills normal	Dysphonia; dysarthria	Deafness acquired after language developed			Elective mutism		Stuttering; 'developmental apraxia of speech'
Generalised delay of language development		?With chronic conductive hearing loss	Common with most types of learning difficulties			Result of neglect	?Delayed language
Specific problems with syntax and phonology		?Particularly with selective high frequency loss		With left hemisphere lesions in older children			Phonologic-syntactic syndrome
Specific problems with semantics and pragmatics			Cocktail-party syndrome; infantile autism (mild)				Semantic-pragmatic disorder
Poor understanding and limited verbal expression		With severe of profound prelingual deafness	Severe learning difficulties	With bilateral lesions of language areas; LKS			Congenital auditory imperception
Severe impairment of non-verbal/verbal communication			Severe learning difficulties; infantile autism	Ultimate outcome of degenerative disorders			

Table 9. 4: Two-way classification of childhood language disorders, from Bishop and Rosenbloom (1987)

9.5.2 Information processing models

A simple information processing model can be reduced to three main components: production, transmission and reception. Feedback and feedforward act as control mechanisms: feedback allows ongoing monitoring of motor activity and listener reactions from the sensory information generated at each stage and feedforward allows comparison between incoming information and the established pattern so that errors can be anticipated prior to output.

The essential characteristics of the medical and behavioural models are encapsulated in a model such as the 'communication chain' or 'speech chain' (Crystal and Varley, 1998; Gardner, 1997), which presents a series of behavioural processes along with a description of the physical bases underlying those processes (figure 9.6). The impairments resulting from disruptions at each stage are also listed (categories of disorder in italics and specific disorders in regular font), although they are not isolated to that particular level. Some disorders disrupt multiple stages of the communication chain and others may primarily affect one stage but have a secondary impact on other stages.

Stage		
Pre-linguistic stage ⇩	*Cognitive disorders*:	Thought disorders Autism Learning difficulty
Language encoding ⇩	*Language disorders*:	Aphasia Developmental language disorders
Motor programming ⇩ (Feedback systems)		Apraxia
Motor execution ⇩		Dysarthria
	Disorders of voice *Disorders of fluency* *Disorders of articulation*	
Transmission ⇩		
Reception ⇩		Hearing impairment
Perception/Recognition ⇩		Agnosia
Language decoding ⇩	*Language disorders*:	Aphasia Developmental language disorders
Message interpretation	*Cognitive disorders*:	Thought disorders Autism Learning difficulty

Figure 9. 6: Stages and disruptions within the communication chain, adapted from Crystal and Varley (1998)

There is no direct anatomical correlation between the language centres of the brain and the stages described in a model. However, the small body of literature on neurological and cognitive impairments following cerebral malaria in children may provide some indication of the stages of the communication chain that may be disrupted by malaria. A detailed review of these studies can be found in Chapter Two: the pertinent points raised by their findings will be discussed below.

The mechanisms of action for CM (section 2.3.2) indicate global and diffuse involvement of the CNS, suggesting that neurological impairments are likely to be widespread, diffuse and difficult to characterise (Newton and Krishna, 1998). As discussed above, malaria with complicated seizures may result in a more localised pattern of damage.

Although cognition is not entirely separable from language, disruptions at the pre-linguistic and message interpretation stages indicate broad deficits across a range of cognitive and other abilities that extend beyond language. Previous studies have cited learning difficulties (Meremikwu, et al., 1997), memory impairment (Bondi, 1992) and developmental regression (van Hensbroek, et al., 1997) following CM. In addition, (Brewster, et al., 1990) suggests that intellectual impairment is a probable consequence of CM. Studies that have specifically investigated elements of cognitive and neuropsychological functioning following severe malaria have consistently reported deficits in attentional capacity (Boivin, in press; Holding, et al., 1999), visual-spatial processing (Boivin, in press), aspects of memory (Boivin, in press; Dugbartey, et al., 1998), executive functioning (Boivin, in press; Holding, et al., 1999) and somatosensory discrimination deficits (Dugbartey, et al., 1998).

Disorders of language encoding and/or decoding may have a cognitive underpinning but one which has more discrete consequences than disorders in the previous category. Disorders at this level are particularly heterogeneous and may involve different levels of language organisation. The archetypal acquired disorder is aphasia, which is the most commonly-reported neuro-cognitive deficit in short-term studies of CM (Bondi, 1992; Brewster, et al., 1990; Carme, et al., 1994; Meremikwu, et al., 1997). Aphasia is also reported in studies of persisting deficits (van Hensbroek, et al., 1997). None of these studies describe the aphasic symptoms presented by the affected children.

There has been no evidence in previous studies of disorders of motor programming and little evidence of disorders of motor execution. Van Hensbroek and colleagues (1997) report cases of dysarthria, although their report is unclear on the actual nature of the disorder as they state that 'cases of aphasia resolved to the level of dysarthria' (p128), which is not indicative of neuromuscular damage. Similarly, disruptions at the levels of reception, perception and recognition have rarely been reported. Hearing loss was reported by van Hensbroek and colleagues (1997), although they give no information on whether it was conductive or sensori-neural. There is no pathological evidence of damage to the cochlea or the VIII nerve as a result of malaria.

9.6 Summary

Ellis and Young (1996) comment that one of the original purposes of syndrome-based models was to assist in the determination of probable lesion sites in the days before more direct scanning techniques became available. They comment that traditional frameworks for the categorisation of speech and language disorders are too coarse-grained. Indeed, in terms of language acquisition, different facets of language are highly interdependent and later language function is more integrated than the models proposed in this chapter would suggest (Bates, 1997). However, such a 'coarse' approach is necessary in the context of a study that is measuring a behaviour about which we know little in the ordered or disordered population.

The C/F/U model provides a broad classificatory framework, which encompasses the universal aspects of language content, form and use. As the model was developed in the context of a large body of knowledge on normal language development in groups of English-speaking children, it is not possible to reproduce the same level of detail in Kigiryama, which has not been studied in terms of acquisition or structure to any depth. Therefore, a framework was constructed which draws upon the major domains of the behavioural and C/F/U models but maintains a structure that reflects the current level of knowledge of the language (figure 9.7).

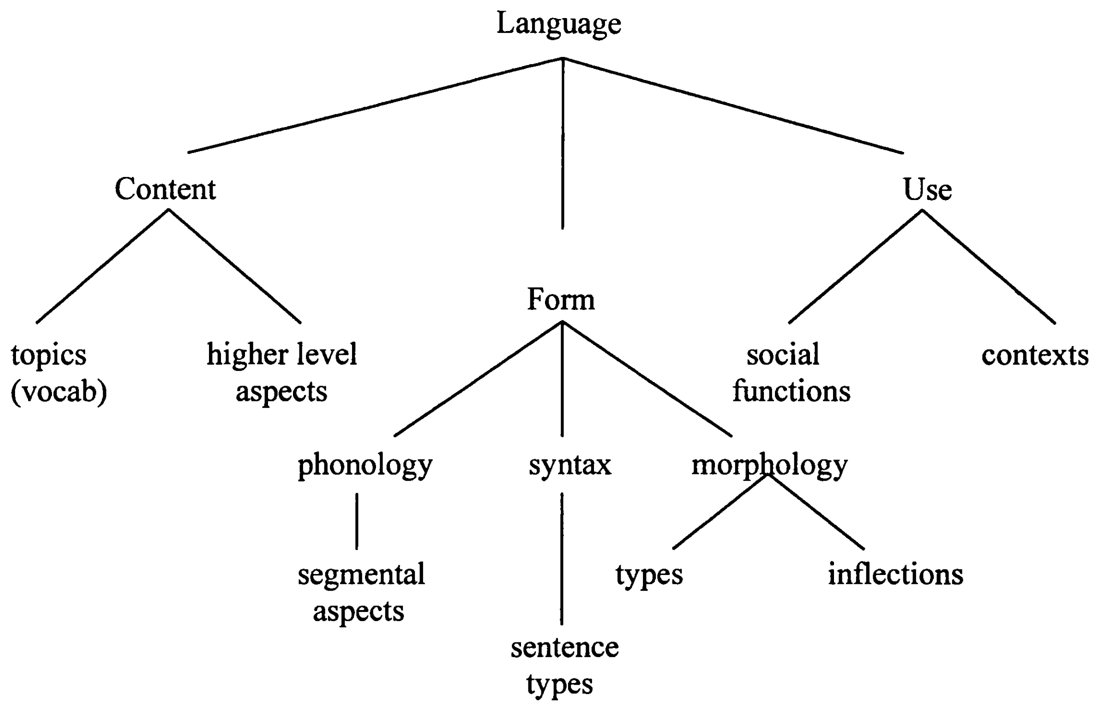

Figure 9. 7: Theoretical framework for the speech and language battery

Chapter Ten: Development and Piloting of the Speech and Language Assessment Battery

10.1 Introduction

This chapter will address issues concerning the development, initial validation and piloting of the speech and language assessment battery. Validity is concerned with the question of whether a test measures what it was designed to measure: it is a multi-step process with various procedures implemented at different stages of test construction and use. Estimates of validity are not inherent in the assessment instrument but are conditional and depend upon the context of assessment, population, response modes and goals of the study (Haynes, et al., 1999; Haynes, et al., 1995).

The chapter will commence with a discussion of different validation procedures but the greater part of the chapter will concentrate on content validation techniques. A framework for using these techniques in test construction and adaptation will be presented and used to describe the initial stages of development of the speech and language assessment tools. Finally, a pilot study, which aimed to examine the cultural validity of the tools, their suitability for children in this context and discriminatory ability will be described. Conclusions from this preliminary investigation into the presence of persisting speech and language impairments in children with a history of severe malaria will be discussed. Assessment refinement in the light of these findings will be described in Chapter Eleven.

10.2 Validation issues

The three types of validation generally employed in measuring the psychometric properties of an assessment are criterion-related, content and construct validity, although the current view is that all three are components of construct validity. Criterion-related and content validity will be discussed below. Construct validity will be considered in Chapter Eleven.

10.2.1 Criterion-related validity

Validity is most powerfully estimated through criterion-related validity – covariance with previously validated or 'gold standard' measures of the same construct (Haynes, et al., 1999). Criterion measures vary according to the specific uses of the assessment. Commonly-used criteria in the validation of cognitive tests are previously validated tests, academic achievement or schoolteacher ratings (Anastasi and Urbina, 1997).

In the Kenyan context, none of these criteria were applicable. There were no validated assessments of speech and language in Kigiryama. Academic achievement or schoolteacher ratings were not considered to be an appropriate means of validation for a number of reasons. School attainment may be influenced by factors other than the child's cognitive abilities, such as the quality of teaching, the availability of teaching materials and the presence of a class environment conducive to learning (Connolly, 1998). Performance at school is also influenced by other phenomena, which may have an interactive effect with neuropsychological functioning. For example, a child with left-hemisphere-related impairments may experience more difficulty as he/she progresses in school, whereas a child with impairments related to right-hemisphere functioning may appear to outgrow difficulties experienced in the early school years (Hartlage and Templer, 1996). In addition, there are issues specific to the coastal Kenyan situation. First, many Giryama children do not attend school and there is evidence to suggest that those with CM may be less likely to attend (see section 12.3). Secondly, class numbers are much larger than in the UK, so schoolteachers may not have the opportunity to observe and accurately rate individual children. Due to these limitations, other methods of validation were employed and are described in the following sections.

10.2.2 Content validity

Content validity is the degree to which the elements of an assessment battery are relevant to and representative of the targeted construct and is, in that sense, a component of construct validity (Haynes, et al., 1995). Haynes and colleagues (1999) describe the concepts of relevance and representativeness of an assessment instrument as central aspects of content validity. Relevance is defined as how appropriate the elements of an assessment are for measuring the targeted construct.

Representativeness is described as the balance of elements to proportionately sample the facets of the construct.

The construct validity of an assessment instrument is limited by the degree to which its elements were initially designed to measure the targeted construct (Haynes, et al., 1999), thus making the content validation or developmental phase of assessment design particularly important. This phase of assessment development and the application of content validation techniques will be described in the next section.

10.3 Development of the speech and language assessments: initial instrument development

There were no pre-existing, standardised assessments of speech and language in Kigiryama, therefore new instruments had to be developed according to the parameters outlined in Chapter Six and the framework discussed in the previous chapter.

The procedure for content validation in assessment development and refinement was based on processes designed for the construction of novel assessment instruments (Clark and Watson, 1995; Haynes, et al., 1995; Smith and McCarthy, 1995; Streiner and Norman, 1995). The current assessments were derived from tools specifically designed for the rural Kenyan context, validated instruments in common use in the UK or used assessment methods routinely in use in the UK, therefore the procedures used in assessment development were modified to reflect this (table 10.1). Stage one – initial instrument development – will be discussed in this chapter and stage two – instrument refinement – will be considered in Chapter Eleven.

STAGE 1	
1	Conception of target construct (Clark and Watson, 1995; Haynes, et al., 1995)
2	Literature review (Clark and Watson, 1995)
3	Creation of item pool (Clark and Watson, 1995; Haynes, et al., 1995; Streiner and Norman, 1995)
4	Matching items to facets and dimensions (Haynes, et al., 1995; Streiner and Norman, 1995)
5	Examination of item structure and face validity (Haynes, et al., 1995; Streiner and Norman, 1995)
6	Establishment of quantitative parameters (Haynes, et al., 1995)
7	Development of instructions (Haynes, et al., 1995)
STAGE 2	
8	Instrument refinement (Clark and Watson, 1995; Smith and McCarthy, 1995; Streiner and Norman, 1995)

Table 10. 1: Procedures for instrument development and refinement

10.3.1 Conception of target construct

Defining the scope or generality of the target construct is important in ensuring that the resulting instruments are embedded in a theoretical framework. Based on the framework outlined in section 9.6, the target constructs of the assessment battery are depicted in figure 10.1.

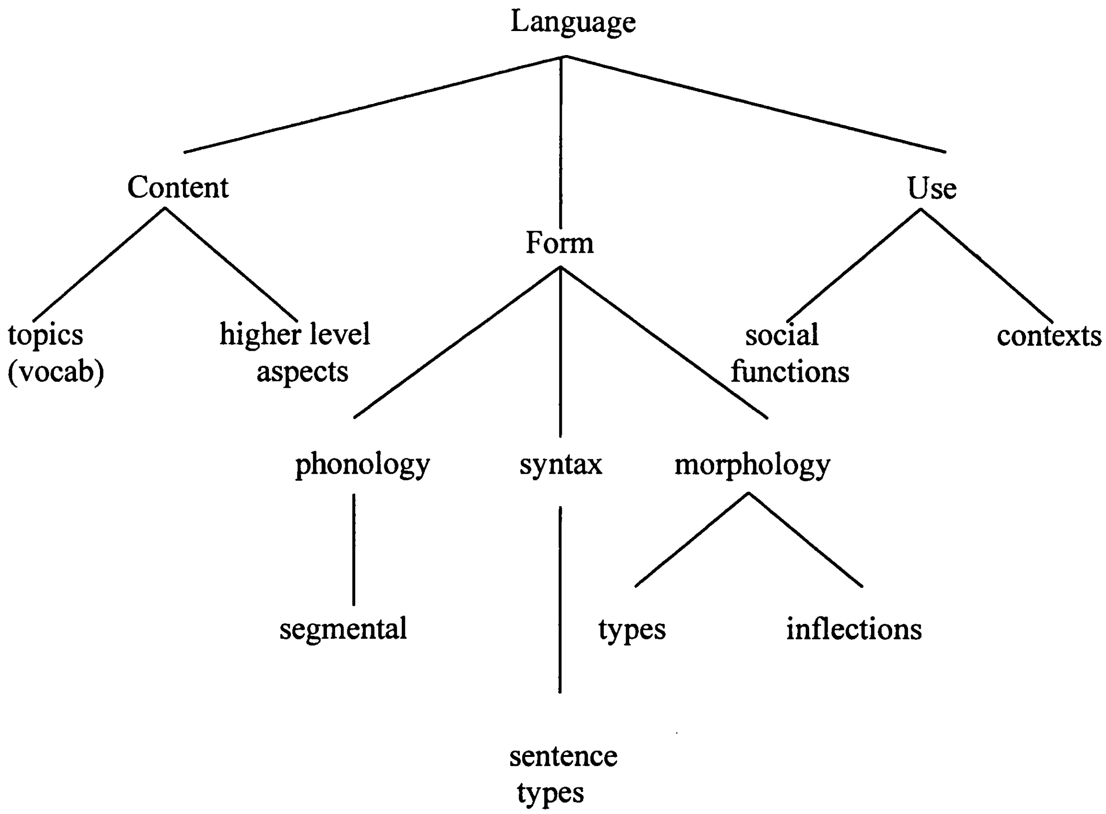

Figure 10. 1: Target constructs of the speech and language assessment battery

10.3.2 Literature review

Clark and Watson (1995) state that reviewing the literature aids the test developer by illustrating how other researchers have approached similar problems. In addition, a review clarifies the nature and range of the content of the construct, may help to identify problems with existing measures and indicates whether a new instrument is actually needed. Coastal Kenya has few language assessment resources so the literature pertaining to relevant assessment models and techniques was drawn from the general African, European and North American literature. The nature and range of the target construct was reviewed in Chapter Nine. The literature reviews in Chapters Four and Six highlight the reasons why existing instruments in their original form are problematic in this context and why new or adapted assessment instruments were necessary for this study.

10.3.3 Creation of item pool

The creation of the item pool is an essential component of content validation since psychometric analysis cannot compensate for missing aspects of the target construct (Streiner and Norman, 1995). Clark and Watson (1995) state that the two key aspects of the initial item pool are that (i) it should be more comprehensive than the designer's theoretical view of the target construct and (ii) it should include items that will eventually be shown to be tangential to the construct.

Sources of item generation are listed by Haynes and colleagues (1995) and Streiner and Norman (1995) as:

- rational deduction
- clinical experience and observation
- theories relevant to the construct
- other assessment instruments with demonstrated validity
- expert opinion
- focus groups or key informants from the target population

The primary source of assessment structure for this battery was from existing assessment instruments, mostly UK-based instruments but also two designed for a previous studying examining cognitive impairments following malaria in the same area (Holding, et al., 1999). Although the content of the Kenyan assessments was maintained, the content and materials of the UK assessments had to be altered to make them culturally-valid. Sources of item content were expert opinion and key informants from the target population. The origins of and alterations to each assessment are discussed below.

10.3.3.1 Receptive language

Measures of receptive language were amalgamated into one assessment (Appendix 10) based on a test of receptive vocabulary used in a previous study in the same area (Holding, et al., 1999). This assessment was developed in another Kenyan study to investigate the relationship between cognitive abilities and nutrition, family characteristics and educational experience (Sigman, et al., 1991; Sigman, et al., 1989) and was based on the Peabody Picture Vocabulary Test (Dunn and Dunn, 1981). The test consisted of 40 items ranging from common nouns to more abstract words, each stimulus word being accompanied by a selection of four black and white drawings, from which the child selects the correct one by pointing. Test validity was measured against school examination scores, which yielded a significant correlation ($r = 0.56$, $p < 0.0001$). For Holding and colleagues' study, the items were translated into Kigiryama and some of the picture stimuli were altered (for example, the house shapes) to make them more appropriate for the target population.

For the current study, items that had proved to be problematic during Holding and colleagues' study were removed to leave 23 items. In addition, more complex measures of receptive language were included. Based upon the facets of the theoretical framework (form, content and use), a measure of syntax - understanding of simple and complex commands – was also included in the final score. The content of these items was devised with the assessors.

10.3.3.2 Syntax

A measure of expressive grammar (Appendix 11) was based on the format of the South Tyneside Assessment of Syntactic Structures (STASS) (Armstrong and Ainley, 1989). The STASS was designed as a rapid measure of expressive language at the grammatical level based on the Language Assessment Remediation and Screening Procedure (LARSP) (Crystal, et al., 1976) and more specifically, an elicited LARSP developed in South Tyneside. The test is designed for use with children up to the age of 7 years and consists of a series of 32 pictures, each one presented to the child to elicit one or more grammatical structures. The child's responses are recorded verbatim to be analysed later by the assessor for the word, clause and phrase level structures defined in the LARSP and auxiliary verbs, pronouns and prepositions.

The state of knowledge of the grammar of the Kigiryama language is not yet sufficient to permit the level of analysis in the original STASS (section 7.3.1). In consequence, although the structure and format of this assessment were maintained, the content and grammatical elements targeted were revised. To determine the particular elements that would be appropriate to local children in the age group targeted, a series of meetings was held with a local schoolteacher. His suggestions were supplemented by elements decided upon by rational deduction of the hypothesised level of syntactic development in Giryama children of 6-9 years of age, knowledge of the language and comments from the assessors. The elements targeted in the assessment were prepositions, plurals, conjunctions, comparatives, adverbs, adjectives, past tense, locatives, negatives, WH-questions ('where', 'who'), passives and future tense. Pictures were drawn by the candidate according to the style of the STASS, one picture per question with a total of 20 questions. Although the assessment tested expressive syntax and morphology, the title was abbreviated to 'syntax assessment'.

10.3.3.3 Lexical semantics

The measure of expressive vocabulary (Appendix 18) was based on the Profile in Semantics – Lexicon (PRISM-L) (Crystal, 1992), a naturalistic method of assessing vocabulary size and breadth from the child's spontaneous language. Due to children's lack of familiarity with testing situations and test materials (section 6.4), it was important to attempt to reduce the number of formal, picture-based tasks. In view of the knowledge limitations of the form and structure of Kigiryama discussed above and the difficulty of assessing receptive abilities in a more naturalistic format, expressive vocabulary was considered to be one of the assessments most amenable to this style of testing.

The PRISM-L is intended as a profile rather than an assessment. Utterances from a spontaneous language sample are transcribed and classified by semantic category (referred to as 'major' or content words) or grammatical usage ('minor' or functional words). The types - the total number of *different* words the child has said – are divided by the tokens - the total number of words the child has spoken – to calculate the 'type-token ratio' for minor and major words.

The format of the profile was maintained for the current study, although the function words sections were altered to reflect the different grammatical categories in Kigiryama and the tool was referred to as an 'assessment'. Three methods were used to generate spontaneous language production: picture description, conversation and storytelling. A picture book depicting various animals was used for picture description and the spontaneous language session was recorded using a dictaphone for later transcription.

10.3.3.4 Higher level language

According to the theoretical framework presented in section 10.3.1, there are aspects of semantics other than vocabulary that need to be considered as part of a comprehensive assessment of language. Higher level language can be described as the level at which the basic aspects of language integrate and interact. The persistence of impairments in this aspect of language has been shown to be an indication of poor prognosis in acquired childhood aphasia (ACA) (Lees, 1997). In addition, assessments of more complex language usage can be useful in identifying subtle language deficits and have been used in the evaluation of residual deficits following ACA (Cooper and Flowers, 1987; Crosson, 1996).

As it was difficult to know the types of questions that would be sensitive and applicable to Giryama language and culture, a wide variety of question types was identified from a range of standardised and non-standardised assessments for a higher level language assessment (Appendix 12). Semantic tasks such as word associations, word classes and formulated sentences from the Clinical Evaluation of Language Fundamentals – Revised (CELF-R) (Semel, et al., 1987) were adapted for use in a Giryama context. In addition, discussions with a local schoolteacher and the assessors generated questions testing synonyms, homonyms, similarities and differences, antonyms, word definitions, figurative language, convergent and divergent semantic tasks and a range of inferential reasoning and problem solving questions.

10.3.3.5 Pragmatics

The assessment of pragmatics (Appendix 13) was divided into three parts. The measure of language use adopted in Holding and colleagues' (1999) study comprised the first part. This approach was chosen because it had been used successfully in the same area and the data could be collected from the same sample of spontaneous speech used for the lexical semantics assessment, thus reducing the number of formal assessments the child had to undertake. The method was an analysis of functional errors taken from a study of Spanish/English bilingual speakers (Damico, et al., 1983). Damico and colleagues found that functional criteria were more successful in the identification of language disorders in children with a mean age of 6 years 11 months and had greater predictive validity for academic achievement compared to 'surface-oriented criteria' (syntactic criteria) judged by the "...grammatical intuitions of native speakers with training in linguistics and clinical experience in speech-language pathology" (p387). The analysis comprised the identification of linguistic nonfluencies, revisions, delayed responses, nonspecific vocabulary, inappropriate responses, poor topic maintenance and need for repetition from a spontaneous language sample.

An observational component formed the second part of the assessment, the content of which was decided by reference to clinical experience and elements of pragmatic theory (Andersen-Wood and Smith, 1997). Discussions were held with a local schoolteacher on cultural norms: Payne and Taylor (2002) comment that culture affects conversational and discourse rules. The candidate observed the child during the assessment session for evidence of the following skills: appropriate physical proximity to the communicative partner; appropriate eye contact; appropriate facial expression; appropriate amount of presupposition; not easily distracted; use of language appropriate to the situation and people present and amount of language. Each skill observed was awarded a score of '1'.

The final part of the assessment comprised a parental questionnaire to investigate the child's range of communicative intents. The initial list was drawn from Lees and Urwin (1997) and Andersen-Wood and Smith (1997) and supplemented by ideas from a local schoolteacher and members of the assessment team.

10.3.3.6 Phonology

The test of phonology (Appendix 14) aimed to assess the integrity of the child's phonological system. As discussed in section 10.3.3.3, where possible, the use of formal, picture-based tasks was minimised: phonology was considered amenable to a more naturalistic style of testing. The first one hundred different words from the child's recorded spontaneous language sample were transcribed and profiled by the candidate using the International Phonetic Alphabet on a chart of all the consonant phonemes used in Kigiryama. The language has no word or syllable final consonant phonemes; word initial and word medial (syllable initial) phonemes were assessed separately. A phoneme was assessed as 'correct' if the child produced it correctly in all words in which it featured in either the initial or medial position.

10.3.4 Matching items to facets and dimensions

Table 10.2 matches the assessments in the speech and language battery to the dimensions and constructs depicted in figure 10.1 to illustrate that all the target constructs are included in the battery.

Domain	Construct	Assessment
Content	Topics (Vocabulary)	Lexical semantics
	Higher level aspects	Higher level language
Form	Phonology	Phonological
	Syntax	Syntax
	Morphology	
Use	Social functions	Parental questionnaire
	Contexts	Observation Analysis of functional errors

Table 10. 2: Items and constructs in the speech and language assessment battery

10.3.5 Examination of item structure and face validity

The structure of the battery was examined in two ways: first, as a component of content validation and secondly to measure the face validity of the assessments. Each item in the assessment battery was examined by the candidate and assessor with reference to the appropriateness for each facet of the target construct. Secondly, the interpretability of the items was examined, focussing on their clarity and specificity. Streiner and Norman (1995) comment that ambiguity, double-barrelled questions (items asking two or more questions at the same time), jargon and lengthy questions may reduce the interpretability of test items. Each item was reviewed by the candidate and assessors then tested on a sample of ten children (siblings of children waiting in the out-patient department of Kilifi District Hospital) of the same age (9 years) as the target population. The children's responses indicated that the items were comprehensible and unambiguous.

Face validity is a surface examination of the instrument by an untrained observer to determine whether the language and context of test items would *appear* valid to the target population. Golden and colleagues (1990) state that the importance of face validity lies in the fact that it is the "...characteristic through which the subject receives an impression of what the test is measuring" (p.33). The participants' perceptions of the test's difficulty or appropriateness will affect their level of co-operation and the acceptance of the instrument (Streiner and Norman, 1995). The applicability and usefulness of measures of face validity in psychometric evaluation is controversial: some authors argue that such superficial judgements are irrelevant or ambiguous (Anghoff, 1988). However, it may be considered important in a context in which there is a paucity of developmental assessments and an unfamiliarity amongst prospective participants with testing procedures and situations. Accordingly, a local schoolteacher and several members of unit staff working on unrelated projects were asked to rate battery items for face validity. Minor modifications to the language were suggested before the face validity of the assessments was considered to be acceptable.

10.3.6 Establishment of quantitative parameters

When the study assessments were based upon existing instruments, the response formats were maintained. The format of the receptive language, syntax and higher level language assessments was question and answer. A simple 1/0 scoring scheme was employed in each assessment. The lexical semantics, phonology and section one of the pragmatics assessments were based on the profiling and analysis of a recorded sample of spontaneous speech comprising conversation, picture description and storytelling (a traditional activity in this area). Sections two and three of the pragmatics assessment were based on observation of the child's behaviours and a question and answer format with the parent respectively.

10.3.7 Development of instructions and test procedure

Instructions for each assessment were developed by the candidate and assessor. The test procedure was designed by the candidate and assessor with input from a local schoolteacher and other workers at the unit with field-based experience. The test procedure for the main study was outlined in section 8.8.

10.4 Pilot study

The aim of the pilot study was twofold. First, to pilot the tools whose development was described in this chapter, with the particular objectives of establishing their cultural validity and suitability for children in this context and collecting data to examine their discriminatory ability, using the measures of item difficulty and response distributions discussed in Chapter Eleven. Second, although long-term studies of impairments associated with malaria suggest that speech and language deficits persist (section 2.3.3), including a previous study in this geographical area (Holding, et al., 1999), there are few such reports and none that have employed instruments of the same detail as described in this chapter. Therefore, a second aim was to conduct a preliminary investigation into the presence of persisting speech and language impairments associated with severe malaria in children.

10.4.1 Materials and methods

Children were selected from a database of patients admitted to Kilifi District Hospital (KDH) with severe malaria using the following criteria: children born in 1990-1991, who lived in a clearly defined study area under demographic surveillance. Children who had been admitted to KDH with severe malaria were recruited to the study. Severe malaria included CM, defined as a deep level of unconsciousness with inability to localise a painful stimulus (Blantyre coma score of ≤ 2 for 4 or more hours), a peripheral asexual parasitaemia and exclusion of other causes of encephalopathy (Newton, et al., 2000) and severe non-cerebral malaria ('severe non-CM'), defined as parasitaemia with prostration, multiple seizures or severe anaemia but without such a reduction in level of consciousness (Marsh, et al., 1995). Twenty-five children were identified using these criteria: 13 with CM and 12 with severe non-CM.

Twenty-seven children who had not been exposed to severe malaria were recruited from the community as a comparison group. They were the same age (8-9 years) and lived in the same villages as the children exposed to severe malaria. All children were from rural homesteads and spoke Kigiryama. The two assessors were blind to each child's group status. Informed consent was obtained from the parent and child before the testing procedure. The location for the assessments was the child's home, as experience in previous studies has shown that children can be reluctant to communicate when in the hospital setting. The basic format of the session followed the main study procedure described in section 8.8. The specific order of the session was as follows: first, the child was invited to look at the picture to stimulate spontaneous speech. This was followed by conversation and storytelling with each individual child. This section was tape-recorded for later analysis. After the spontaneous speech session, the child was given a break. The order of the assessments was first the receptive language assessment, followed by the syntax assessment and finally the higher level language assessment. The candidate carried out the pragmatics observation during the play and testing sessions. Including the break, each session took about one hour.

Analysis was carried out using STATA version 6. Multiple regression was used to estimate the difference between the exposed and unexposed group scores, adjusting for age and sex.

10.4.2 Results

On discharge, eight children exposed to severe malaria were reported to have impairments, four of whom had been admitted with CM and four with severe non-CM. Two of the cases were mute, four had limited speech and language (single words) including two with visual impairment and two had motor deficits (one of whom had disordered behaviour). Seventeen children were reported to have no neurological deficits on discharge from hospital. Twenty children were assessed 5 to 6 years after admission to KDH and five, 2 to 4 years after admission. Children exposed to severe malaria had a median age of 8 years 8 months (range 8 years 3 months to 9 years 9 months). Twelve were female and 13 were male. The 27 comparison children had a median age of 8 years 11 months (range 7 years 8 months to 10 years 4 months). There were 11 females and 16 males. None had been admitted to hospital with severe malaria. All of the children were able to communicate verbally.

Children who survived severe falciparum malaria had significantly lower scores for the receptive language, syntax and both components of the lexical semantics assessments than children unexposed to the disease (table 10.3). The exposed group's mean scores were lower in the higher level language and pragmatics assessments but the difference was not statistically significant. Due to difficulties with sections two and three of the assessment (section 11.2.6), only the results from section one of the pragmatics assessment are included in table 10.3. Only two children (both from the exposed group) had minor phonological problems so this was not included in the statistical analysis.

A qualitative analysis of the language samples indicated the occurrence of word finding difficulties in 46% of the CM group, 33% of the severe non-CM group and 7% of the unexposed group. These manifested as consistent pauses and use of fillers, paraphasias and perseveration.

Assessment (maximum score)	Exposed mean (SD) n=25	Unexposed mean (SD) n=27	Est. difference exposed vs. unexposed *	95% C.I.	p-value
Receptive language (36)	30.88 (4.32)	33.52 (2.56)	-2.35	-4.36 – -0.34	0.02
Syntax (34)	18.27 (3.83)	21.35 (3.35)	-2.64	-4.91 – -0.37	0.02
Lexical semantics – function (n/a)	0.28 (0.09)	0.34 (0.08)	-0.06	-0.11 – -0.01	0.02
Lexical semantics – content (n/a)	0.54 (0.09)	0.63 (0.09)	-0.08	-0.14 – -0.03	0.004
Higher level language (31)	14.46 (4.79)	17.24 (3.89)	-2.35	-4.84 – 0.15	0.07
Pragmatics (n/a) **	4.03 (3.24)	3.13 (3.15)	0.80	-1.05 – 2.64	0.39

Table 10. 3: Results of speech and language assessments for exposed and unexposed groups

* Estimated differences are adjusted for age and sex

** A lower score indicates a superior performance

The distribution of scores was in general lower in children from the exposed group compared to children from the unexposed group, suggesting an overall effect rather than one or two very impaired children (see figures 11.1 to 11.6). There was no evidence that the scores of exposed children reported to have no impairments on discharge were significantly different to the scores of those discharged with impairments.

To illustrate the possible clinical significance of these results, one child from the exposed group is described. SS was assessed 6 years after admission to KDH with CM: she had no reported neurological deficits on discharge from hospital. Her scores were two standard deviations (SD) lower than the unexposed group mean on the receptive language, syntax and higher level language assessments and on the content word component of the lexical semantics assessment. Other scores were one SD lower. During spontaneous speech, she exhibited poor turn-taking skills, word finding difficulties and perseveration. Despite being friendly in demeanour, she dominated the conversation, showing poor listening skills, frequently made inappropriate comments and was avoided by the other children in her village. SS did not attend school, although it was not ascertained whether this was due to financial reasons or her behaviour.

10.4.3 Conclusions from the pilot study

Children who had previously been admitted to KDH with severe malaria had, in general, significantly lower scores on the language assessments. These findings suggest that children who have had severe malaria have impairments in language functions, which persist two to 6 years after discharge. The children's phonological systems appear unaffected: the minor phonological deficits seen in two of the children from the exposed group did not impair intelligibility. Alternatively, moderate or severe phonological impairments may have occurred in the immediate post-onset period and resolved by the time of assessment.

The improvement in the six children with speech and language problems on discharge implies that initial deficits may improve beyond the stage of mutism or severe aphasia but do not completely resolve by 6 years post-onset. Indeed, the pattern of scores indicates that basic language functions are still affected years after the malarial episode. If the deficits in these children have any parallels with those of children with acquired childhood aphasia (ACA) as a result of other aetiologies, this would suggest that many of the cases had not reached the final stage of recovery, usually characterised by high level deficits (Lees and Neville, 1990). As all of these children had passed the first 2 years post-insult, it may be postulated that they will never fully recover their language functions. As highlighted in section 3.5, other infectious disease aetiologies are associated with a poor prognosis (Loonen and van Dongen, 1991; Paquier and Van Dongen, 1993), although the pathophysiology is different to malaria.

Although the numbers are small, the finding that children discharged with impairments achieve scores that are not significantly different to children discharged without impairments indicates that this assessment battery is more sensitive to neuro-cognitive impairment associated with severe malaria than the neurological assessment performed on hospital discharge. This also suggests that language deficits may be an important but under-reported sequela of severe malaria.

A striking observation, possibly due to the small numbers, was that there was no difference between the scores of children who had suffered CM and those who had severe non-CM. The prevalence of acquired neurological impairment following severe non-CM has not previously been investigated but it is possible that certain manifestations of severe malaria other than CM may also be associated with impairments. This represents one of the central issues of this thesis and will be discussed further in the presentation of the main study results (Chapters Twelve to Sixteen).

10.5 Summary

This chapter has outlined the development of the speech and language assessment battery, the initial stages of instrument validation and piloting. A two-stage procedure was described for the development and adaptation of assessment tools using the principles of content validation. Six speech and language assessments were developed using these principles, two adapted from tasks previously used in Kilifi and the remainder based on tests or procedures in common use in the UK. The chapter concluded with a presentation of the pilot study methodology and results, suggesting that deficits in speech and language may persist for up to 6 years post-malaria and that impairments may be associated with manifestations of severe malaria other than CM. Alterations to the battery following these results will be presented in the next chapter.

Chapter Eleven: Refinement of the Speech and Language Assessment Battery

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11.1 Introduction

This chapter outlines refinements and alterations to the speech and language battery following the pilot study results described in the previous chapter. The specific reasons underlying alterations made to each test will be discussed in the relevant sections but in outline, were because too many children were at baseline or ceiling on certain tasks or because selected items or materials were not culturally appropriate. In addition, as the target population for the main study was extended from 9 year olds to include children between 6 and 9 years, alterations were necessary to reflect the younger population.

Instrument refinement techniques may be qualitative, in terms of content or form or quantitative, using empirical techniques such as item difficulty and response distributions. These techniques will be discussed where appropriate in the following sections, which present an analysis of the success of each assessment on a test by test basis. The chapter concludes with further evidence of the validity and reliability of the assessments in the speech and language battery.

11.2 Refinement and alterations to the speech and language assessments

When analysing item difficulty, items of varying levels of difficulty are necessary to discriminate along a broad continuum of abilities (Smith and McCarthy, 1995). Item endorsement – the proportion of participants who give each response alternative to an item or assessment – is one function of the difficulty of the item or assessment (Streiner and Norman, 1995). In examining response distributions, two considerations are important. First, items with unbalanced or highly skewed distributions should be removed or altered. Items that draw similar answers from all participants convey little information and have limited variability, meaning that they are unlikely to correlate highly with other test items (Clark and Watson, 1995). Conversely, items with broad distributions should be retained as such questions can discriminate at different points along the continuum of the construct. In the case of items with binary scores, widely varying endorsement percentages indicate items with discriminatory ability (Clark and Watson, 1995).

11.2.1 Receptive vocabulary assessment

The distribution of the receptive vocabulary section of the receptive language assessment in the groups exposed and unexposed to malaria (figure 11.1) indicates that the assessment had insufficient test ceiling for the children in the study. Fifty-seven percent of children from the combined groups achieved one of the top three scores (21–23) and none of the children scored less than 11. The scores of the exposed group have a wider distribution than those of the unexposed group but still indicate that the assessment was too easy.

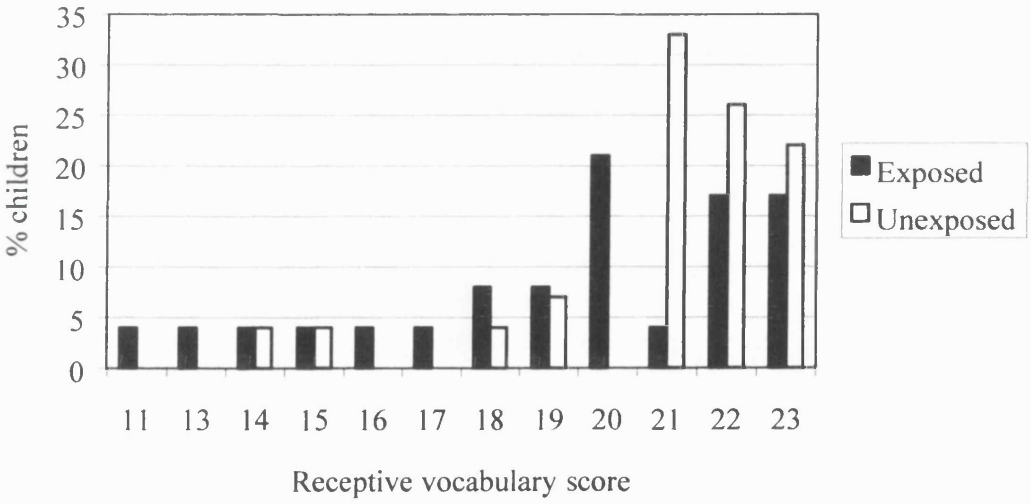

Figure 11. 1: Distribution of receptive vocabulary scores by exposure group

As this assessment was developed from a strong theoretical background in a Kenyan context and has previously been used successfully in this area, it was considered that measures should be adopted to alter the content of the assessment rather than replacing it. In conjunction with the educational psychologist who had developed the test, the range of vocabulary was extended using the version of the test employed in Holding and colleagues' (1999) study and the word frequency list described in the word finding assessment section, to include a series of more difficult items. In addition, using item response data from the pilot study and Holding and colleagues study, pictures that were ambiguous or unclear were redrawn by a local artist. The final version of the assessment, administered during the cognitive assessment battery (Appendix 2), comprised a list of 30 items of increasing difficulty, from which each child would be presented with 25. For older children, the first five items were omitted and for younger children, the last five items were omitted.

11.2.2 Receptive grammar assessment

The distribution of the scores from the second part of the receptive language assessment, the test of simple and complex commands, also indicated that the ceiling was too low (figure 11.2). Sixty-seven percent of children from the unexposed group and 38% of children from the exposed group achieved the highest score (13). Only one child (exposed to severe malaria) scored less than 10.

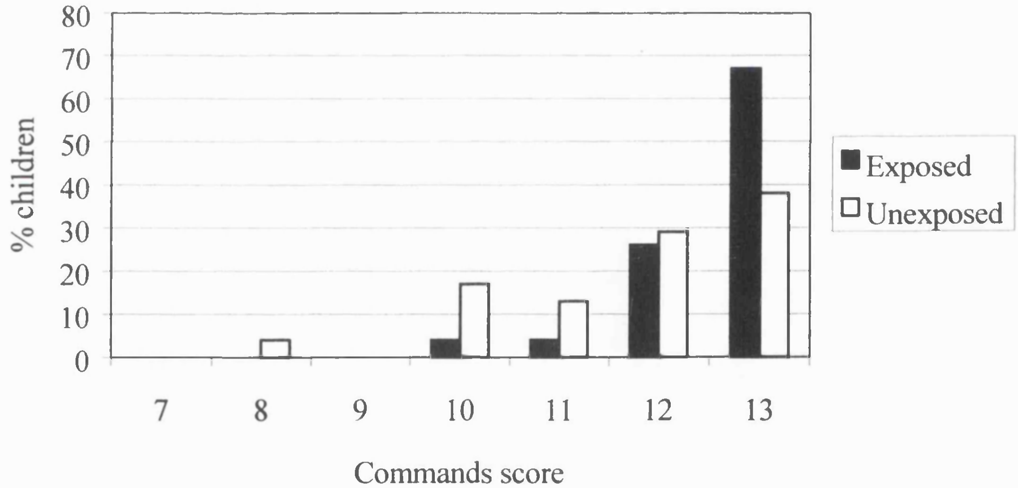

Figure 11. 2: Distribution of commands scores by exposure group

As a result of these findings, it was decided that a more complex measure of receptive grammar was required for the main study. The Test for Reception of Grammar (TROG) (Bishop, 1983) provided the basis for a new receptive grammar assessment (Appendix 15). The TROG is a multiple-choice test designed to assess auditory-verbal comprehension of grammatical contrasts in children between the ages of 4 and 13. The test has been used with children with Landau Kleffner syndrome (LKS) and acquired childhood aphasia (Lees, 1993; Lees and Neville, 1990) and to measure language dysfunction in childhood epilepsy syndromes (Staden, et al., 1998). The test comprises 80 items, each with a target picture and three distractors: the participant is required to point to the picture that corresponds to the phrase or sentence spoken by the assessor. The items are arranged into 20 sections of increasing complexity from single words to complex sentences.

The first step in altering the TROG for use in this community was to identify any items irrelevant to Kigiryama and conversely, any items relevant to the language not included in the English version. This was performed in conjunction with the assessor and a local schoolteacher. Items included in the original TROG and removed from the current receptive grammar assessment were the third person pronoun ('he' and 'she' are both represented by the pronoun 'a' in Kigiryama) and some of the complex sentence structures. The singular/plural item was expanded to take account of the Kigiryama noun classes (section 7.3.1) and the comparative/absolute item was altered to become a simple comparative. The content of all the items was altered for cultural validity, although the principles of using a restricted vocabulary, easily-recognisable pictures and lexical and grammatical distractors were maintained. The whole assessment was administered to each child: there were no start/discontinue rules.

A local artist drew the pictures: each one was piloted with children from the target population for level of recognition. The group of children was selected to include those at school and those not attending school, as the latter would be less likely to have experience of seeing and interpreting pictures yet would certainly form a proportion of the main study group. If 80% of children recognised the picture, it was accepted, otherwise it was redrawn or discarded. This process of recognition testing was repeated for each assessment using picture stimuli.

The final version of the assessment comprised an example picture, a practice picture and 34 items in seventeen groups. Four items per section are included in the TROG, reducing the probability of achieving correct scores on all items by chance (Bishop, 1983). Due to time constraints in the development of the receptive grammar assessment and the fact that this assessment was only one part of a relatively long battery, only include two items per section were included. Thus, the decision was made to give each item an individual score rather than a section score, making the assessment total 34. The receptive grammar assessment was designed primarily to provide a quantitative measure of this aspect of comprehension. However, a set of vocabulary cards was drawn to provide a basic indication of the nature of any impairments identified.

11.2.3 Syntax assessment

The scores on the syntax assessment were normally-distributed (figure 11.3) and the children responded well to the question-answer format.

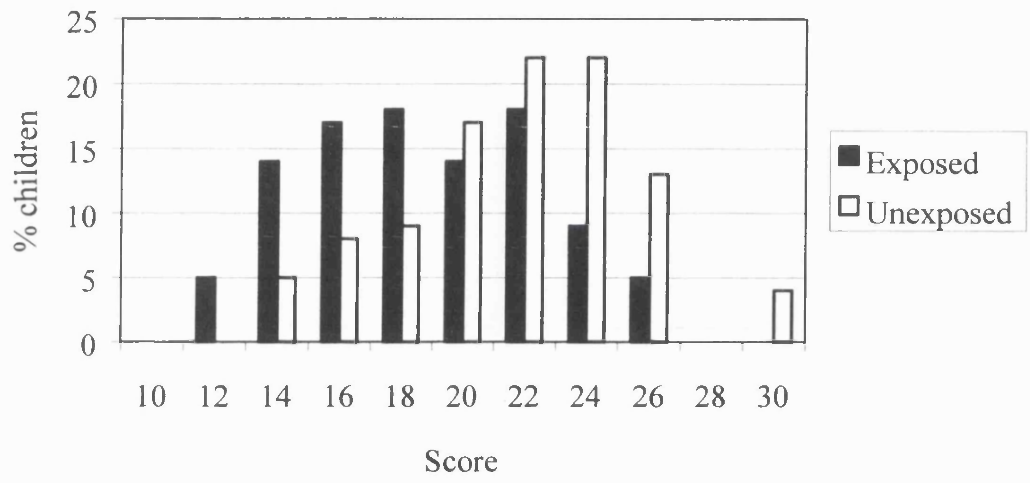

Figure 11. 3: Distribution of syntax assessment scores by exposure group

Several of the items were unsuccessful and were removed or altered. First, the use of pictures to test prepositions was not effective. The prepositions 'infront' and 'behind' were particularly problematic: 24% of children responded 'on top' and 26% said 'under' for each one respectively, which may be due to the fact that the pictures were a two-dimensional representation of a three-dimensional concept. This is supported by Serpell (1972), who asserts that children in resource-poor countries often have difficulty understanding the manner in which depth is represented in two dimensions. Therefore, it was decided to use real objects (a cup and banana) to test prepositions in the main study, by questioning the child on the position of the banana in relation to the cup.

Pictures were also not a useful means of representing past and future tense questions: many children expressed confusion about them during the assessment. In consequence, the two pictures were removed and tenses were tested through questions modelling the target, indirectly related to the pictures. For example, the picture for the 'passives' question showed two boys, one with a mango and one with a banana. After the child has given the answer 'this boy was given a banana', the assessor asks 'what will he do with it?' to elicit the future tense.

All new pictures were subject to recognition testing as described above. The final version of the assessment (Appendix 16) comprised five preposition questions and fifteen picture-based items testing plurals, conjunctions, comparatives, adverbs, adjectives, tenses, locative, negation, passive and WH-questions. There was an example item and a practice item for the preposition section and the picture-based section. The total score was 40.

The 0/1 scoring system was also altered to allow for more complex analysis. The scoring system from the Renfrew Action Picture Test (RAPT) (Renfrew, 1988) formed the basis of the new system, whereby answers that are not correct but show some evidence of the development of syntactic principles are awarded a score. For example, a child who says 'catched' instead of 'caught' in English knows the principle of using the past tense but not the irregular exceptions. To devise the new scoring system (Appendix 17), all of the answers given by children in the pilot study were listed and the types and frequency of responses analysed to determine common response-types for each syntactic element.

11.2.4 Lexical semantics assessment

The spontaneous language tasks used in the pilot study were enjoyed by the participants and resulted in large samples of conversation and storytelling. However, the picture book was not successful, as many of the children did not recognise some of the animals depicted. For example, many children had heard of a crocodile and knew what type of creature it was but had never seen one pictorially or in reality. In consequence, a composite picture was designed by the candidate, the assessor and other staff at the research unit and drawn by a local artist. Several drafts were piloted as described above. The final picture depicted a typical household scene familiar to rural children, comprising people and animals engaged in various activities to stimulate broad descriptions (figure 11.4). This picture is illustrative of the style and content of other pictures used in the battery.

Figure 11. 4: Picture employed in the spontaneous language task

The scores for the function word (figure 11.5) and content word (figure 11.6) elements of the assessment were broadly distributed in both exposure groups, indicating that the assessment can discriminate at different points along the continuum of the construct. Therefore, the format of the assessment was maintained for the main study (Appendix 18). Minor changes were made to the profile form to remove categories that had not been utilised by children in the pilot study and were judged not to contain concepts within the experience of the target population (for example, air travel). In addition a booklet of guidelines outlining which words to include in each category was produced using response data from children in the pilot study (Appendix 18). In order to achieve a representative score, it was decided that each child should produce a minimum of 100 words (tokens) in the language sample for the score to be calculated.

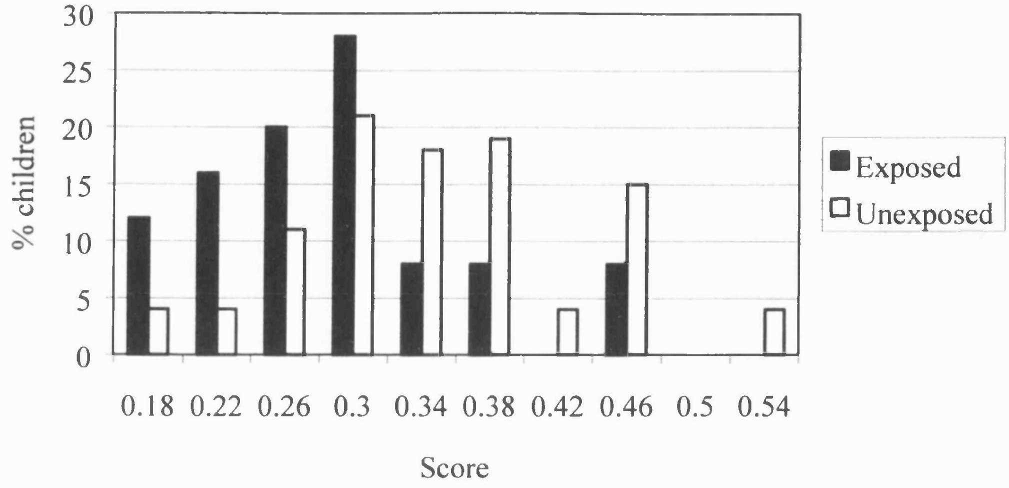

Figure 11. 5: Distribution of lexical semantics function words scores, by exposure group

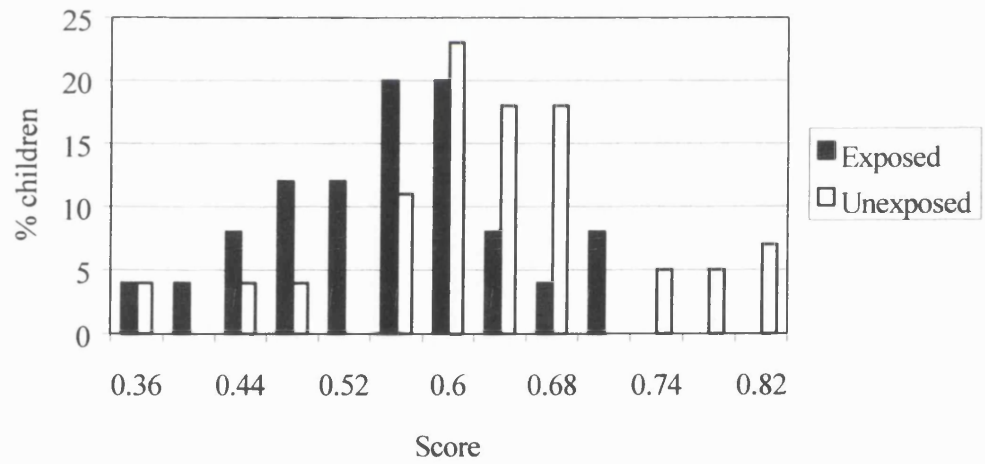

Figure 11. 6: Distribution of lexical semantics content words scores, by exposure group

11.2.5 Higher level language assessment

The pilot higher level language assessment was designed to be over-inclusive because it was difficult to know the types of questions that would measure this construct in Kigiryama. The direction of the association between the exposed and unexposed groups on the pilot higher level language assessment suggested poorer performance in the former group (table 10.3): it was surprising that there was a significant difference between results on tests of basic language functions but not in higher level functions, although this may be indicative of difficulties with the assessment.

An analysis of item endorsement suggested that some of the items did not discriminate between the two groups (table 11.1). The figurative language and convergent semantic tasks drew the same answer from almost all of the children in each exposure group. The response distributions for the synonyms task were also very similar between the groups and the proportion of children with a score of '0' indicated that this task was too difficult. Over 70% of children attained a '0' score on the antonyms task, again indicating an inappropriate level of difficulty.

	Unexposed group n (%)			**Exposed group n (%)**		
Score	**0**	**1**	**2**	**0**	**1**	**2**
Antonyms	19 (70)	5 (19)	3 (11)	19 (76)	1 (4)	5 (20)
Homonyms	4 (15)	16 (59)	7 (26)	6 (24)	16 (64)	3 (12)
Definitions	3 (11)	15 (56)	9 (33)	6 (24)	8 (32)	11 (44)
Figurative lang.	27 (100)	0	0	24 (96)	1 (4)	0
Convergent task	1 (4)	26 (96)	0	0	27 (100)	0
Sentence form.	13 (48)	5 (19)	9 (33)	13 (52)	7 (28)	5 (20)
Synonyms	24 (89)	3 (11)	0	22 (88)	3 (12)	0

Score	**0**	**1**	**2**	**3**	**4**	**0**	**1**	**2**	**3**	**4**
Categorisation	0	0	1 (4)	3 (11)	23 (85)	0	0	3 (12)	4 (16)	18 (72)
Similarities / Differences	7 (26)	7 (26)	5 (19)	6 (22)	2 (7)	13 (52)	6 (24)	3 (12)	2 (8)	1 (4)
Divergent task	2 (7)	2 (7)	9 (33)	8 (30)	6 (22)	1 (4)	4 (16)	9 (36)	3 (12)	8 (32)

Table 11. 1: Item endorsement on the pilot higher level language assessment

The use of a picture for the inferential reasoning section of the assessment proved to be problematic. Observation of the assessment sessions by the candidate suggested that many of the children found the use of a picture to complete an abstract task confusing.

The results also suggested that this task was very difficult. Only one child (unexposed group) was able to complete the inferential reasoning question and a '0' score was attained by 48% and 74% of the unexposed group on the explaining an inference and applying general knowledge tasks respectively. The younger children included in the main study would probably have less exposure to pictures and abstract tasks than the 9-year olds in the pilot study so this section of the assessment was removed.

In order to increase the reliability and homogeneity of the main study assessment, the number of different items was reduced and the number of questions per item increased. To maintain an assessment of reasonable length, five items were selected for the main study assessment, each of which comprised at least four questions. The homonyms, definitions, similarities/differences and sentence formulation tasks were selected on the basis that they were each chosen by a local schoolteacher as the items most familiar to schoolchildren of the same age as the target population, had broad response distributions and varying levels of difficulty. The categorisation task, which required children to name as many items within a group (for example, animals) as possible within one minute, was selected as word fluency tasks are often sensitive to word finding difficulties (Crosson, 1996). Although items that had proved very difficult for 9 year olds were removed for the reasons discussed above, it was important to retain some of the more difficult items (for example, homonyms and similarities and differences) in order that the assessment would discriminate more subtle impairments (Crosson, 1996).

The low mean score attained by the unexposed group in the pilot study suggested that in addition to the issue of individual item difficulty discussed above, lack of familiarity or understanding of the test requirements may have contributed to poor scores. Therefore, a test booklet was devised to include detailed explanations of each task in addition to examples and in some instances, discussion of the task with the child to establish his/her understanding of its requirements. Pictures were included with the homonyms and similarities/differences tasks to be used if the child found this useful.

The final alteration to the higher level language assessment was to change the scoring systems of the categorisation and sentence formulation tasks in accordance with the CELF-R (Semel, et al., 1987) word associations and formulated sentences tasks on which they were based. The final assessment is shown in Appendix 19. Based on the responses given by children in the pilot study, scoring guidelines (Appendix 20) were produced to maintain consistency of scoring in the main study.

11.2.6 Pragmatics assessment

The first section of the pragmatics assessment, the measure of functional errors adapted from Damico and colleagues (1983) was included in the original battery because it had previously been used in the same area (Holding, et al., 1999). There was no evidence of a difference between the groups, although the direction of the association suggested poorer performance among children from the exposed group. Damico and colleagues found that functional criteria were more sensitive to language disorders and later academic difficulties than surface-oriented (syntactic) criteria in Spanish/English bilingual speaking children. The use of functional criteria arose from the hypothesis that grammatical errors in second language learners may be due to "normal interlanguage processes" (p386), in other words a normal developmental phase common to first language acquisition. Such processes would not be expected to result in any future scholastic or language difficulties and children classified as language-disordered on the basis of such 'errors' would be considered to have been misdiagnosed. The context of Damico and colleagues' study was different to that of the current study, in which children may have been exposed to a second language (Kiswahili) but were assessed in their mother tongue (in most cases, Kigiryama). In the current study, the exposed group displayed poorer performance relative to the unexposed group on three assessments using 'surface-oriented criteria' (as defined by Damico and colleagues). The authors assert that the correlation between surface-oriented and functional criteria is weak: these results may support that assertion but suggest that in the Giryama population, 'surface-oriented criteria' are more sensitive than the functional criteria proposed in Damico and colleagues' study.

The other sections of the assessment were included to address aspects of pragmatics not featured in the analysis of functional errors, although both proved to be problematic in the pilot study. The observational section was designed to assess the child's ability to adapt to the needs of the listener and his/her awareness and use of conversational devices and status relations. However, it was difficult to obtain a representative measure of these pragmatic behaviours, first because the length and setting of the observation was limited and secondly because several of the behaviours were affected by the situation or cultural norms. For example, traditional Giryama families teach their children that it is disrespectful to make eye contact with adults who are in an authoritative position, such as a teacher (which is the role most parents saw the assessor as fulfilling). Also, the fact that the child knew there were strangers present immediately altered his/her behaviour. Consequently, the results of the observation were not deemed to be a representative measure of these aspects of pragmatics.

The parental questionnaire, investigating the child's range of communicative intents, was also problematic to administer. The format was successful in that most parents were responsive and gave detailed and informative answers to questions they understood. However, some of the questions were very specific and despite the use of examples, many parents commented that they were obscure or confusing. The assessor performing the questionnaires also reported that she felt some parents were randomly answering questions because they were unclear of the meaning but did not want to say so. In consequence, the results were considered to be unreliable.

The findings of the pilot study indicated that the second and third sections of the pragmatics assessment were not appropriate tasks for the main study. The analysis of functional errors used alone did not measure the construct of pragmatics defined in the theoretical framework for the study (section 10.3.1) and was not necessarily a sensitive measure of pragmatic abilities in the Giryama community. As the parental questionnaire format was successful, a broad-based, accessible questionnaire was designed to replace all three sections, based on the Pragmatics Profile of Everyday Communication Skills in Children (Dewart and Summers, 1995). The Pragmatics Profile was developed to "...provide the practitioner with a picture of the child as a communicator *outside* the clinical context and *within* the context of everyday life" (p2), concentrating on three aspects of the development of pragmatics. First, the development of communicative functions; second, the child's response to communication and third, the way the child participates in interaction and conversation. The Profile also includes a fourth section measuring the way that variations in context, such as time, place and people involved, affect the expression of the three aspects described above.

The Pragmatics Profile was adapted to the cultural context of the current study by the candidate and assessors, with several consultations with a local schoolteacher. The fourth section of the original profile was omitted for several reasons. First, to reduce its length; second, because some of the items were not appropriate for the Giryama community (for example, 'books as a context for communication') and third, because too little is known of the current context to make an assessment of appropriate contextual variation. The adapted profile (Appendix 21) comprises three sections with twenty questions, representing the major language use constructs described by Lahey (1988): social functions, conversational devices, adapting to the needs of the listener and linguistic contexts. Items are presented in the context of everyday skills, making questions more relevant to parents and providing information on possible service requirements. The current profile was designed to be quantifiable (and henceforth referred to as a 'questionnaire') for ease of analysis and group comparisons: the scoring system (Appendix 22) was based on a version of the Profile quantified for use with children with Landau Kleffner syndrome (Hand, 1996). To ensure that the scores reflected cultural expectations of pragmatic abilities in the Giryama community, a scoring system was developed in consultation with unit workers from the local area. The questioner seeks to engage the parent in discussion about various aspects of the child's pragmatic skills. The parent's answers are recorded on a response sheet and later scored on a 0 – 5 scale.

The first section of the pragmatics questionnaire assesses communicative functions through nine questions about the child's ability to direct another's attention, make requests, give information or instructions and express humour and emotion. The second section measures the child's response to communication with six questions on the child's reaction to sarcasm, humour and attempts to gain his/her attention; his/her metalinguistic awareness and his/her ability to negotiate and request clarification. The third section comprises five questions on interaction and conversation, concerning the child's interest in interaction; ability to maintain, repair and terminate a conversation and his/her use of presupposition.

11.2.7 Phonological assessment

A profile of the first 100 different words produced by the child during the spontaneous speech session formed the phonological assessment in the pilot study. The results of the pilot study suggested that persisting phonological impairment is not associated with severe malaria, although the study numbers were small.

The pilot assessment was time-consuming and a qualitative analysis of the results indicated a subset of phonemes that appeared frequently in words and a subset that were rarely used by any of the children. In order to reduce the transcription time and target commonly-used phonemes, a 40-word picture-based assessment was devised (Appendix 23). This assessment was also used as a word finding assessment: the method of item selection is described in the section detailing that assessment.

To attain a score of '1' for a phoneme in a particular position, the child was required to produce it correctly in each word it appeared in that position. The methodology meant that less common phonemes may only be included in one of the 40 words, therefore only assessed once. In consequence, if a child did not produce the correct word, it would not be possible to assess that particular phoneme. As a result, it was decided to use the percentage of all the phonemes used that were produced correctly to score the assessment.

11.2.8 Word finding assessment

Anomia is a common finding in diffuse CNS disorders such as encephalitis, increased intracranial pressure, subarachnoid haemorrhage, concussion and toxic-metabolic encephalopathy (Love and Webb, 2001). Unlike other aphasic symptomatology, anomia is a non-localising, which has been interpreted to mean that the lexical store required for semantic concepts has broad representation throughout the brain.

The persistence of word finding difficulties has been found to be an indication of a poor prognosis in ACA (van Hout, et al., 1985) and a qualitative analysis of the pilot study language samples indicated that 46% of children with previous CM showed signs of anomia. In addition, word finding difficulties have been associated with language disorders, learning difficulties and low reading achievement (German, 1989). Therefore, a word finding assessment was devised for the main study, based on the Test of Word Finding (TWF) (German, 1986). The TWF evaluates children's word finding skills in multiple naming formats, using words of different syntactic and semantic categories, characterised by accuracy, speed, response types and presence of gestures and extra verbalisations (German, 1989). The test is divided into five sections. Three sections assess picture naming of nouns, verbs and categories, respectively; one measures sentence completion naming and one, description naming. Performance is measured by three indices: an accuracy score measuring the number of correct first responses; an assessment of time taken to respond and a response analysis identifying types of substitutions made on incorrect responses. Finally, the TWF comprises a comprehension assessment to differentiate naming errors due to word finding difficulties and those due to lack of knowledge of the target word.

The word finding assessment (Appendix 24) developed for the current study was based on the principles of the TWF but was more simple in structure and format, due to the fact that this assessment was only one part of a relatively long battery. The first stage of development of the current assessment was to construct a vocabulary frequency list from the target population. Sixty children between the ages of 6 and 9 years were asked to name as many words as possible. Few verbs, adjectives, adverbs or abstract nouns were included in the list: any were discarded as they would be difficult to present pictorially. The first twenty and last twenty nouns were selected from the frequency list and analysed for phonemic content, so the assessment would also fulfil the requirements of the phonological assessment. The analysis showed that one commonly-used medial phoneme was not represented by any of the words so one noun was replaced by a more appropriate word from the frequency list.

Pictures representing the 40 nouns were drawn by a local artist. The process of recognition testing was carried out as described above, although the accepted recognition level was raised to 90% because the test requires children to name the word depicted quickly and without the cues included in other assessments in the battery, meaning each picture had to be immediately recognisable. The test procedure and scoring system was based on the TWF, measuring both response accuracy and delay. Each accurate response was awarded a score of '1'. A delayed response was categorised as a response >4 seconds after the presentation of the picture: an estimated time was used as it was thought that the use of a stopwatch would interfere with the fluidity of the assessment procedure. A response analysis was carried out on the assessments of children assigned an 'impaired' score (section 16.5). A comprehension test was not included due to time constraints: as the words had been selected from a frequency list generated from the target population, it was assumed that the majority of children would know them. The assessment was tape-recorded in order that transcription and analysis for the phonological assessment could be carried out after the administration of the battery.

11.3 Further validation: construct validity

Construct validity refers to the extent to which a test may be said to measure a theoretical construct or trait. An estimate of the construct validity of an assessment instrument is informed by a pattern of covariance with theoretically related and unrelated constructs, covariance with a previously validated or 'gold standard' test being the most powerful estimate (Haynes, et al., 1999).

Construct validity usually results from the gradual accumulation of evidence after multiple applications of the assessment over time (Anastasi and Urbina, 1997; Clark and Watson, 1995; Litwin, 1995). Two specific techniques – age differentiation and principal components analysis – were employed to provide initial evidence of the construct validity of the speech and language assessments. Both procedures were performed retrospectively on the group of 179 children unexposed to severe malaria recruited to the main study, in order that the large numbers would increase the reliability of the results.

11.3.1 Age differentiation

Age differentiation has been used in the validation of many traditional intelligence tests (Anastasi and Urbina, 1997). Performance on speech and language assessments would also be expected to exhibit a progressive increase with advancing age, although the increase in this group may be less marked in some facets of language because of the age of the children. Tables 11.2 and 11.3 show summary statistics for each speech and language assessment, stratified by age. Yearly age bands were used, following the age stratification procedures employed in the main study analyses due to issues of validation of month of day of age (section 12.2). Means were calculated for normally-distributed data and medians for skewed data.

	Receptive grammar	Syntax	Higher level language	Lexical semantics (function)	Lexical semantics (content)
Age	**Mean score (SD)**				
6	20.0 (3.9)	22.2 (6.0)	14.9 (7.3)	0.23 (0.04)	0.57 (0.06)
7	21.7 (5.0)	23.0 (7.2)	17.0 (6.0)	0.23 (0.04)	0.57 (0.06)
8	25.2 (4.7)	29.3 (6.4)	20.7 (7.0)	0.22 (0.04)	0.58 (0.06)
9	25.9 (4.8)	30.7 (6.1)	23.9 (7.7)	0.23 (0.04)	0.58 (0.06)

Table 11. 2: Mean scores showing the age differentiation of normally-distributed tests

	Receptive vocabulary	Word finding	Pragmatics	Phonology
Age	**Median score (IQR)**			
6	20.5 (2.7)	36 (31-37)	85 (81-92)	100 (100-100)
7	21.3 (2.8)	37 (33-39)	86 (82-89)	100 (100-100)
8	23.1 (2.1)	38 (36-39)	87 (81-92)	100 (100-100)
9	22.5 (2.5)	39 (36-40)	88 (82-91)	100 (100-100)

Table 11. 3: Median scores showing the age differentiation of tests with skewed distributions

A progressive increase in scores with advancing age is shown in the assessments of receptive grammar, syntax, higher level language, word finding and pragmatics. The receptive vocabulary assessment displays progressively increasing scores in 6 to 8 year old children. The largest increase in scores is seen in the higher level language assessment, reflecting the fact that this test targets advanced functions more likely to be present in older children. Scores remain almost static over the age range for the lexical semantics assessment, possibly reflecting the fact that many children do not attend school (section 12.3), thus do not exhibit increases in vocabulary as a function of education. Indeed, when non-schoolers were removed from the analysis, the content word component did exhibit a progressive increase with age, with the exception of the 9 year-olds category (6 years: mean=0.59 (SD=0.07); 7 years: 0.61 (0.05); 8 years: 0.63 (0.05); 9 years: 0.62 (0.06)). The function word scores remained the same as in table 11.2. The median phonological assessment score and the inter-quartile range across the age groups is the maximum possible score, suggesting that the Kigiryama phonological system, as measured by the current study's tools, is fully developed by 6 years of age.

11.3.2 Principal components analysis

The investigation of the factor structure of an assessment instrument is to assess the degree to which elements of an instrument or battery covary in patterns that are consistent with expectations based on the underlying theory (Floyd and Widaman, 1995). Convergence between the language assessments in the battery would be expected if the instruments were valid. A principal components analysis was used to examine the correlation matrix of the variables. Four components accounted for 81% of the total variance of the measured variables. A scree plot shows that factor 1 explains most of the variables' combined variance with the other Eigenvalues falling at or below 1.0 (figure 11.7).

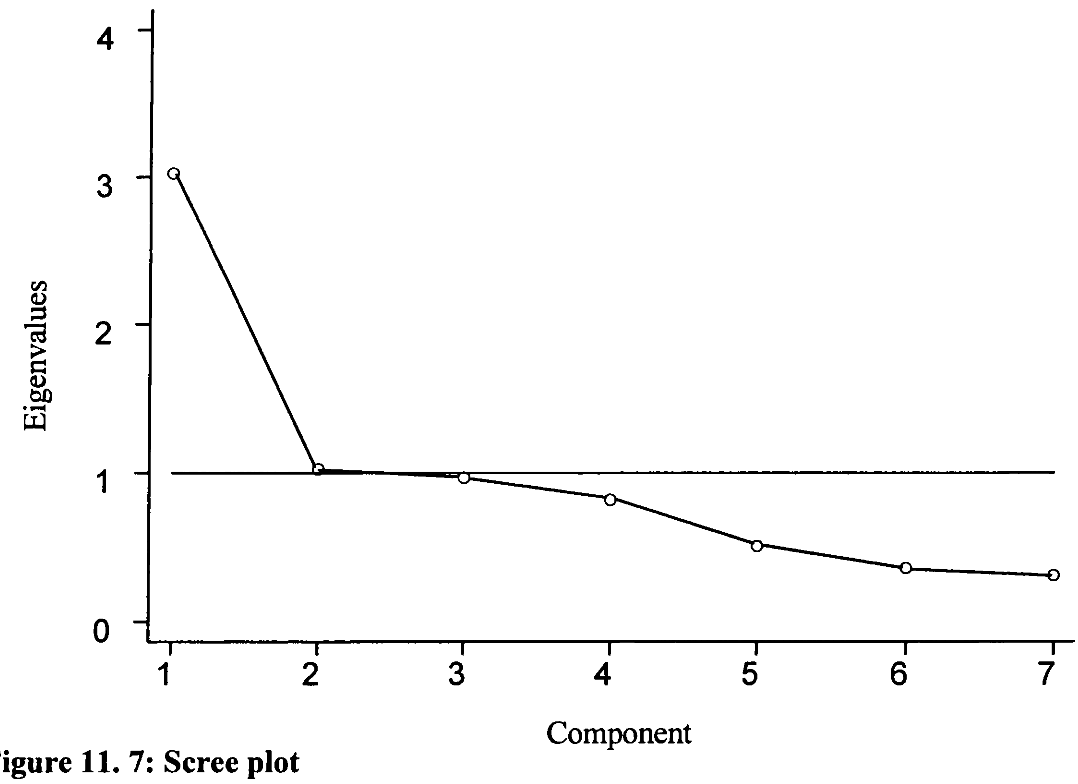

Figure 11. 7: Scree plot

Assessment	Principal Components			
	1	2	3	4
Receptive grammar	**0.45**	-0.08	-0.14	-0.02
Receptive vocabulary	**0.43**	0.18	-0.01	-0.05
Syntax	**0.42**	-0.15	-0.28	-0.07
Higher Language	**0.38**	-0.26	-0.16	-0.24
Lexical semantics	0.18	**0.79**	0.21	0.29
Word Finding	**0.43**	0.21	-0.03	0.03
Pragmatics	0.21	-0.39	0.35	**0.79**
Phonology	0.17	-0.11	**0.85**	-0.37

Table 11. 4: Principal components of the speech and language assessment battery

All of the variables are pure variables with loadings of 0.4 or greater on only one component (table 11.4: shown in bold font). Examination of the items on factor 1 indicates a 'general language ability' component with positive loadings on all variables. Factor 2 seems to specifically relate to 'vocabulary' or aspects of word meaning with a high loading for expressive vocabulary and positive loadings for receptive vocabulary and word finding. Factor 3 relates to phonology and the fourth factor indicates a pragmatics component. The covariance on factor 1 provides evidence for the convergent validity of the language measures. The other three factors relate to distinct components of the assessment framework (section 10.3.1) from the three major categories of content, form and use: although they formed distinct factors, these variables still had positive loadings on the 'general language ability' factor.

11.4 Reliability of the speech and language battery

The measurement of assessment reliability allows the tester to estimate the proportion of the total variance of test scores due to 'error variance' or factors irrelevant to the purpose of the test (Anastasi and Urbina, 1997).

Twenty children were recruited for reliability testing. Retesting was carried out two weeks after the first administration of the assessment by the same assessor, at the same venue and where possible, at a similar time of day. Inter-rater reliability was carried out at the time of the first administration of the assessments.

11.4.1 Test-retest reliability

Test-retest reliability measures the temporal stability of an assessment instrument. Many studies give the product-moment correlation coefficient (r) as an indicator of agreement between the two measures of interest. Bland and Altman (1986) argue that this method of analysis is inappropriate because the correlation coefficient is a measure of association, dependent on the range of measures used: a good correlation is likely because two measures over the whole range of possible values are usually compared. Second, Bland and Altman contend that the test of significance is not relevant because two measurements of the same tool or method will inevitably be related to some degree. Therefore, test-retest and inter-rater (section 11.4.2) reliability were measured using an alternative method proposed by Bland and Altman: the mean difference between the two measures, as an estimate of the overall bias and the 95% limits of agreement as an indication of the range of variability in individual scores. Thus, the mean difference between the first and second administrations of the receptive grammar assessment was 1.2 and the second administration varied from 2.27 points less to 4.67 points more than the first (table 11.5). Clinical judgement is required to decide whether this is an acceptable level of agreement.

The mean difference in scores indicates a high level of repeatability in all of the speech and language assessments (table 11.5). The highest level of individual variability relative to the maximum assessment score was on the receptive grammar assessment, the direction suggestive of a practice effect. Ascertaining the clinical acceptability of the limits of agreement is difficult in the context of novel assessments but the figures are suggestive of an acceptable level of variability as they represent less than 10% of the mean score of the main study unexposed group.

Assessment	Mean difference (SD)	95% limits of agreement		Maximum assessment score
Receptive grammar	1.2 (1.77)	-2.27	4.67	34
Receptive vocabulary	-0.62 (1.89)	-4.32	3.08	25
Syntax	0.7 (1.56)	-2.36	3.76	40
Higher level language	0.05 (1.7)	-3.28	3.38	39
Lexical semantics (function words)	0.008 (0.04)	-0.09	0.07	n/a
Lexical semantics (content words)	0.01 (0.03)	-0.07	0.05	n/a
Pragmatics	1.0 (2.45)	-3.8	5.8	100
Phonology	0.15 (1.5)	-3.09	2.79	100
Word finding	-1.15 (1.04)	-0.89	3.19	40

Table 11. 5: Measures of test-retest reliability of the speech and language assessments

11.4.2 Inter-rater reliability

The speech and language and cognitive batteries were each performed by two assessors. Several procedures were put into place to reduce the amount of scorer variance in the assessments (section 8.4.8). First, each assessor independently scored the other's tests on a daily basis. Any discrepancies in scoring were resolved through discussion, although the number of discrepancies was low as there were detailed descriptions for scoring. Second, detailed scoring guidelines were produced (Appendices 17, 18, 20 and 22) to reduce variability and subjectivity in the assignment of scores. Third, the candidate regularly observed the assessors, providing feedback on performance. Finally, an 'assessment refresher day' was held every few months whereby the assessors had the opportunity to act as peer educators, observing each other and resolving any differences in test administration.

Statistical measurement of inter-rater reliability indicates an acceptable level of congruence between assessors: again, the mean difference in scores is less than 10% of the mean score for the main study unexposed group (table 11.6).

Assessment	Mean difference (SD)	95% limits of agreement		Maximum assessment score
Receptive grammar	-0.2 (0.79)	-1.75	1.35	34
Receptive vocabulary	0.3 (0.55)	-1.44	1.25	
Syntax	0.4 (0.52)	-0.62	1.42	40
Higher level language	0 (1.05)	-2.06	2.06	39
Lexical semantics (function words)	0.004 (0.01)	-0.06	0.05	n/a
Lexical semantics (content words)	0.01(0.03)	-0.08	0.04	n/a
Pragmatics	-0.5 (2.22)	-4.85	3.85	100
Phonology	0 (0)	0	0	100
Word finding	0 (0.47)	-0.92	0.92	40

Table 11. 6: Measures of inter-rater reliability of the speech and language assessments

11.4.3 Internal consistency

The internal or inter-item consistency of an assessment instrument refers to the magnitude of covariance among its elements. Each of the speech and language assessments was intended to measure a unitary construct: Haynes and colleagues (1999) comment that in the case of assessments measuring a unidimensional construct, it is important that all items tap that particular construct. However, a particularly high level of covariance between items may indicate that some are redundant and lead to some aspects being overemphasised, thus reducing the content validity (Bland and Altman, 2002; Clark and Watson, 1995). The internal consistency of the speech and language assessments was established using Cronbach's alpha, in addition to item-level statistics – the impact on the alpha if an item is deleted – and item-total correlations. The item-test correlation is the basic item-total correlation and the item-rest correlation measures item-total covariance when that item is removed, thus avoiding distortion to the scale from poorly fitting items. Four of the assessments consisted of aggregated measures: the receptive grammar, syntax, higher level language and pragmatics assessments. The results are presented in tables 11.7 to 11.10.

11.4.3.1 Receptive Grammar Assessment

Test item	Item-test correlation	Item-rest correlation	Alpha coefficient
Noun	0.34	0.31	0.8
Verb	0.55	0.49	0.79
Adjective	0.6	0.53	0.79
Two elements	0.4	0.35	0.8
Negation	0.4	0.28	0.8
Three elements	0.57	0.49	0.79
Reversible active	0.55	0.45	0.79
Comparative	0.5	0.38	0.8
Plural (N-class)	0.59	0.49	0.79
Plural (Ki/Vi)	0.41	0.29	0.8
Plural (M/Mi)	0.28	0.21	0.81
Plural (M/A)	0.57	0.48	0.79
Reversible Passive	0.6	0.51	0.79
Preposition 1	0.53	0.43	0.79
Preposition 2	0.36	0.24	0.81
Postmodified subject	0.62	0.53	0.79
Relative Clause	0.58	0.47	0.79
		Scale Coefficient	**0.8**

Table 11. 7: Internal consistency of the receptive grammar assessment

11.4.3.2 Syntax Assessment

Test Item	Item-test correlation	Item-rest correlation	Alpha coefficient
Prepositions: 'On'	0.45	0.37	0.82
'In'	0.55	0.49	0.82
'Beside'	0.47	0.37	0.82
'Under'	0.59	0.51	0.82
'Between'	0.59	0.53	0.82
Plural (N-class)	0.45	0.38	0.82
Conjunction	0.42	0.36	0.82
Comparative	0.52	0.42	0.82
Plural (Ki/Vi)	0.44	0.37	0.82
Adverb	0.41	0.32	0.83
Adjective	0.63	0.58	0.81
Plural (M/A)	0.5	0.43	0.82
Past tense	0.38	0.26	0.83
Plural (M/Mi)	0.53	0.47	0.82
Locative	0.47	0.39	0.82
Negation	0.44	0.34	0.83
'Wh'-question 1	0.61	0.52	0.81
Passive	0.35	0.24	0.83
Future tense	0.39	0.34	0.83
'Wh' question 2	0.66	0.58	0.81
		Scale Coefficient	**0.83**

Table 11. 8: Internal consistency of the syntax assessment

11.4.3.3 Higher Level Language Assessment

Test Item	Item-test correlation	Item-rest correlation	Alpha Coefficient
Categorisation 1	0.65	0.59	0.74
Categorisation 2	0.64	0.58	0.74
Categorisation 3	0.64	0.58	0.74
Definitions	0.64	0.51	0.73
Homonyms	0.71	0.6	0.71
Similarities/diffs	0.78	0.62	0.69
Sentence formulation	0.85	0.62	0.76
		Scale Coefficient	**0.76**

Table 11. 9: Internal consistency of the higher level language assessment

11.4.3.4 Pragmatics questionnaire

For two items on this assessment – directing attention to him/herself and gaining attention – all children attained the maximum score, therefore these items were omitted from the analysis.

Test Item	Item-test correlation	Item-rest correlation	Alpha coefficient
Attention: others	0.5	0.45	0.79
Request assistance	0.49	0.38	0.79
Request information	0.56	0.47	0.79
Give information	0.65	0.6	0.78
Give instructions	0.57	0.49	0.79
Humour	0.5	0.42	0.79
Express pleasure	0.29	0.25	0.8
Express upset	0.37	0.3	0.8
Sarcasm	0.52	0.4	0.79
Metalinguistic	0.46	0.36	0.79
Amusement	0.4	0.32	0.8
Negotiation	0.34	0.23	0.8
Request clarification	0.53	0.38	0.8
Initiate interaction	0.44	0.4	0.8
Maintain interaction	0.51	0.43	0.79
Presupposition	0.57	0.46	0.79
Conversation repair	0.56	0.42	0.79
End interaction	0.62	0.44	0.78
		Scale Coefficient	**0.8**

Table 11. 10: Internal consistency of the pragmatics questionnaire

Bland and Altman (1997) suggest that when comparing groups, α values of 0.7 to 0.8 are satisfactory. The four language assessments have α values of 0.76 to 0.83, indicating that their internal consistency is acceptable. The α does not increase markedly with the exclusion of any of the items in the assessments, suggesting that none of the individual items detract from the consistency of the assessment. Item-total correlations are usually recommended to be above 0.20 (Streiner and Norman, 1995), a criterion met by all items on the battery.

11.5 Summary

The pilot study results were analysed using quantitative (item difficulty, response distributions and item endorsement) and qualitative (acceptance and response of participants) techniques for indications of areas for assessment refinement. Alterations were carried out according to the content validity principles described in Chapter Ten.

The receptive vocabulary element of the pilot receptive language assessment was maintained, although with some alterations and additions at the item level to increase the difficulty of the assessment. Conversely, the commands element of the pilot assessment was replaced with a receptive grammar assessment based on the TROG (Bishop, 1983). Item level alterations to pictures and question content were made to the syntax assessment and a more complex scoring system was devised to increase assessment reliability. The lexical semantics assessment was retained, although an alternative picture stimulus was designed. The higher level language assessment was subject to major alterations, removing redundant items to reduce the number of individual tasks from sixteen to five, while increasing the number of questions per task. The pilot pragmatics assessment was replaced with a parental questionnaire, adapted from the Pragmatics Profile of Everyday Communication Skills in Children (Dewart and Summers, 1995). The format of the phonological assessment was altered from a transcription of the spontaneous language sample to one of 40 words targeting the most commonly-used phonemes in Kigiryama. The same collection of words formed the basis of a novel assessment of word finding, designed following the finding of anomic errors in a qualitative analysis of the pilot study language samples. Psychometric measures indicated that the eight assessments have an acceptable level of construct validity, internal consistency and reliability.

Part Four: Results and Discussion

The final part of the thesis presents the findings of the study, their interpretation and possible ramifications for clinical practice across sub-Saharan Africa. Due to the size of the study, the results are presented in five chapters, each focussing on a particular domain of development. This study aimed to provide a broad overview of impairments associated with malaria across the spectrum of developmental domains, therefore the level of detailed analysis possible in a more narrowly-focussed study was not performed in these chapters. Chapter Twelve presents background data, concentrating on variables such as schooling, nutritional status and socioeconomic status, which were hypothesised to be factors influencing child development in the Kenyan context. Chapter Thirteen presents the results of investigations into the occurrence of epilepsy and the findings of the neurological examination, hearing test and visual screening. Chapter Fourteen focuses on the speech and language data and Chapter Fifteen presents the results of the cognitive and behavioural assessments. While these chapters concentrate on differences between the exposure and epilepsy groups, Chapter Sixteen describes the 'impaired' group, a subgroup of children with particularly poor comparative performance. Finally, Chapter Seventeen discusses the implications of the study's findings and possible directions for further study.

Chapter Twelve: Background Data

12.1 Introduction

This chapter presents background data to set the subsequent results chapters in context. The chapter first outlines the demographic characteristics of the cohort, followed by their level of school attendance, admissions data, pre- and perinatal history and developmental milestones. Socioeconomic and nutritional data are presented and the process of selection of variables for the regression models is described. Finally, assessment variables and the process of regression modelling are discussed.

12.2 Demographic characteristics

Seven hundred and forty-eight children were identified from the KEMRI unit databases, including all children previously admitted to Kilifi District Hospital (KDH) with previous CM who were 6-9 years of age at the time of the search and an equal number of children with a history of M/S. These children were identified from databases of admissions to KDH and children unexposed to CM or M/S were identified from surveillance databases (section 8.6). Of the 748 identified, 25 had subsequently died (14 CM, 5 M/S), 25 were found to be under/overage on confirmation of their birthdates (6 CM, 7 M/S), 211 were no longer at the same address (72 CM, 63 M/S), representing a follow-up of 70%. In addition, eight children from the unexposed group were transferred to the exposed groups due to admissions subsequent to the creation of the surveillance database (described in section 12.4.1). There were no refusals, although some children refused particular assessments: this will be detailed in each assessment section. Four hundred and eighty-seven children were recruited to the study, 152 children who had previously been hospitalised with CM, 156 children who had been in hospital with a diagnosis of M/S and 179 children unexposed to either condition. These numbers were less than the original recruitment aim of 300 children per group, due to the fact that the CM and M/S groups were limited to those of the required age, traceable from the unit databases, living within the designated study area.

Verification of the child's age proved to be an issue during the study, as some parents were unsure of the exact age of their child. Each parent was asked to provide the child's health card: this is issued to mothers who give birth in hospital or bring the child into hospital soon after birth for immunisations and gives an accurate record of the child's date of birth. If the parent had no health card, he/she was asked to provide a written document showing the child's birthdate. This usually took the form of a record sheet that some fathers keep of their children's birthdates.

Exposure group	Age verified with documentation		No documentation
	Health card (%)	Other (%)	provided (%)
CM	106 (70)	21 (14)	25 (16)
M/S	83 (53)	34 (22)	39 (25)
Unexposed	114 (64)	27 (15)	38 (21)

Table 12. 1: Method of age verification in the study cohort

Age verification by day and month was not possible with 21% of the children, a proportion that was slightly higher in the M+S group (table 12.1). However, when the two 'verification by documentation' subgroups were collapsed into one group, there was no significant difference between the three groups in the proportion of children with documentation compared to those without documentation (χ^2=3.41 p=0.18). Although the year of birth could be verified from the hospital records, month of birth was less certain in some cases, therefore children were divided into age categories by year in all statistical analyses.

The distribution of children among the age and sex groups was approximately equal (table 12.2). Two children had an age of 10:0, having just had a birthday before the day of assessment. These children were amalgamated into the 9 year age group.

	CM (%)	M/S (%)	Unexposed (%)
Male	77 (51)	72 (46)	93 (52)
Age 6 years	43 (28)	45 (29)	42 (23)
7 years	43 (28)	45 (29)	37 (21)
8 years	34 (22)	28 (18)	48 (27)
9 years	32 (21)	38 (24)	52 (29)
Total	152	156	179

Table 12. 2: Age and sex distributions in the study cohort

12.3 School attendance

School attendance is not obligatory in Kenya and schools. Although education is technically free, charges are levied in the form of fees for tuition, equipment, buildings, examination papers and security. In consequence, a child's attendance at school is usually determined by factors such as family income and size, although there have been no formal studies in the area to investigate the factors influencing school attendance. The official school starting age is 6 years but children often start later, particularly in rural areas.

There was a discrepancy between the three diagnostic groups in schooling status (table 12.3), with fewer children from the exposed groups attending school (χ^2=11.72 p=0.003). Of the children attending school, there was a higher proportion of children from the unexposed group in more advanced standards, although the difference was not significant (χ^2=3.59 p=0.47).

	CM (%)	M/S (%)	Unexposed (%)
No schooling	74 (49)	67 (43)	55 (31)
Nursery	47 (31)	54 (35)	62 (35)
Standard 1	19 (13)	24 (15)	39 (22)
Standards 2-4	12 (8)	11 (7)	23 (13)

Table 12. 3: Schooling status of the study cohort

It was unclear whether the lower rates of school attendance in the exposed groups were a cause or a consequence of exposure status. Therefore, a logistic regression model was created to measure the association between attending school and covariates that may be expected to have an effect on school attendance: diagnosis, age of child, sex of child, mother's education level and family income (represented by father's occupation) (table 12.4). The results suggest an association between a previous diagnosis of CM and not attending school.

	Variable	Odds ratio	95% C.I.	p-value
Exposure group	CM	0.48	0.3 – 0.77	0.002
	M/S	0.69	0.43 – 1.1	0.11
Age	7 years	1.55	0.94 – 2.59	0.001
	8 years	1.81	1.06 – 3.09	
	9 years	3.24	1.88 – 5.59	
Sex	Female	0.76	0.52 – 1.11	0.16
Mother's education	Lower primary	1.39	0.69 – 2.82	0.43
	Upper primary	1.81	1.13 – 2.89	
	Secondary/tertiary	1.84	0.62 – 5.42	
Income level	Large-scale farmer	1.01	0.49 – 2.05	0.04
	Casual worker	0.87	0.53 – 1.44	
	Small business	1.2	0.55 – 2.66	
	Large business /Professional	1.01	0.58 – 1.75	

Table 12. 4: Odds of school attendance between children with previous CM or M/S and children from the unexposed group

12.4 Admission data

12.4.1 Admissions in the unexposed group

Parents of children from the unexposed group were interviewed to see whether any admissions for severe malaria had taken place since the construction of the surveillance databases. All information was cross-checked on the databases using the in-patient numbers provided by the mothers, where available. As a result, eight children were transferred to the exposed groups (one to CM, seven to M/S) because they had previously been admitted with the respective diagnoses. Any children for whom the information given by the mother could not be verified with hospital records or did not fulfil the criteria for the exposed groups remained in the unexposed group (table 12.5).

Diagnosis	No. Children	Study ID number	Verified with hospital records?
CM	3	096, 108, 214	No
Malaria	7	022, 071, 102, 359, 387, 442, 453	Yes
Malaria/Anaemia	2	203, 437	Yes
URTI	1	032	Yes
LRTI	3	050, 207, 233	Yes
Pneumonia	1	110	No
Haemorrhoids	1	075	No
Corneal Perforation	1	226	Yes

Table 12. 5: Hospital admissions in the unexposed group

12.4.2 Age at admission

There was a broader range of ages and a trend towards older age at admission among children from the CM group compared to the M/S group (figure 12.1). The median age of admission among children with previous CM was 28 months (IQR 19-44 months) and among children with a history of M/S, 23 months (IQR 12-35 months).

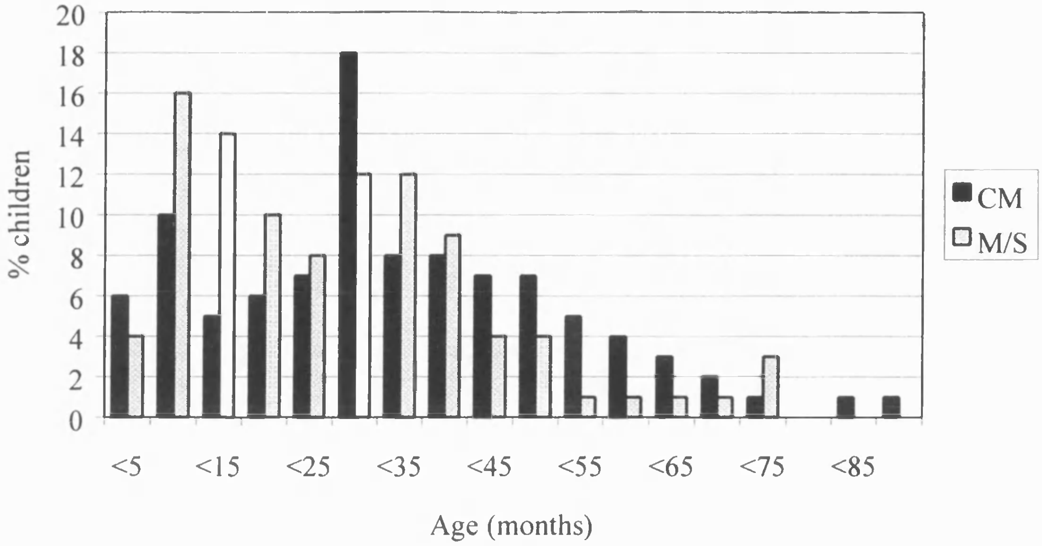

Figure 12. 1: Age of admission with CM or M/S

12.4.3 Time since admission

There was a larger proportion of children from the CM group with lower times since admission relative to the M/S group (figure 12.2). The median time since admission in the CM group was 64 months (IQR 40-78 months) compared to 71 months (IQR 55-85 months) in the M/S group. The minimum time since admission in either group was 20 months and the maximum was 112 months.

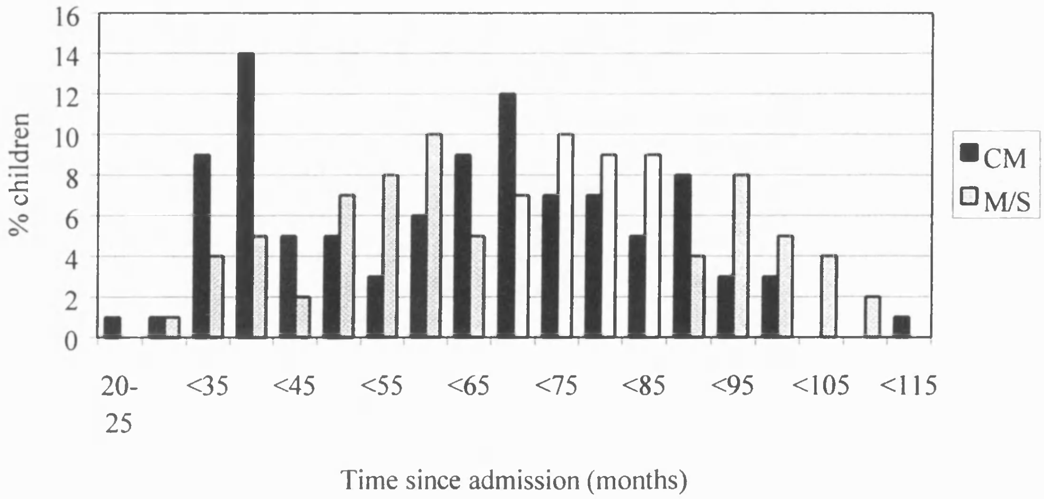

Figure 12. 2: Time since admission with CM or M/S

12.5 Obstetric and perinatal history

The obstetric and perinatal history was taken from the adult accompanying the child to hospital on day three of the protocol (section 8.8). On day two, the assessors requested that the mother accompany the child but in some cases, this was not possible, accounting for the 'don't know' responses in this section. The 'unspecified' category comprises instances in which the mother stated there was a problem but gave too little detail to ascertain whether the problem could result in harm to the foetus.

The CM group had the lowest number of problems during pregnancy (table 12.6) or during and after birth (table 12.7). The difference between the CM and unexposed groups in proportion of pregnancy-related problems was not significant (χ^2=0.48 p=0.49), although there was a significant difference in the relative frequency of perinatal difficulties, with 7.9% of the CM group having problems compared to 15.6% of the unexposed group (χ^2=4.64 p=0.03). Differences in proportions of problems between the M/S and unexposed groups were not significant (prenatal: χ^2=0.1 p=0.75; perinatal: χ^2=1.19 p=0.28). Individual children's results will be related to performance on developmental assessment in subsequent chapters, where applicable.

Problem	CM (%)	M/S (%)	Unexposed (%)	Total (%)
Anaemia	2 (1)	2 (1)	1 (0.5)	5 (1)
Haemorrhage	0	1 (0.5)	3 (1.5)	4 (1)
Pre-eclampsia	0	2 (1)	0	2 (0.5)
Unspecified	2 (1)	2 (1)	2 (1)	7 (1.5)
Don't know	2 (1)	3 (2.5)	4 (2)	9 (2)
None	146 (96)	146 (94)	169 (95)	461 (94)

Table 12. 6: Problems in pregnancy, reported by the mother

Problems	CM (%)	M/S (%)	Unexposed (%)	Total (%)
Prematurity	0	2 (1)	2 (1)	4 (1)
Twin birth	0	1 (0.5)	1 (0.5)	2 (0.5)
Foetal distress	3 (2)	4 (2.5)	6 (3.5)	13 (2.5)
Seizures after delivery	1 (0.5)	0	1 (0.5)	2 (0.5)
Neonatal jaundice	1 (0.5)	0	1 (0.5)	2 (0.5)
Unspecified	3 (2)	2 (1)	4 (2)	9 (2)
Don't know	4 (3)	9 (6)	13 (7)	26 (5)
None	140 (92)	138 (89)	151 (85)	429 (88)

Table 12. 7: Problems during or after delivery, reported by the mother

12.6 Developmental milestones

Information on the group's developmental status before hospital admission was collected to provide information on the proportion of children who may be expected to display poor performance on study assessments for reasons unrelated to exposure to severe malaria. These data were gleaned from each child's hospital records as this was considered to be a more reliable measure of pre-admission status than asking parents during the current study, years after the period in question. Only 87% of CM records and 34% of M/S records were found to contain this information. The discrepancy between the groups was due to the fact that most of the former group but only a proportion of the latter group would have been admitted to the high dependency unit, where neurological investigation is more detailed. In the 60% of cases where this information was elicited from parents, four questions were asked to determine whether the parent considered the child's ability to sit, stand, walk and speak to be age appropriate.

The proportion of children with possible delays in motor or language development was higher in the M/S group relative to the CM group (table 12.8). There was no indication of severity but more of the M/S group were reported to display delays in multiple domains than the CM group (6% vs 2%). Where appropriate, individual children's results will be related to developmental assessment performance in subsequent chapters.

	Sit (%)	Stand (%)	Walk (%)	Speak (%)	Total (%)
CM	0	1 (1)	2 (2)	8 (6)	9 (7)
M/S	2 (4)	3 (6)	3 (6)	3 (6)	5 (9)

Table 12. 8: Developmental milestones reported by the parent at the time of hospital admission

12.7 Socioeconomic status data

There are no established measures of socioeconomic status (SES) that predict child development in this area. The SES questionnaire comprised eight measures, of which the most relevant will be selected for inclusion in the analysis. The questionnaire results are presented in table 12.9 (except for 'number of siblings, which is graphically presented in section 12.7.2), although each measure will be discussed separately in sections 12.7.1 to 12.7.9.

	Variable	CM (%)	M/S (%)	Unexposed (%)
Respondent	Mother	130 (85)	136 (87)	153 (86)
	Father	4 (3)	8 (5)	6 (3)
	Other	18 (12)	12 (8)	20 (11)
Mother's education	No schooling	95 (63)	97 (62)	109 (61)
	Lower Primary	20 (13)	8 (5)	18 (10)
	Upper Primary	35 (23)	43 (28)	45 (25)
	Secondary	2 (1)	6 (4)	7 (4)
	Tertiary	0	2 (1)	0
Speaks English	Yes	21 (13.8)	36 (23.1)	33 (18.5)
Father's occupation	Subsistence farmer	65 (43)	62 (40)	90 (51)
	Large-scale farmer	15 (10)	17 (11)	10 (6)
	Casual labourer	37 (24)	33 (21)	33 (18)
	Small business	7 (5)	12 (8)	13 (7)
	Large business	28 (18)	32 (20)	33 (18)
Meals per day	Two	5 (3)	7 (4)	10 (6)
	Three	147 (97)	149 (96)	169 (94)
Flour milling	Grind	80 (53)	75 (48)	51 (28)
	Buy	72 (47)	81 (52)	128 (72)
Owns home	Yes	148 (97)	148 (95)	176 (98)
Owns other land	Yes	106 (70)	117 (75)	127 (71)
Mother's radio listening	Daily	53 (35)	40 (26)	50 (28)
	Weekly	7 (4)	6 (4)	8 (4)
	Irregularly	42 (28)	53 (34)	55 (31)
	Never	50 (33)	57 (36)	66 (37)

Table 12. 9: Results of the SES questionnaire, presented by exposure group

12.7.1 Respondent

The respondent was usually the child's mother, although other relatives (most often an aunt or grandmother who resided with the family) or the child's father occasionally provided the data if the mother was unavailable at the time (table 12.9). The proportion of different respondents was similar across the three groups (χ^2=2.94 p=0.57), therefore would not be expected to introduce any bias into one particular group.

12.7.2 Number of siblings

The distribution of sibling numbers was similar across the three groups (figure 12.3). The maximum number of siblings was 13. A multiple regression analysis comparing the groups' means showed no significant differences between the CM and unexposed groups (est. diff.=0.01 95%C.I.=-0.48 – 0.51 p=0.95) or the M/S and unexposed groups (est. diff.=0.06 95%C.I.=-0.43 – 0.55 p=0.81).

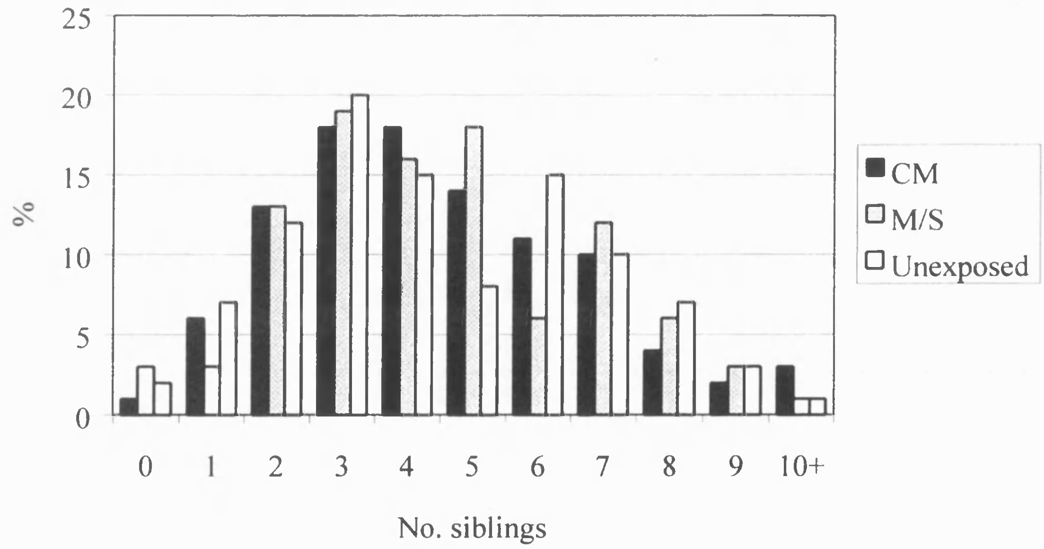

Figure 12. 3: Number of siblings, presented by exposure group

12.7.3 Mother's level of education

Over half of the mothers in the study had never attended school, in similar proportions in each group (χ^2=0.1 p=0.95) and very few had progressed to secondary or tertiary education (table 12.9). Those who had attended school were divided into two groups: those with lower-primary level education (between seven and 9 years of age) and those with any level higher than this. There was a significant difference in the proportions of mothers in each group (χ^2=7.28 p=0.03), primarily due to the difference between the CM and M/S groups.

12.7.4 Mother speaks English

Less than one quarter of mothers were able to speak English. There was a lower proportion of mothers of children from the CM group who were able to speak English, although the difference between the three groups was not significant (χ^2=4.38 p=0.11).

12.7.5 Father/main breadwinner's occupation

In most cases, the main breadwinner in the family was the father, therefore this measure will henceforth be referred to as 'father's occupation'. Almost half of the fathers were subsistence farmers (table 12.9). When the results were divided into subgroups of subsistence farmers compared to income-generating occupations, there was no evidence of a difference between the groups (χ^2=4.03 p=0.13). Twenty-six percent ran a business or had regular professional or skilled employment, which would tend to offer a regular income and more security (Hoorweg, et al., 1995). Although the categories were ordered according to the research team's perceptions of which occupations would confer higher status and economic resources, it is possible that the category of casual labourer would offer less because of the insecure nature of the work.

12.7.6 Meals per day

The locally-based assessors administering the questionnaire expressed surprised at the lack of variation in responses and the high number of families consuming three meals per day (table 12.9), commenting that this was not what their experience of the community would have suggested. These results may not be reliable as feedback from mothers indicated that the question was inappropriate, as it would be considered demeaning to admit to providing less than three meals per day. Koram and colleagues (1995) comment that some SES questions may not be answered reliably if the respondent thinks that a 'correct' or 'appropriate' answer is expected and particularly if he/she believes that the future care of the child depends upon the answer.

12.7.7 Flour milling

On administering the questionnaire, it became clear that most families combine grinding with buying flour, depending on the season. Families who grind their own maize are locally considered to be of higher SES status as they usually own land and have smaller families to feed. However, by the end of the dry season, even these families will often resort to buying flour as their stocks run low. After this became apparent, the question was altered to specify how the family obtains flour *most* of the year but it is possible that responses given before the alteration are unreliable due to confusion about whether the respondent was referring to the family's general practice or how they were obtaining flour at the time of interview .

The proportion of families from each diagnostic group grinding their own flour was significantly different (χ^2=22.76 p<0.001), primarily due to the lower proportion of grinding in the unexposed group compared to the exposed groups (table 12.9).

12.7.8 Land ownership

The majority of people responded that they owned the land they lived on (table 12.9), although less than half could produce a title deed. Land registration is only complete in some parts of the district (Hoorweg, et al., 1995). Families living in such areas have usually lived there for so long that they consider the land to be theirs. All pieces of other land were allotments or plots of farmland. Fewer families owned other land apart from that they lived on, in similar proportions in each group. There was no evidence of a difference between exposure groups (χ^2=1.17 p=0.56).

12.7.9 Mother listens to radio

This variable was selected in preference to ownership of a radio because community opinion was that some people, despite not owning one, regularly listen to radio broadcasts, a factor considered to represent a level of educational achievement and societal awareness. There was no evidence of a difference between the groups in percentage of mothers who ever listened to a radio compared to those who never did (χ^2=0.67 p=0.72) or between mothers who regularly (daily or weekly) listened compared to those who rarely or never did (χ^2=3.64 p=0.16).

12.7.10 Selection of SES variables

The results of the SES questionnaire suggested a high degree of homogeneity between the exposed and unexposed groups. The only significant difference was in method of obtaining flour, although difficulties in the administration of this item raised questions about the reliability of the responses. Thus, there are no measures that clearly differentiate between the exposure groups. In consequence, mother's level of education and father's occupation were selected as covariates in further analyses, on the basis that they are commonly used as measures of SES in studies of child development. Mother's level of education is often regarded as a predictor of child health and development in resource-poor countries (Coreil, 1997; Kvalsvig and Connolly, 1994). Father's occupation has been found to correlate with income level in previous studies on the Kenyan coast (Hoorweg, et al., 1995).

For mother's level of education, a dummy variable was created with 'no schooling' taking the value '0' and 'any level of schooling' taking the value '1'. A similar process was carried out for father's occupation, with 'farmer' (subsistence or large-scale) taking the value '0' and 'casual labourer', 'small business' and 'large business' combined taking the value '1'.

12.8 Nutritional data

The mean heights (cm) and weights (kg) of the cohort are presented by age and sex categories in table 12.10.

Sex	Age	Mean height (SD)	Mean weight (SD)
Male	6	110.74cm (5.88)	18.06kg (2.19)
	7	117.14 (6.31)	20.46 (2.53)
	8	120.47 (6.61)	21.41 (3.32)
	9	124.67 (6.51)	23.14 (3.07)
Female	6	110.84 (5.68)	17.77 (2.21)
	7	114.39 (6.03)	18.7 (2.54)
	8	120.55 (5.61)	21.1 (2.51)
	9	123.38 (6.43)	22.43 (2.74)

Table 12. 10: Mean height and weight of the cohort

Classifications of stunting, wasting or underweight were based on height or weight measurements more than two standard deviations below that expected on the basis of international growth references for a child's age and sex (Frongillo Jr., 1999). The prevalence of stunting (HAZ), wasting (WHZ) and underweight (WAZ) (table 12.11) is lower than the prevalence of 50.5%, 3.7% and 30.4% respectively, previously reported in Coast Province in Kenya (Ngare and Muttunga, 1999). However, classifications were based on z-scores *at* –2 or less in that study. If the current results are categorised on this basis, similar prevalence rates of 51%, 10% and 48% are found

	CM (%)	M/S (%)	Unexposed (%)	Total (%)
Stunted	36 (24)	28 (19)	25 (14)	89 (19)
Wasted	2 (1)	1 (1)	2 (1)	5 (1)
Underweight	19 (13)	16 (11)	13 (7)	48 (10)

Table 12. 11: Children diagnosed with low nutritional status

12.8.1 Weight/height scores

The distribution of weight/height z-scores is shown in figure 12.4. A multiple regression analysis, adjusted for age and sex, showed a significant difference in weight/height z-scores between the M/S and unexposed groups (est. diff.=0.17

95%C.I.=0.003 – 0.33 p=0.05) but not between the scores of the CM and unexposed groups (estimated difference=0.06 95%C.I.=-0.11 – 0.23 p=0.46).

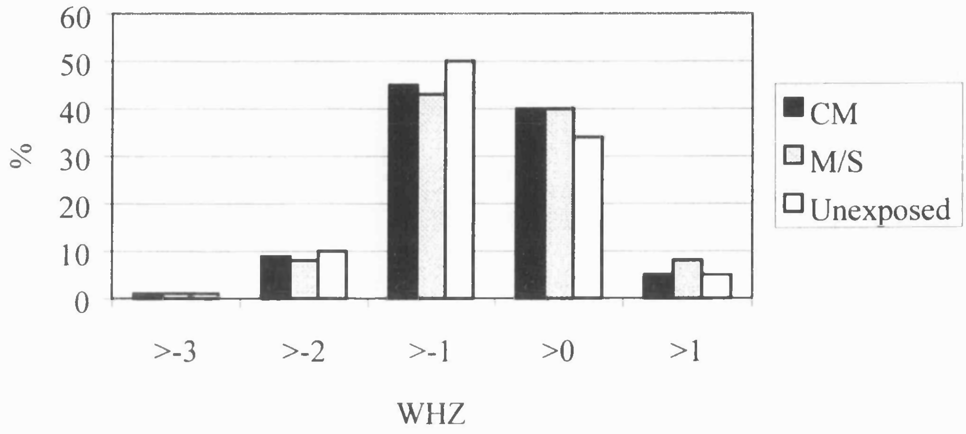

Figure 12. 4: Weight/Height z-scores (WHZ) by exposure group

12.8.2 Height/age scores

The distribution of weight/height z-scores is shown in figure 12.5. The height/age z-scores of children in the exposed groups were more broadly distributed than those of children in the unexposed group, although the differences, adjusted for age and sex, between the CM and unexposed groups (est. diff.=-0.14 95%C.I.=-0.39 – 0.11 p=0.28) and M/S and unexposed groups were not statistically significant (est. diff.=-0.05 95%C.I.=-0.29 – 0.2 p=0.72).

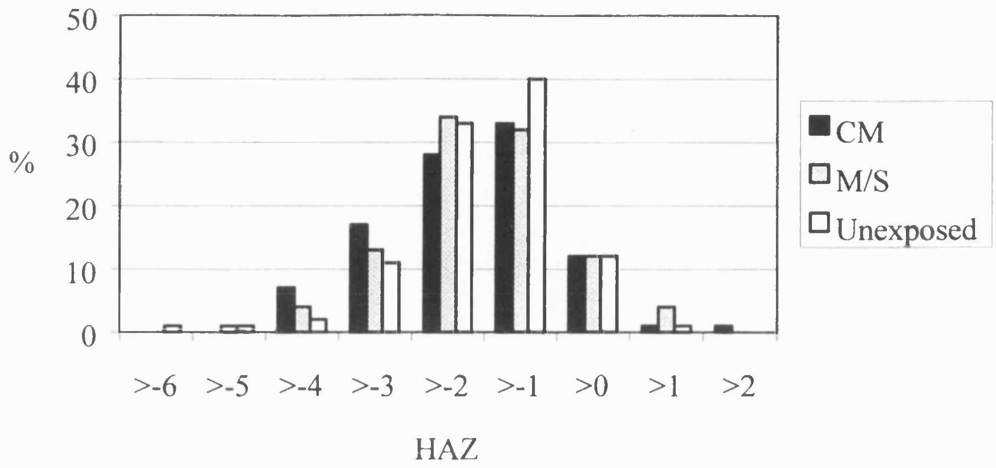

Figure 12. 5: Height/Age z-scores (HAZ) by exposure group

12.8.3 Weight/age scores

The distribution of weight/height z-scores is shown in figure 12.6. There was no evidence of a difference, adjusted for age and sex, in weight/age z-scores between the CM and unexposed groups (est. diff.=-0.03 95%C.I.=-0.21 – 0.16 p=0.76) or the M/S and unexposed groups (est. diff.=0.09 95%C.I.=-0.09 – 0.28 p=0.32).

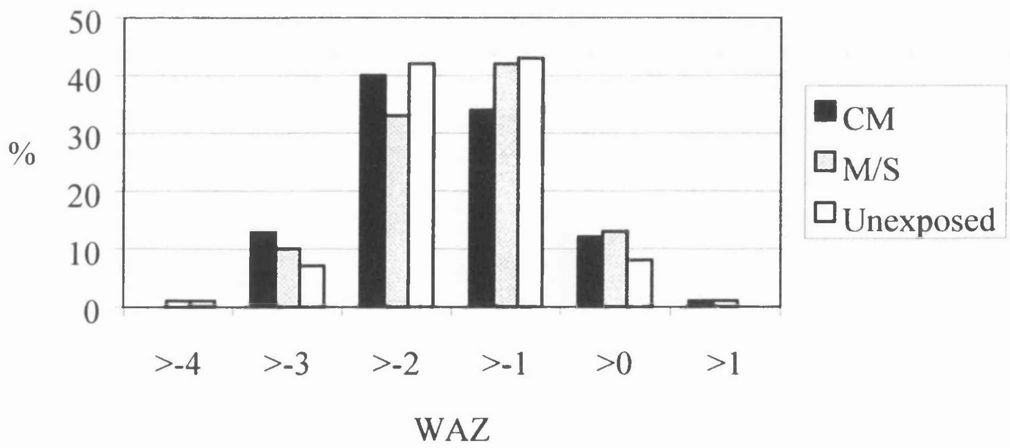

Figure 12. 6: Weight/Age (WAZ) z-scores by exposure group

12.9 Assessment variables

12.9.1 Assessor effect

The speech and language, cognitive and neurological assessments each had two assessors involved in their administration. Inter-rater reliability testing was carried out as part of the development of the speech and language battery (section 11.4.2). However, assessor variability was not directly tested for the cognitive or neurological assessments, therefore estimated differences in performance were examined to analyse the overall effect of different assessors.

Assessor 3 performed more cognitive assessments than assessor 4, although in similar proportions across the exposure groups (table 12.12). Multiple and logistic regression analyses of the cognitive assessments showed that there was a significant assessor effect on the number of errors made on the attention assessment, despite adjustment for age, sex, schooling status and diagnosis (OR=0.47 95%C.I.=0.24-0.91 p=0.03). There was no evidence of an effect on the other components of the cognitive battery.

Assessor ID	CM (%)	M/S (%)	Unexposed (%)	Total (%)
3	89 (59)	93 (60)	105 (59)	287 (59)
4	63 (41)	63 (40)	74 (41)	200 (41)

Table 12. 12: Number and proportion of cognitive assessments performed by each assessor

There was also a discrepancy in the numbers of children assessed on the neurological examination by each of the assessors involved in its administration. Assessor 5 saw more children than assessor 11, although in similar proportions across each group (table 12.13). A logistic regression analysis of assessor effect on the outcome of the examination (neurological deficit: yes/no) showed no evidence of any effect (OR=1.04 95% C.I.=0.48 – 2.25 p-value=0.92).

Assessor ID	CM (%)	M/S (%)	Unexposed (%)	Total (%) *
5	111 (74)	109 (72)	129 (73)	349 (73)
11	39 (26)	43 (28)	48 (27)	130 (27)

Table 12. 13: Number and proportion of neurological assessments performed by each assessor
* There were some refusals

12.10 Regression modelling

As stated in section 8.9.2, an *a priori* decision was made to adjust all estimates for speech/language, cognition and behaviour for age, sex, schooling status, nutritional status and socioeconomic status and estimates for the neurological assessment for age and sex. All variables were categorical. Age was divided into yearly brackets because of the difficulties with age verification (section 12.2) and because it was not possible to assume a linear relationship between age as a continuous variable and outcome. The creation of dummy SES variables is described in section 12.7.10. For nutritional status, three dummy variables were generated. For weight/age and height/age, a z-score of more than –3 took the value '0' and one of less than –2 took the value '1'. For weight/height, a z-score of more than –2 took the value '0' and one of less than –1 took the value '1'.

12.11 Summary and discussion

The aim of this chapter was to provide background information on the cohort's medical history and the variables that had been selected as covariates in the analysis of the developmental measures.

There were few differences between the exposure groups in socioeconomic status, indicating that the group was generally homogeneous in nature. Due to the lack of previous information on apposite measures of SES in this community, it is unclear whether this is a genuine finding or merely a indication of the insensitivity of the measures selected for the study, although a previous study in this geographical area also found a high level of homogeneity among the Mijikenda community (Holding, 1998). Measures such as 'flour milling' may prove to be useful means of stratifying the community in future but there is little evidence at present of what they are actually assessing.

As expected, the nutritional level of the cohort was lower than that of their US counterparts but similar to that found in other studies on the Kenyan coast (Ngare and Muttunga, 1999). Few children attained z-scores of more than 0 on any of the nutritional measures, indicating that a large proportion of the group have experienced chronic inadequacies in nutrition and/or health. The only significant difference between the exposed and unexposed groups was found in the M/S group measure of weight/height, on which children with previous M/S had significantly higher z-scores.

Few children were reported to have experienced perinatal insults and developmental milestones were adequate in the majority of children for whom this information was available, establishing a baseline developmental level for the groups. Individual cases will be referred to, where appropriate, in subsequent chapters.

In summary, these data have established that the groups are comparable on most of the major determinants of cognitive and language development. Variables exhibiting group differences, such as schooling status, will be included as covariates in further analyses, as outlined in the previous section. This chapter has also confirmed there was no evidence of selection bias in the recruitment procedure. All children in the target age range previously admitted to Kilifi District Hospital with a history of CM or M/S were identified and a random sample of children unexposed to these conditions was selected from surveillance databases. This avoids the potential selection bias incurred when unexposed participants are chosen by asking members of the community or by visits to local households to identify eligible children.

Chapter Thirteen: Neurological Results

13.1 Introduction

Most previous studies of neurological impairment associated with CM have focussed on deficits in motor and movement, in addition to gross deficits in other domains (section 2.3.3). Almost 11% of survivors of CM are reported to have neurological deficits on discharge from hospital: motor and visual deficits often appear to improve within six months of discharge (Newton and Krishna, 1998), although there has been no long-term follow-up of such problems. In addition, there are few data on epilepsy and no published studies comparing prevalence of epilepsy in children with a history of severe malaria to that in children unexposed to the condition.

This chapter presents the results of the epilepsy questionnaire, electroencephalogram (EEG), neurological examination and visual acuity and hearing screening. The characteristics of children diagnosed with epilepsy will be reported and comparisons made between the exposure groups made using logistic regression.

13.2 Epilepsy questionnaire

13.2.1 Prevalence of epilepsy

A diagnosis of epilepsy was based on the findings of the epilepsy questionnaire administered to parents. Children whose parents reported two or more seizures, at least one of which was unrelated to fever in those under 6 years of age were classed as having epilepsy. There was an increased prevalence of epilepsy in children who had previously been admitted with CM (OR=4.4 95%C.I.=1.42 – 13.69 p=0.01) or M/S (OR=6.1 95%C.I.=2.02 – 18.25 p=0.001) compared to the unexposed group (table 13.1).

	CM (%)	M/S (%)	Unexposed (%)
Epilepsy	14 (9.2)	18 (11.5)	4 (2.2)
Active epilepsy	7 (4.6)	10 (6.4)	2 (1.1)
Inactive epilepsy	7 (4.6)	8 (5.1)	2 (1.1)
Total	152	156	179

Table 13. 1: Prevalence of epilepsy by exposure group

Although the prevalence of epilepsy was higher in the M/S group compared to the CM group, there was no evidence of a significant difference between the M/S and CM groups (OR=1.29 95%C.I.=0.62 – 2.69 p=0.5).

The father of one boy (age 8:4) from the CM group came to the hospital several months after assessment, requesting help for the child's seizures, which were occurring up to three times per week. On questioning, he said that the child was having seizures at the time of assessment but that he was too embarrassed to admit it at the time. The boy remained in the 'no epilepsy' group on the basis that according to the design of the study, epilepsy status was determined by the parental interview taken at the time of assessment.

13.2.2 'Active epilepsy' group

Active epilepsy was defined as two or more seizures (not related to fever in those aged 6 years) with at least one in the previous 12 months. Nineteen children were reported to have active epilepsy, seven from the CM, ten from the M/S and two from the unexposed groups (table 13.2).

Seizure type was determined according to the ILAE classification (section 3.2). The most commonly reported seizure types were tonic-clonic (42%), partial becoming secondary generalised (16%) and both (21%). Only two instances of other seizure types – one each of complex partial seizures without secondary generalisation and tonic seizures, both in children from the M/S group – were reported. One of the seizure types described was unable to be classified.

Seizures ranged from 'infrequent' (less than one per month) to several times per week. As seven of the children had two seizure types, the age of onset and occurrence of provoking factors sometimes varied with type. Data on age of onset from the current study indicated that seizure onset occurred after hospital admission in 11/17 cases. Review of the parental comments recorded in the hospital notes at the time of admission indicated that 9/17 parents reported no previous seizures at that time, including three (ID 053, 191, 487) of those who indicated an age of onset indicative of pre-admission seizures in the current study. Three parents reported previous febrile seizures when interviewed on the child's admission to hospital, although the separation of febrile and unprovoked seizures is not clear. Five notes gave no information on pre-admission seizure history. Thus, there was a discrepancy between parental reports at the time of hospital admission and during the current study.

Only two of the children were receiving any medication: one child was taking Sodium Valproate (400mg/day) and the other, Phenobarbitone (90mg/day). Another child (ID 487) was reported to have taken Phenobarbitone before the age of six. All other children were referred to the Neurology Clinic at Kilifi District Hospital for treatment after participation in the study.

						Seizure Characteristics				
ID no.	Grp	Sex	Age y:m	Age adm	Time adm*	Age of onset	Type/s	Freq. **	Provoked	AED
034	CM	F	9:4	2:10	6:6	1 day	TC/SG	3 pw	No	No
036	CM	F	9:7	3:1	6:6	3:1	TC	1 pm	No	No
053	CM	M	9:11	2:0	7:11	1:0	TC/US	1 pm	No	No
193	CM	M	7:0	1:2	5:10	0:9	SG	1 pm	No	No
306	CM	F	6:10	4:2	2:8	6:0	TC	infreq	No	No
435	CM	M	8:0	5:8	2:4	2 wks/7:5	TC/SG	3 pw	FI/FI	No
487	CM	F	7:4	3:1	4:3	2:5	TC	1 pw	No	No
028	M/S	F	8:4	1:3	7:1	1:0/2:0	CP/TC	1 pw	FI/No	SV
062	M/S	F	7:9	3:0	4:9	4:0	TC	1 pm	No	No
094	M/S	M	9:5	1:7	7:10	2:0/9:0	TC/US	infreq	FI/FI	No
191	M/S	F	7:8	0:10	6:10	0:3	TC	infreq	No	No
241	M/S	M	6:3	3:9	2:5	5:0	TC/SG	infreq	FI/NFI	No
253	M/S	F	7:7	3:0	4:7	1:0/6:0	TC/SG	5 pw	FI/No	No
265	M/S	M	7:4	0:10	6:6	0:11	TA	infreq	No	No
268	M/S	F	9:0	3:3	5:9	4:0	TC	infreq	No	No
404	M/S	F	8:0	6:7	1:5	6:8	SG	1 pm	No	PB
428	M/S	F	6:3	4:2	2:1	2:0	SG	2 pm	No	No
444	Un	M	7:0	n/a	n/a	2:0	TC	infreq	No	No
458	Un	M	6:10	n/a	n/a	2:6	TC	infreq	No	No

Table 13. 2: Characteristics of children with active epilepsy

Seizure type: TC tonic-clonic
SG partial becoming secondary generalised
CP complex partial
TA tonic
US unclassifiable

Seizure frequency: pw per week
pm per month
infreq infrequent

Provoked: FI febrile illness
NFI non-febrile illness

Anti-epileptic drugs (AED): SV Sodium Valproate
PB Phenobarbitone

* Time since hospital admission
** Indicates the highest frequency at which seizures have been experienced

13.2.3 'Inactive epilepsy' group

Inactive epilepsy was defined as two or more seizures (at least one of which was not related to fever in those at or below 6 years of age), none of which occurred within the past 12 months. There were seventeen children with inactive epilepsy: seven from the CM, eight from the M/S and two from the unexposed groups (table 13.3).

As with the active epilepsy group, tonic-clonic (41%) and partial becoming secondary generalised (41%) seizures were the most commonly reported seizure types. Simple partial seizures and occurrences of two seizure types (secondary generalised/tonic-clonic and simple partial/tonic seizures) were each reported by one parent.

Seizure frequency ranged from infrequent to three times per week. Information on age of onset from the questionnaire indicated that seizure onset occurred after hospital admission in 6/14 cases. At the time of admission, eight of the parents reported no previous seizures, including seven who reported an age of onset indicative of previous seizures when interviewed for the current study. The eighth parent from this group (ID 190) reported previous febrile seizures at the time of the child's admission to hospital. Five sets of notes gave no information. The children's last seizures ranged from 1 year to 7 years and 9 months before the date of assessment.

None of these children had received anti-epileptic medication.

						Seizure Characteristics				
ID no	**Grp**	**Sex**	**Age y:m**	**Age adm**	**Time adm**	**Age of onset**	**Last seizure (age)**	**Type/s**	**Freq.**	**Provoked**
138	CM	M	8:11	3:3	5:8	1:0	5:0	TC	3 pm	No
167	CM	M	6:6	2:4	4:2	4:0	5:6	SG	infreq	No
190	CM	F	9:3	1:6	7:9	0:6	4:2	SG	1 pm	FI
279	CM	M	6:3	1:2	5:1	3:0	5:0	TC	1 pw	No
333	CM	M	9:0	3:2	5:10	3:2	7:1	SG	infreq	No
395	CM	F	6:0	3:3	2:9	3:3	4:1	TC	infreq	No
469	CM	F	7:10	no info*	no info	4:0	4:7	SG	infreq	No
086	M/S	M	9:8	1:4	8:4	8:0/8:0	8:3/8:3	SP/TA	infreq	FI/FI
093	M/S	F	9:11	2:10	7:1	2:0	7:0	SG	3 pm	No
121	M/S	F	9:10	2:6	7:4	0:8	2:1	SP	infreq	No
124	M/S	F	9:11	2:3	7:8	1:0	3:0	SG	2 pm	No
176	M/S	F	9:3	2:4	6:11	0:8	8:0	TC	3 pw	No
201	M/S	F	7:3	2:11	4:4	2:0	2:6	TC	infreq	No
228	Un	M	7:9	n/a	n/a	6:6	6:6	TC	infreq	No
307	M/S	M	7:3	2:7	4:8	2:11/2:11	4:6	SG/TC	infreq	FI/NFI
446	M/S	M	9:5	5:7	3:10	0:10	7:0	SG	1 pw	No
476	Un	M	8:8	n/a	n/a	0:9	6:8	TC	1 pw	No

Table 13. 3: Characteristics of children with inactive epilepsy

Key same as Table ** except:
Seizure type: SP simple partial
* Hospital records unavailable

The families of a subgroup (n=81) of the current cohort completed a seizure history questionnaire as part of a related study, which the candidate assisted in, investigating the evidence for a familial predisposition for seizures in children exposed to CM or M/S. The results suggested an increased prevalence of seizures in relatives of the CM and M/S subgroups compared to relatives of the unexposed subgroup, although the methodology precluded investigation of whether causation was genetic or environmental (Versteeg, et al., 2002).

13.3 Electroencephalographic data

All participants consented to undergo the EEG, although 37 children (18 CM, 9 M/S, 10 unexposed) refused to hyperventilate and one child (CM) refused the photic stimulation procedure. The EEGs were interpreted by an experienced neurophysiologist. Twenty children (6 CM, 8 M/S, 6 unexposed) had abnormalities on their EEG recording (table 13.4). Epileptiform activity, defined as spikes, sharp waves and spike and wave complexes, occurred in only nine of the total cohort. The EEG focal features categories included both epileptiform abnormalities and non-specific focal slow wave abnormalities: both were uncommon. Activation procedures resulted in abnormalities in three children with photic stimulation and five children with hyperventilation.

	EEG abnormality	CM (%)	M/S (%)	Unexposed (%)
Epileptiform activity	Epileptiform activity	2 (1.3)	6 (3.8)	1 (0.6)
	Focal temporal	0	3 (2.0)	1 (0.6)
	Focal extra-temporal	2 (1.3)	4 (2.6)	0
	Multifocal	0	1 (0.7)	0
	Generalised	0	2 (1.3)	0
Focal features	All	5 (3.3)	6 (3.8)	3 (1.7)
	Temporal	3 (2.0)	4 (2.6)	3 (1.7)
	Parieto-occipital	2 (1.3)	5 (3.3)	1 (0.6)
	Photosensitivity	0	2 (1.3)	1 (0.6)
	Hyperventilation	2 (1.3)	1 (0.7)	2 (1.1)

Table 13. 4: Electroencephalographic (EEG) abnormalities

Five children from the epilepsy groups presented with EEG abnormalities (table 13.5), representing 26.3% of the active epilepsy group or 13.8% of both epilepsy groups. Three (ID 404, 428, 446) had been diagnosed with secondary generalised seizures, one (ID 034) with tonic clonic and secondary generalised seizures and one (ID 053) with tonic clonic and unclassifiable seizures.

There were six children from the non-epilepsy groups who had epileptiform activity on their recording. They were invited back to Kilifi District Hospital and re-interviewed with specific questions to probe for complex partial seizures or Benign Rolandic epilepsy. None of the children were reported as having these or any other forms of epilepsy.

	Active epilepsy group		**Inactive epilepsy group**	
Abnormality	**Yes**	**ID no**	**Yes**	**ID no**
Epileptiform activity	2	404/428	1	446
Focal temporal	1	404	1	446
Focal extra-temporal	1	404	1	446
Multifocal	2	404/428	0	-
Generalised	1	404	0	-
Focal features: All	4	034/053/404/428	1	446
Temporal	4	034/053/404/428	1	446
Parieto-occipital	3	053/404/428	0	-
Photosensitivity	1	428	0	-
Hyperventilation	0	-	0	-

Table 13. 5: EEG abnormalities in children with epilepsy

13.4 Neurological examination

The candidate was not involved in the design or execution of the neurological examination, despite overseeing the logistics of its administration and analysing the results, and it did not comprise a focal part of the current study. Therefore, the findings will only be presented in outline.

The examination comprised an assessment of cranial nerve function, motor function and minor neurological dysfunction. Thirty-four children had abnormalities detected, with 10.5% and 8.3% of children exposed to CM and M/S respectively having neurological abnormalities. These findings represent a significantly higher proportion of problems on univariate analysis in the exposed groups compared to the unexposed group (CM vs unexposed: χ^2=8.27 p=0.004; M/S vs unexposed: χ^2=5.03 p=0.03).

The abnormalities were categorised according to a hierarchical classification of spasticity, ataxia and fine motor dysfunction (table 13.6). Children diagnosed with 'spasticity' also showed signs of ataxia and fine motor dysfunction and children categorised as 'ataxic' also displayed fine motor dysfunction. Ataxia was the most common deficit found in each exposure group: this broad term disturbance in control of posture and movement and does not necessarily imply cerebellar dysfunction. The results are presented in detail in Appendix 25.

Neurological abnormality	CM (%)	M/S (%)	Unexposed (%)
Yes	16 (10.5)	13 (8.3)	5 (2.8)
No	136 (89.5)	143 (91.7)	174 (97.2)
Spasticity	6 (3.9)	4 (1.3)	1 (0.6)
Ataxia	9 (5.9)	8 (5.1)	3 (1.7)
Fine motor	1 (0.7)	1 (0.6)	1 (0.6)

Table 13. 6: Prevalence and type of neurological abnormalities by exposure group

Exposure to CM or M/S did not significantly increase the odds of having a neurological abnormality in a multivariate analysis (table 13.7). The odds were significantly higher for children with active epilepsy: eight children with active epilepsy and three children with inactive epilepsy were diagnosed with neurological abnormalities. Thirty-six percent (n=4) of this subgroup were diagnosed with spasticity, 55% (n=6) with ataxia and 9% (n=1) with fine motor dysfunction.

	Variable	Odds ratio	95% C.I.	p-value
Exposure group	CM	2.17	0.82 – 5.71	0.12
	M/S	1.42	0.5 – 3.99	0.51
Epilepsy status	Active epilepsy	9.22	3.03 – 28.04	<0.001
	Inactive epilepsy	2.92	0.72 – 11.88	0.13
Age	7 years	1.89	0.64 – 5.58	0.54
	8 years	1.37	0.41 – 4.59	
	9 years	2.1	0.71 – 6.16	
Sex	Female	1.37	0.65 – 2.9	0.4
Nutritional status	Weight/height	0.8	0.22 – 2.89	0.74
	Height/age	2.36	0.82 – 6.79	0.11
	Weight/age	2.04	0.56 – 7.44	0.28
SES status	Mother's education	1.13	0.52 – 2.47	0.75
	Father's occupation	1.39	0.66 – 2.92	0.39

Table 13. 7: Odds of neurological deficits in children with previous CM or M/S and children from the unexposed group

Neurological assessment of gross developmental skills, performed by a physician, is the mainstay of diagnosis of malaria-related impairments across Africa. The current study presented interesting anecdotal evidence on the capacity of such assessment techniques to identify children with deficits in cognition or language. Although not part of the specific remit of the current neurological assessment, the assessors reported any gross impairments of this nature apparent during the course of the examination. Eight children were identified with impairments in cognition and language, four of whom (ID 184, 253, 451, 471) were part of a 'low functioning' group, described further in section 16.2, and four of whom (ID 098, 138, 151, 174) presented no evidence of impairment on the cognitive and language assessments (Appendix 28).

13.4.1 Fronto-occipital circumference

There were no significant differences in fronto-occipital circumference measurements (table 13.8), adjusted for age and sex, between the CM and unexposed groups (est. diff.=-0.21 95%C.I.=-0.51–0.1 p=0.18) or M/S and unexposed groups (est. diff.=0.01 95%C.I.=-0.29–0.32 p=0.94).

	Mean (SD)	Minimum	Maximum
CM	50.1cm (1.6)	45.5cm	53.5cm
M/S	50.3 (1.49)	46.5	55
Unexposed	50.4 (1.51)	46.5	54.8

Table 13. 8: Fronto-occipital circumference measurements, by exposure group

13.5 Visual screening

Before assessment, parents were asked to report any possible visual problems. The visual acuity screening test was administered to these children before the other assessments to ensure that any impairments were detected before participation in other study activities requiring visual skills. Eight parents reported possible visual problems, although only one of the eight children was diagnosed with an impairment on screening. After further discussion with the seven other parents, the remaining positive responses were thought to be due to misunderstanding of the question or possible attention deficits in the children. Alternatively, these findings may be partly explained by the possibility that continued research work in this community has created expectations among some of the local population that participation in research projects will lead to improved health care (Dr S Molyneux, personal communication).

Visual acuity measurements were uncorrected. One child (unexposed) scored 6/18 in each eye, which is classed as moderate visual impairment according to the Sonksen-Silver Acuity System. This child had been admitted to hospital as an infant with corneal perforation (section 12.4.1), therefore the impairment was not caused by a refractive error, so corrected measurements were not taken. This child was excluded from further assessments involving the use of pictorial material. No other visual impairments were detected.

13.6 Hearing screening

Parents were asked to report possible hearing problems before assessment, resulting in forty positive responses, including those of four of the 11 diagnosed with impairments on screening. No impairment was detected for the other 36 children and after discussion with the parent, most of the positive responses were thought to be due to misunderstanding of the question, intermittent hearing difficulties resulting from infections or attention deficits in the children.

Seven children, who formed part of a low functioning group of children (section 6.2), could not complete the examination due to lack of understanding of task demands. A simple distraction test was performed with these children to determine the presence of severe or profound hearing loss. All of the children responded appropriately and none of their parents reported noting difficulties with their hearing.

Detected impairments were mild and in one case, moderate (table 13.9). There were no severe or profound deficits. The numbers are too small for group comparisons, although there is little difference in prevalence between the three groups. Of the 11 children with impairments, three were male, one was 6 years, five were 7 years, three were 8 years and two were 9 years of age. Two of the children, both with mild impairments, had abnormalities (debris and excess wax) detected on otoscope examination. Diagnostic audiometry was not available to determine whether detected impairments were conductive or sensori-neural.

	Mild (%)	**Moderate (%)**
CM	4 (2.6)	0
M/S	2 (1.3)	0
Unexposed	4 (2.2)	1 (0.6)

Table 13. 9: Hearing impairments detected by audiometric screening

Children with impairments were referred to the hospital's ENT department for further examination. These levels of hearing loss were not considered to preclude participation in the cognitive and speech/language assessments. Assessors were informed of the screening findings in these cases and asked to ensure that the assessment venue was quiet and that they spoke clearly to the child and checked that the child heard and understood all test instructions.

Three children (27%) were subsequently found to have impaired performance on some of the language and cognitive assessments (section 16.5). The child with moderate hearing loss (ID 484) demonstrated impaired performance on the lexical semantics, higher level language and pragmatics assessments. One child from the CM group with mild hearing loss (ID 375) was impaired on a broad range of speech and language assessments (receptive grammar, receptive vocabulary, higher level language, word finding, phonology) and on the test of attention. The third child, from the unexposed group, had an impairment-level performance on the receptive vocabulary and syntax assessments. Although it is possible that their hearing deficits prevented these children from understanding assessment task demands, thus from giving a performance representative of their abilities, it may be expected that if this were the case, impaired performance would have been found on the majority of tasks in which verbal instructions were given. In addition, the child with a moderate hearing deficit was impaired in pragmatics, which was assessed using a parental questionnaire. Conceivably, these hearing deficits had contributed to the speech and language impairments detected.

13.7 Summary and discussion

CM and M/S were both associated with an increased prevalence of epilepsy compared to children unexposed to these conditions. The prevalence of epilepsy in the CM group was similar to that hypothesised from the evidence of encephalitic CNS infection (10%) (Annegers, et al., 1988) and that found in the reports of bacterial meningitis reviewed in Chapter Two (8.7% mean prevalence). The prevalence of epilepsy in the M/S group was much higher than that hypothesised from the evidence of complicated febrile seizures (4.5%) (Annegers, et al., 1979), which suggests that the complicated seizures experienced in severe malaria are associated with an increased risk of CNS damage relative to complicated febrile seizures. Seizures occurring in CM, particularly those witnessed during hospital admission, are associated with increased risk of subsequent death (Molyneux, et al., 1989): if the occurrence of seizures during the malaria episode is also implicated in the later development of epilepsy, it is possible that a proportion of these children may have died, thus reducing the numbers surviving with epilepsy.

In other studies of CNS infections, the prevalence of epilepsy increases up to 20 years post-infection (Annegers, et al., 1988), so the prevalence in the exposed groups may also increase over time. However, a previous study in the same geographical area has suggested that people with epilepsy have a higher risk of death (Snow, et al., 1994), which may affect the prevalence.

The prevalence of epilepsy in the unexposed group was higher than that found in other studies of children without previous seizures or CNS infection (0.5%) (Hauser and Kurland, 1975). Both incidence and prevalence estimates are often higher in resource-poor countries (Sander and Shorvon, 1996; Senanayake and Roman, 1993), although international comparisons can be problematic because of lack of uniformity in case definitions. Snow and colleagues (1994) reported that 0.3% of 6-9 year olds from the same geographical area as the current cohort had epilepsy. The discrepancy between these and the current findings may be explained by the fact that the current study employed a detailed questionnaire to elicit information about all types of seizures, whereas the method of questioning adopted by Snow and colleagues was limited to questions to a key informant about the occurrence of 'kifafa' or 'vitsala' (Kigiryama terms to describe mainly tonic-clonic epilepsy).

The link between hospital admission and seizure onset was difficult to determine because of the prevalence of febrile seizures in this population, the problems of separating these from epileptic seizures and the difficulties of ascertaining ages accurately. The most commonly reported seizure types were tonic-clonic and partial becoming secondary generalised. There was only one reported case of complex partial seizures. These seizures are often not recognised as forms of epilepsy in resource-poor countries (Senanayake and Roman, 1992) and as mentioned above, the most commonly used terms for epilepsy specifically relate to the tonic-clonic type. Therefore, it is possible that the epilepsy questionnaire was not sensitive enough to identify other seizure types. However, the EEG data provided little evidence of epileptiform activity in the temporal lobe.

There was little evidence of an association between epileptiform activity on the EEG and a diagnosis of either active or inactive epilepsy: more children without reported epilepsy presented with epileptiform activity than children with reported epilepsy.

Flink and colleagues (2002) state that a routine EEG recording in a child with epilepsy will have no epileptiform activity in approximately 50% of cases: the proportion in the current epilepsy group was higher, suggesting that the EEG recording was not sensitive to epileptiform abnormalities. There also seemed to be little association between seizure type and EEG abnormalities.

Plasmodium falciparum appears to be particularly epileptogenic. Falciparum malaria was the most common cause of acute seizures in children admitted to the hospital from which the current exposure group were drawn: 84% of children had no other signs of neurological involvement and seizures were complex in 54% of cases, even at rectal temperatures below 38°C (Waruiru, et al., 1996). A Thai study found that even at similar peak temperatures, seizures were twice as likely to occur in children with falciparum than vivax malaria, even when children with a diagnosis of CM were excluded (Wattanagoon, et al., 1994). The current findings suggest that there is an association between malaria and epilepsy but give no indication regarding causality. A pre-existing susceptibility to epilepsy may result in a propensity to develop seizures during malaria or to suffer subsequent neurological impairment (Versteeg, et al., 2002). Conversely, malaria may result in an increased risk of epilepsy.

The father who admitted giving false information due to embarrassment about his son's seizures is an interesting example of the stigma associated with epilepsy in many resource-poor countries (Birbeck, 2000; Danesi, 1984; Debruyn, 1990). This factor was not directly investigated in the study so it is not possible to know whether his was an isolated case or an indication of a more widespread phenomenon, possibly more prevalent in fathers than in mothers, who were the main respondents of the epilepsy questionnaire. However, it is possible that reliance on reported seizures to determine occurrence in a community in which there may be reluctance to disclose signs of epilepsy resulted in an underestimation of the prevalence of the disorder.

There were significant differences between the exposed and unexposed groups on a univariate analysis of the neurological examination results, although a multivariate analysis suggested that most of the variance was due to epilepsy status. Ataxia, broadly defined as disturbance in the control of posture and movement, was the most common abnormality in each exposure group. Active epilepsy was associated with significantly higher odds of a neurological abnormality on multivariate analysis. Although a large proportion of children with neurological abnormalities also had epilepsy, neither active or inactive epilepsy was associated with higher proportions of more severe abnormalities (spasticity or ataxia) relative to CM or M/S.

No severe impairments were detected on the hearing test and visual screening identified no impairments in either of the exposed groups. Mild to moderate hearing deficits were equally as common in the exposed and unexposed groups. Other studies of CM have also found low levels of impairment in the special senses: 0.7% (van Hensbroek, et al., 1997) and 1.6% (Bondi, 1992) with hearing loss. Cortical visual impairment following CM is common on discharge but tends to resolve. Only two (0.4%) of a cohort of 452 Gambian children admitted with CM were found to have visual field defects 6 months after discharge (van Hensbroek, et al., 1997), indicating the consistency of the current findings, from a smaller cohort after a longer follow-up.

In summary, the increased prevalence of epilepsy found in each of the exposed groups suggests an association between malaria and epilepsy but provides no information on causality. There was little evidence of complex partial seizures, either from the epilepsy questionnaire administered to the parents or from the level of epileptiform activity in the temporal lobe recorded on the EEG. The proportion of children with neurological deficits was higher in the exposed groups relative to the unexposed group, although the odds of impairment on this assessment was highest in children with active epilepsy.

Chapter Fourteen: Speech and Language Results

14.1 Introduction

Persisting impairments in speech and language have been reported but have not been investigated in detail prior to the current study. The speech and language battery comprised eight assessments: receptive grammar, receptive vocabulary, syntax, lexical semantics (expressive vocabulary), higher level language, pragmatics, phonology and word finding. The results for each assessment will be examined in turn, presenting a summary of the performance of each exposure group and an analysis of the differences in performance by exposure group and epilepsy status.

14.2 Summary of results

The volume of data presented in this chapter is quite large, therefore the results will be summarised before being presented in more detail. Table 14.1 summarises the performance of the exposed groups (CM and M/S) relative to the unexposed group and table 14.2 summarises the performance of the epilepsy groups relative to the no epilepsy group.

	CM	**M/S**
Lower estimated scores	Receptive vocabulary Lexical semantics Higher level language Pragmatics Phonology Word finding	Lexical semantics Pragmatics Phonology
Significant difference in estimated scores	Lexical semantics Higher level language Pragmatics	Pragmatics Phonology

Table 14. 1: Summary of speech and language assessment findings in the CM and M/S groups relative to the unexposed group

	Active Epilepsy	Inactive epilepsy
Lower estimated scores	Lexical semantics Higher level language Phonology	Receptive grammar Lexical semantics Word finding
Significant difference in estimated scores	Receptive grammar Receptive vocabulary Syntax Pragmatics Word finding	–

Table 14. 2: Summary of speech and language assessment findings in the active and inactive epilepsy groups relative to the no epilepsy group

14.3 Receptive grammar assessment

One child (M/S) refused the receptive grammar assessment and one child (unexposed) was unable to complete it due to a visual impairment.

The results of the assessment approximated a normal distribution (figure 14.1). In the boxplot presented in figure 14.1 (and all subsequent boxplots), the box illustrates the interquartile range (IQR) and the central horizontal line, the mean or median. Outliers, represented by circles, constitute data points more than 1.5IQR beyond the first or third quartile.

There was a broader distribution of scores, slightly lower mean scores and lower minimum scores in the exposed groups compared to the unexposed group. The maximum possible score was 34.

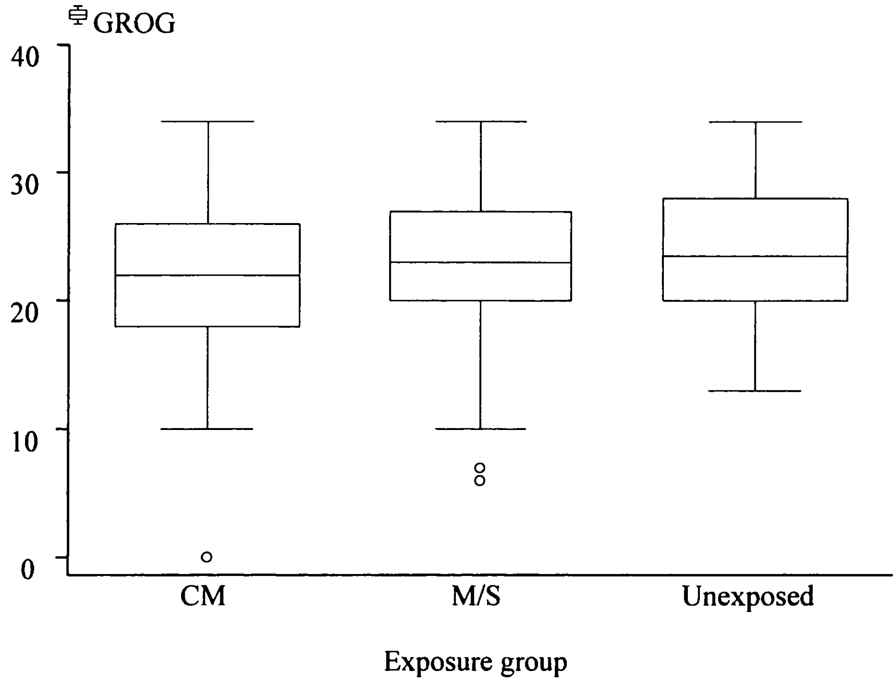

Figure 14. 1: Distribution of receptive grammar (GROG) scores by exposure group

There was no evidence of a difference in performance between the exposed and unexposed groups on the receptive grammar assessment (table 14.3). However, children with active epilepsy had significantly lower scores than those without epilepsy. This effect was not seen in the inactive epilepsy group, although the direction of the association with the no epilepsy group suggested a poorer performance among children with inactive epilepsy.

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	0.25	-0.64 to 1.14	0.59
	M/S	0.87	-0.01 to 1.76	0.06
Epilepsy status	Active epilepsy	-3.34	-5.23 to -1.45	0.001
	Inactive epilepsy	-0.46	-2.36 to 1.47	0.65
Age	7 years	1.69	0.68 to 2.69	<0.001
	8 years	3.35	2.29 to 4.42	
	9 years	3.32	2.19 to 4.46	
Sex	Female	0.15	-0.58 to 0.87	0.69
Schooling status	Nursery	2.25	1.39 to 3.12	<0.001
	Standard 1	6.78	5.63 to 7.93	
	Standard 2	7.72	6.26 to 9.18	
Nutritional status	Weight/height	-0.03	-1.35 to 1.28	0.96
	Height/age	-0.86	-2.06 to 0.33	0.16
	Weight/age	-0.88	-2.49 to 0.73	0.28
SES status	Mother's education	0.45	-0.34 to 1.23	0.26
	Father's occupation	-0.2	-0.94 to 0.54	0.6

Table 14. 3: Estimated differences in receptive grammar scores between the exposed and unexposed groups

14.3.1 Vocabulary check

The receptive grammar assessment was designed primarily to provide a quantitative measure of this aspect of comprehension. Vocabulary cards were designed to provide an elementary level of qualitative analysis on the nature of any impairments identified: however, aspects of the materials and administration of this section of the test proved problematic. One hundred and forty-seven children (30%) from the total cohort failed the vocabulary check, defined as correct naming of less than 85% of the cards. Failure was associated with schooling status (all failures occurred in children either not schooling or attending nursery) and age (51% failure rate in 6 year olds versus 13% in 9 year olds), a pattern replicated in all of the cognitive and speech and language assessments. A logistic regression model, adjusted for age, sex and schooling status suggested no difference in the odds of failure between the CM

(OR=0.93 95%C.I.=0.53 – 1.62 p=0.79) or M/S (OR=0.76 95%C.I.=0.43 – 1.33 p=0.34) groups compared to the unexposed group.

The speech and language assessors suggested that the high failure rate may be partly explained by difficulties with the pictures and the method of naming them. Verbs and adjectives, out of the context of a sentence, were difficult to depict. Certain pictures, such as 'kutsukula' ('to carry'), were particularly problematic, in this case because it became clear during the course of the study that colloquially, this verb specifies carrying a heavy load, whereas the picture showed a person carrying a light load. Adjective naming proved confusing for some children: Kigiryama adjectives must agree with the noun they are qualifying (section 7.3.1), yet the adjectives were named in their 'stem' versions. In addition, the results of the vocabulary tested in the first three sections (nouns, verbs, adjectives) of the assessment itself suggested that poor performance on the vocabulary check may have been influenced by difficulties inherent in its administration and materials. Ninety-seven percent of the cohort (with similar proportions across individual exposure groups) attained the maximum score on the 'nouns' section and 87% on the 'verbs' section. Forty-five percent achieved the maximum score on the 'adjectives' section, although 97% attained at least a score of '1'.

Failure on the vocabulary check was associated with lower mean and minimum scores on the receptive grammar assessment (table 14.4) but the results were not analysed further due to lack of confidence in the reliability of the findings.

Vocab. check pass	Number of children	Mean score Score	SD	Minimum score	Maximum score
N	147	17.9	4.3	0	27
Y	339	24.9	4.5	14	34

Table 14. 4: Summary of receptive grammar scores by vocabulary check results

14.3.2 Error analysis

Four pictures were presented for each assessment question: the target picture, a grammatical distractor, a lexical distractor and an unrelated picture (with the exception of the six questions measuring single nouns, verbs and adjectives, which comprised a target picture and three unrelated pictures). Grammatical errors were more common than lexical errors but error analysis did not identify any obvious patterns in the question types resulting in poorer levels of performance in each exposure group (Appendix 26).

14.4 Receptive vocabulary assessment

Two children did not complete the receptive vocabulary assessment, one (CM) refused and the other (unexposed) had a visual impairment, thus was unable to undertake it. The distribution of results was skewed (figure 14.2), with a broader distribution of scores in the CM group compared to the M/S and unexposed groups. The median scores were the same across the three groups, although the minimum scores were lower in the CM and M/S groups compared to the unexposed group. The maximum possible score was 25.

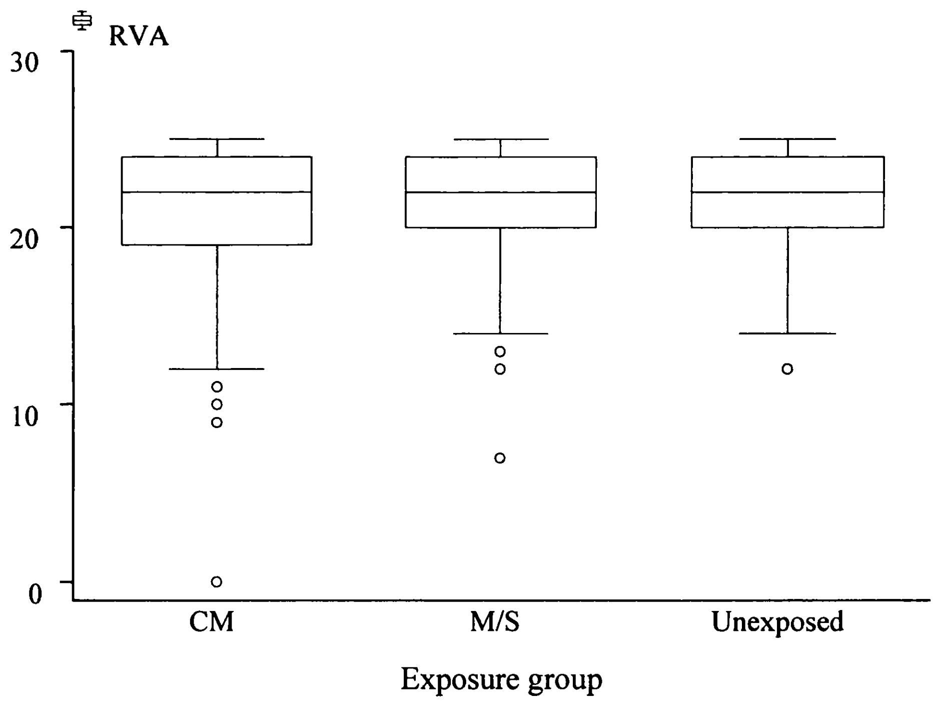

Figure 14. 2: Distribution of receptive vocabulary assessment (RVA) scores by exposure group

A transformation could not be found that produced a normal distribution of this data, thus it was analysed as a binary outcome. A logistic regression analysis of the results (cut-off at 19) showed no evidence of a difference in performance between the CM or M/S groups compared to the unexposed group on this assessment (table 14.5). Children with active epilepsy performed significantly worse than children without epilepsy: this effect was not seen in the inactive epilepsy group.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	1.29	0.65 to 2.58	0.47
	M/S	0.8	0.39 to 1.67	0.55
Epilepsy status	Active epilepsy	6.43	2.01 to 20.56	0.002
	Inactive epilepsy	0.45	0.05 to 4.18	0.49
Age	7 years	0.45	0.23 to 0.87	<0.001
	8 years	0.17	0.07 to 0.42	
	9 years	0.1	0.03 to 0.28	
Sex	Female	1.03	0.59 to 1.8	0.92
Schooling status	Attends school *	0.36	0.19 to 0.66	0.001
Nutritional status	Weight/height	1.24	0.48 to 3.22	0.65
	Height/age	2.09	0.94 to 4.67	0.07
	Weight/age	1.49	0.52 to 4.26	0.45
SES status	Mother's education	0.5	0.25 to 0.98	0.04
	Father's occupation	0.79	0.44 to 1.42	0.43

Table 14. 5: Estimated odds of poorer performance on the receptive vocabulary assessment between the exposed and unexposed groups

* Used because standards 1 and 2 predict failure perfectly

14.5 Syntax assessment

Four children (2 CM, 2 M/S) did not complete the Syntax assessment because they had very limited speech. One of these children (M/S) had active epilepsy. The results of the assessment approximated a normal distribution (figure 14.3). There was a broader distribution of scores in the CM group compared to the M/S and unexposed groups. The mean and minimum scores were lower in the CM group compared to the M/S and unexposed groups. The maximum possible score was 40.

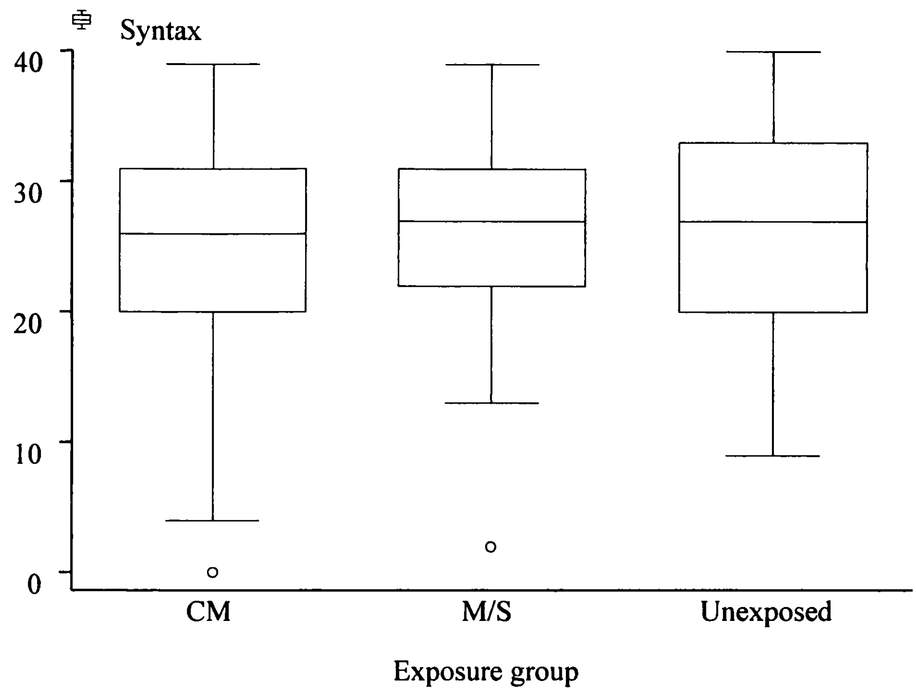

Figure 14. 3: Distribution of syntax assessment scores by exposure group

There was no evidence of a difference in performance between the CM and unexposed groups on this assessment (table 14.6). The M/S group had a significantly better performance than the unexposed group. Children with active epilepsy had a significantly poorer performance than children without epilepsy. There was no evidence of a difference between the scores of children with inactive and no epilepsy, although the direction of the association suggested better performance among the children with inactive epilepsy.

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	0.07	-1.16 to 1.3	0.91
	M/S	1.26	0.05 to 2.48	0.04
Epilepsy status	Active epilepsy	-3.13	-5.8 to -0.47	0.02
	Inactive epilepsy	1.9	-0.74 to 4.55	0.16
Age	7 years	0.81	-0.59 to 2.21	<0.001
	8 years	4.15	2.68 to 5.63	
	9 years	5.59	4.02 to 7.16	
Sex	Female	-1.25	-2.25 to -0.24	0.02
Schooling status	Nursery	2.15	0.94 to 3.35	<0.001
	Standard 1	6.35	4.76 to 7.94	
	Standard 2	7.17	5.15 to 9.19	
Nutritional status	Weight/height	-0.92	-2.72 to 0.89	0.32
	Height/age	-1.71	-3.37 to -0.06	0.04
	Weight/age	-1.27	-3.49 to 0.95	0.26
SES status	Mother's education	1.05	-0.03 to 2.13	0.06
	Father's occupation	0.27	-0.76 to 1.3	0.61

Table 14. 6: Estimated differences in syntax assessment scores between the exposed and unexposed groups

Individual item performance, as measured by the percentage of the maximum score attained for each question, was similar across the three exposure groups (Appendix 26).

14.6 Lexical semantics

The lexical semantics assessment generated two scores, type-token ratios (TTR) for function words (referred to as the 'minor TTR' by Crystal, 1992) and content words (the 'major TTR'; Crystal, 1992). Both ratios have a potential maximum score of 1.0, although in practice such a score would not occur as it would mean that the child had only used each word he/she spoke once. Both the function (minor TTR, abbreviated to MIR) and content word (major TTR, abbreviated to MAR) scores were normally distributed (figures 14.4 and 14.5).

The mean and minimum function word scores were similar across the three groups. Both the CM and M/S groups had a broader distribution of scores and higher maximum scores relative to the unexposed group.

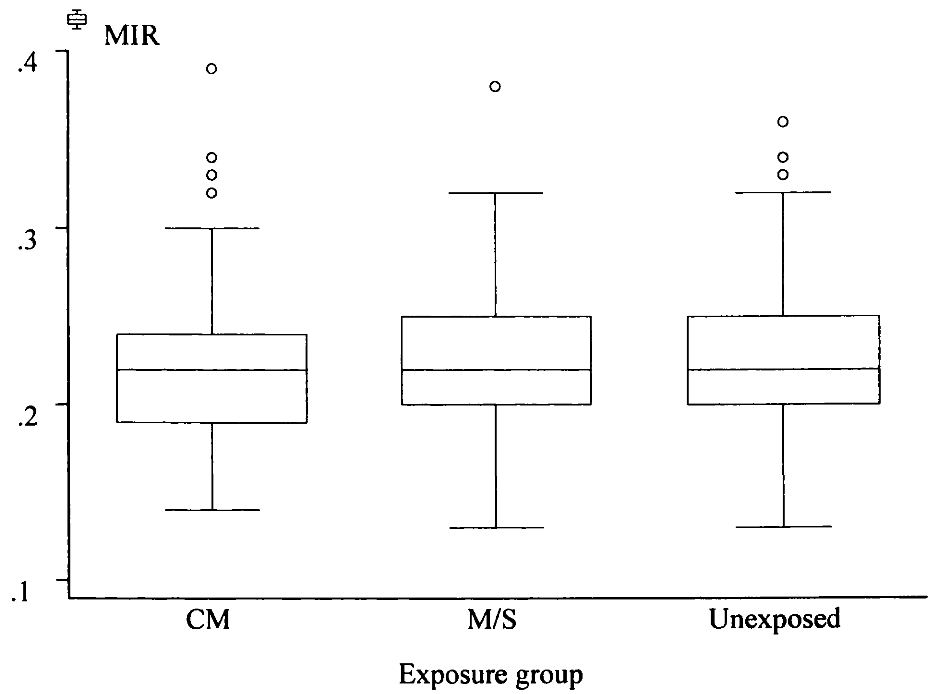

Figure 14. 4: Distribution of function word (MIR) scores by exposure group

In contrast, the mean scores for the content word section were lower in both exposed groups in comparison to the unexposed group. Figure 14.5 illustrates that the distribution of scores in the CM group is shifted down relative to the distributions of the other two groups.

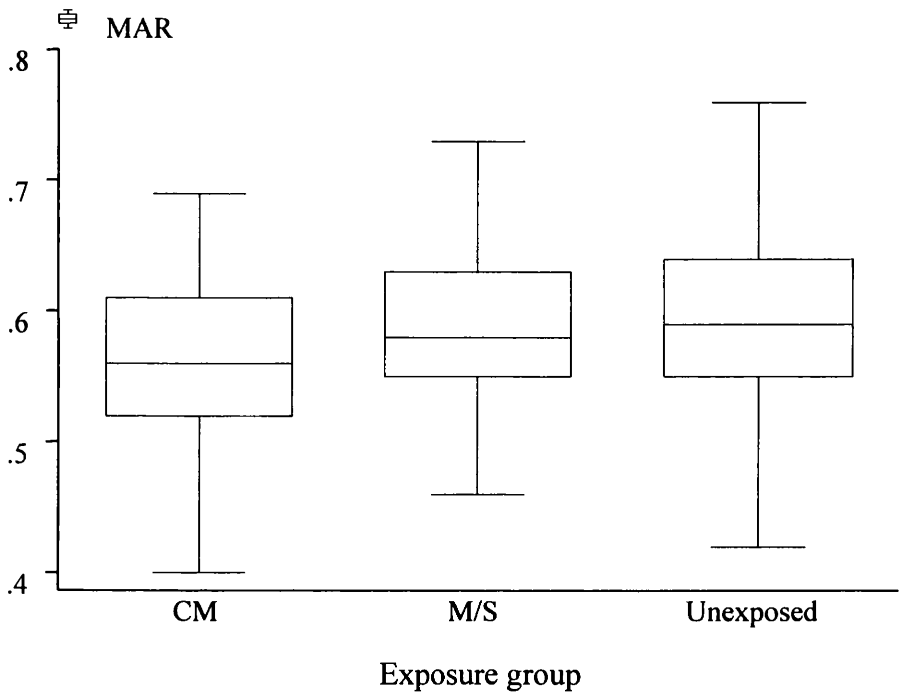

Figure 14. 5: Distribution of content word (MAR) scores by exposure group

In order to obtain a representative measurement of vocabulary, assessors encouraged children to produce language samples of at least 100 words. Forty-six children (23 CM; 12 M/S; 11 Unexposed) were unable to produce a language sample of sufficient length for the lexical semantics assessment. Seventy-two percent of this subgroup were not attending school and 78% were in the younger age groups (6 or 7 years of age). Three (1 CM; 2 M/S) had active epilepsy. However, adjusting for age, sex and schooling status, the estimated odds of producing a limited speech sample were still 2.42 (95% C.I.=1.12 – 5.25 p=0.04) higher in the CM group compared to the unexposed group.

The mean length of utterance (MLU) was calculated to give an indication of the amount of speech this subgroup produced. Four children, two each from the CM and the M/S groups, produced no speech sample at all: they had limited speech, reportedly producing only single words or short phrases, and were unable to attempt many of the assessments in the battery. The MLU for the remaining 42 children ranged from 2.1 to 4.2 with a median score of 3.3, which lay below the 14th centile of MLU scores for the whole study cohort.

There was no evidence of a difference in performance between the exposed and unexposed groups or the epilepsy and no epilepsy groups on function word production (table 14.7).

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	-0.01	-0.02 to 0.003	0.2
	M/S	-0.001	-0.01 to 0.01	0.74
Epilepsy status	Active epilepsy	0.01	-0.01 to 0.03	0.23
	Inactive epilepsy	0.003	-0.02 to 0.02	0.77
Age	7 years	-0.001	-0.01 to 0.01	0.76
	8 years	-0.01	-0.02 to 0.01	
	9 years	-0.001	-0.01 to 0.01	
Sex	Female	-0.002	-0.01 to 0.01	0.49
Schooling status	Nursery	0.003	-0.01 to 0.01	0.89
	Standard 1	-0.001	-0.01 to 0.01	
	Standard 2	-0.001	-0.02 to 0.01	
Nutritional status	Weight/height	-0.01	-0.02 to 0.01	0.47
	Height/age	0.002	-0.01 to 0.02	0.69
	Weight/age	0.01	-0.01 to 0.02	0.52
SES status	Mother's education	0.002	-0.01 to 0.01	0.58
	Father's occupation	-0.01	-0.01 to 0.003	0.22

Table 14. 7: Estimated differences in lexical semantics (function words) assessment scores between the exposed and unexposed groups

There was a significant difference in performance in content word production between the CM and unexposed groups, although not between the M/S and unexposed groups (table 14.8). There was no evidence of a difference between the epilepsy and no epilepsy groups, although the direction of the association between the groups suggested poorer performance among children with epilepsy.

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	-0.02	-0.04 to -0.01	0.002
	M/S	0.001	-0.01 to 0.01	0.9
Epilepsy status	Active epilepsy	-0.01	-0.04 to 0.02	0.49
	Inactive epilepsy	-0.01	-0.03 to 0.02	0.7
Age	7 years	0.01	-0.01 to 0.02	0.52
	8 years	0.01	-0.01 to 0.03	
	9 years	0.002	-0.02 to 0.02	
Sex	Female	0.004	-0.01 to 0.02	0.55
Schooling status	Nursery	0.03	0.02 to 0.05	<0.001
	Standard 1	0.03	0.01 to 0.05	
	Standard 2	0.03	0.01 to 0.05	
Nutritional status	Weight/height	0.01	-0.02 to 0.03	0.63
	Height/age	0.01	-0.01 to 0.03	0.47
	Weight/age	-0.01	-0.04 to 0.02	0.51
SES status	Mother's education	0.01	-0.01 to 0.02	0.43
	Father's occupation	-0.01	-0.02 to 0.01	0.26

Table 14. 8: Estimated differences in lexical semantics (content words) assessment scores between the exposed and unexposed groups

14.7 Higher level language assessment

Four children (CM) refused the higher level language assessment and one child (M/S) was unable to complete any of the tasks because of her limited language. The results of the higher level language assessment were normally distributed (figure 14.6). The exposed groups had lower mean and minimum scores compared to the unexposed group. The total possible score was 39. The distributions of scores in the CM and M/S groups were shifted downwards relative to that of the unexposed group.

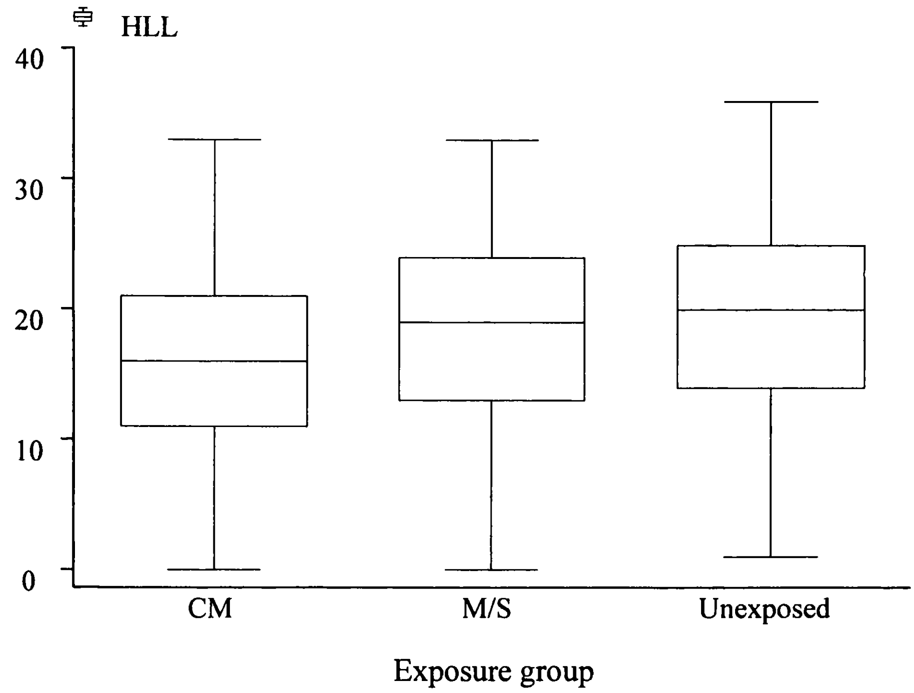

Figure 14. 6: Distribution of higher level language (HLL) assessment scores by exposure group

Analysis of the individual tasks suggested a trend towards poorer performance in the CM group compared to the other groups (Appendix 26). This was particularly marked in the sentence formulation task, although the results indicated that the distribution of scores in the CM group relative to the other groups (figure 14.6) is due to a consistent reduction in performance across the tasks rather than the effect a large difference in one task.

There was a significant difference in performance between the CM and unexposed groups (table 14.9). No evidence of a difference was found between the M/S and unexposed groups or the epilepsy and no epilepsy groups. However, the direction of the association between the active and no epilepsy groups suggested a poorer performance in the former.

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	-1.63	-2.99 to -0.27	0.02
	M/S	0.37	-0.98 to 1.71	0.59
Epilepsy status	Active epilepsy	-0.74	-3.62 to 2.13	0.61
	Inactive epilepsy	0.52	-2.39 to 3.44	0.72
Age	7 years	1.29	-0.25 to 2.83	<0.001
	8 years	3.37	1.73 to 5.0	
	9 years	5.48	3.75 to 7.21	
Sex	Female	-0.13	-1.24 to 0.99	0.83
Schooling status	Nursery	2.71	1.39 to 4.04	<0.001
	Standard 1	6.1	4.34 to 7.85	
	Standard 2	8.8	6.58 to 11.03	
Nutritional status	Weight/height	0.33	-1.67 to 2.34	0.75
	Height/age	-1.16	-2.99 to 0.66	0.21
	Weight/age	-2.27	-4.75 to 0.21	0.07
SES status	Mother's education	1.06	-0.13 to 2.26	0.08
	Father's occupation	0.18	-0.96 to 1.32	0.75

Table 14. 9: Estimated differences in higher level language assessment scores between the exposed and unexposed groups

14.8 Pragmatics questionnaire

The parental pragmatics questionnaire, based on the The Pragmatics Profile (Dewart and Summers, 1995), was divided into three sections comprising nine, six and five questions respectively. Each question had a maximum score of five. The results are presented by section.

14.8.1 Communicative functions

The maximum score for the communicative functions section was 45. The distribution of scores was skewed, with a median score of 42 in each group (figure 14.7). The exposed groups had broader distributions of scores and lower minimum scores than the unexposed group. Item analysis highlighted areas of difference between the exposed and unexposed groups. A smaller proportion of children in the CM group (86%) compared to the unexposed group (96%) attained the maximum score in the 'attention directing to others' question (χ^2=8.01 p=0.01). A larger proportion of children with previous CM (9%) were assigned the minimum scores (gives too much or too little information) on the 'giving information' question relative to the unexposed group (2%) (χ^2=9.58 p=0.002). The minimum score on the 'humour' question (never makes jokes) was given to a larger proportion of children with previous CM (10%) than their unexposed group counterparts (2%) (χ^2=10.73 p=0.001). Six percent of children from the M/S group were also given the minimum score on the latter question, again representing a significant difference to the proportion of unexposed children assigned this score (χ^2=6.08 p=0.01).

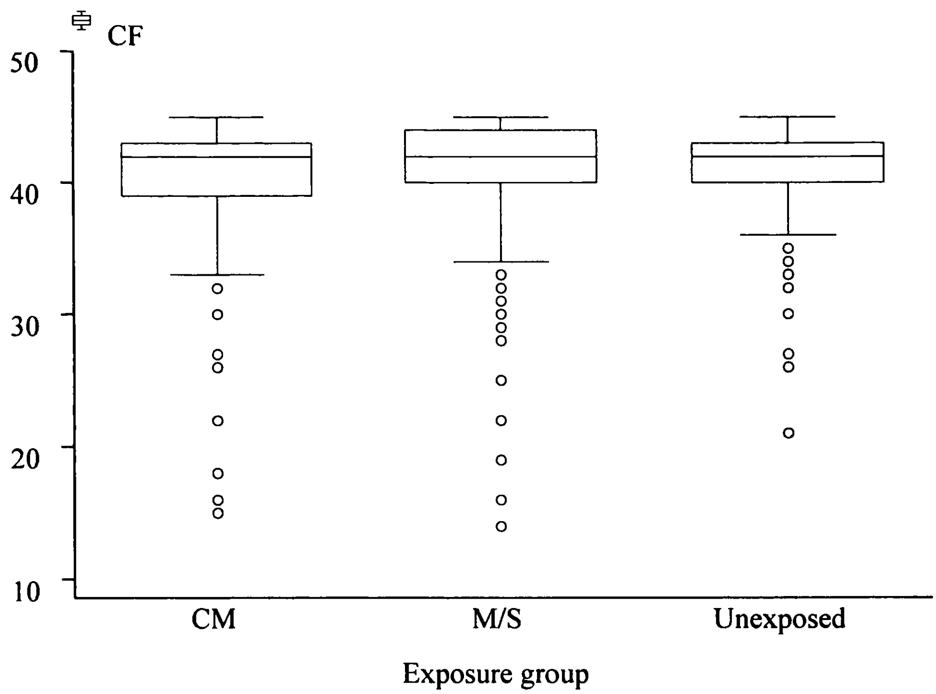

Figure 14. 7: Distribution of communicative functions (CF) scores by exposure group

14.8.2 Response to communication

The maximum score for the response to communication section was 30. The results were skewed with median scores of 24, 22 and 23 for the CM, M/S and unexposed groups respectively (figure 14.8). Both exposed groups had lower minimum scores compared to the unexposed group.

Differences in reported performance between the M/S and unexposed groups were more apparent in this section. Seventeen percent of children with previous M/S were reported to never demonstrate metalinguistic awareness compared to 6% of the unexposed group (χ^2=10.33 p=0.001) and 6% to laugh for no apparent reason ('responding with amusement' question) relative to 1% of the unexposed group (χ^2=5.73 p=0.02). Twenty-five percent of children from the M/S group were reported to never request clarification if asked to carry out an activity that he/she did not understand, compared to 15% of children from the unexposed group (χ^2=5.32 p=0.02). The proportion of low scores was larger in the CM group relative to the unexposed group on all questions apart from the 'gaining attention' and 'sarcasm' items. The differences were statistically significant on the 'metalinguistic awareness' (χ^2=6.35 p=0.01) and 'responding with amusement' (χ^2=5.9 p=0.02) questions.

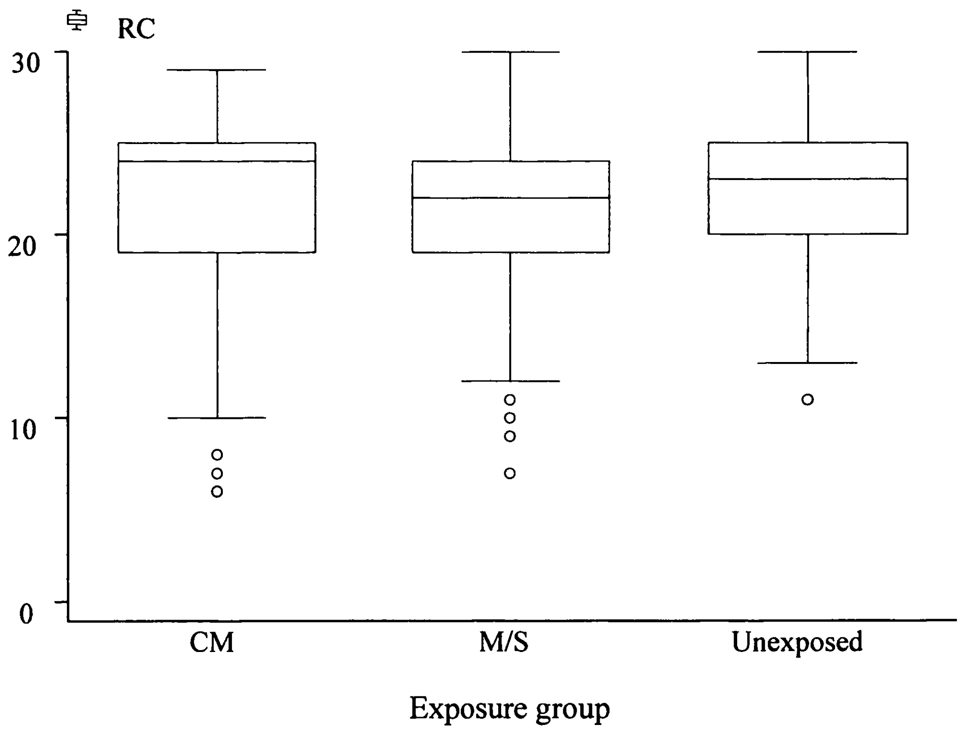

Figure 14. 8: Distribution of response to communication (RC) scores by exposure group

14.8.3 Interaction and conversation

The maximum score for the interaction and conversation section was 25. As with the previous two sections, the distribution of interaction and conversation scores was skewed (figure 14.9). The median scores of the CM, M/S and unexposed groups were 22, 23 and 24 respectively. The exposed groups had broader distributions of scores and lower minimum scores compared to the unexposed group.

Areas of reported difficulty for the CM group were conversational repair and presupposition (appendix 14.9). Twenty-seven percent of children were assigned the minimum score for the 'conversational repair', reportedly becoming upset and giving up if not understood during conversation, compared to 16% of children from the unexposed group (χ^2=5.72 p=0.02). Forty-eight percent of children with previous CM had limited skills in presupposition, offering too much or too little information, compared to 28% of the unexposed group (χ^2=14.26 p<0.001). Children from the M/S group were reported to have little interest in interaction ('is left on the sidelines' or 'only talks to one other child') relative to the unexposed group (χ^2=7.88 p=0.01) and to have no idea how to appropriately terminate a conversation (χ^2=6.03 p=0.01).

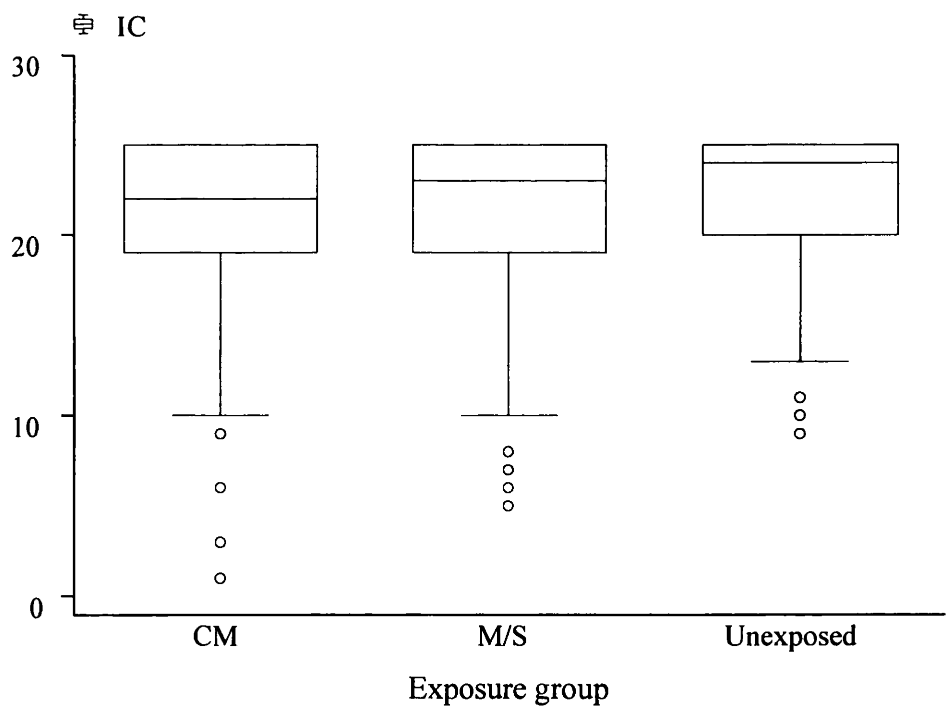

Figure 14. 9: Distribution of interaction and conversation (IC) scores by exposure group

In summary, the trend in scores across the three sections was for little difference in median scores across the three groups, a cluster of children with high scores and larger numbers of outliers in the exposed groups relative to the unexposed group. This pattern can be seen in the distribution of the total questionnaire scores (figure 14.10).

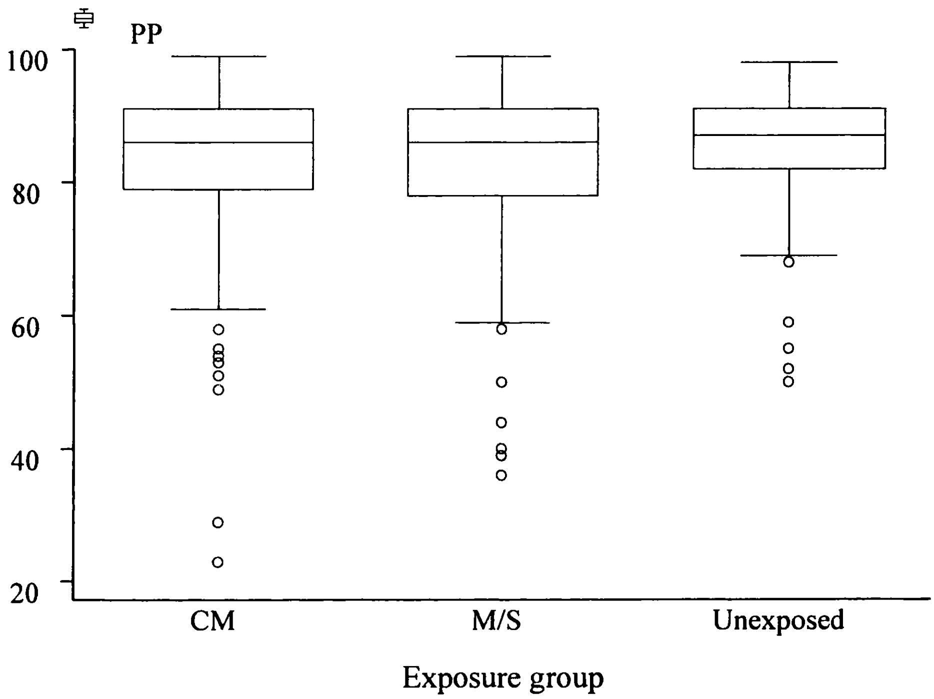

Figure 14. 10: Distribution of pragmatics profile (PP) scores by exposure group

A transformation could not be found that produced a normal distribution of these data, therefore it was analysed as a binary outcome. A logistic regression model (cut-off at 69) was applied to analyse the results. There was a significant difference in the estimated odds of poor performance between both of the exposed groups and the unexposed group (table 14.10). The estimated difference between the active epilepsy and no epilepsy groups was also significant. None of the children with inactive epilepsy had a score of less than 69 and the variable was dropped from the model.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	2.81	1.04 to 7.6	0.04
	M/S	3.23	1.2 to 8.71	0.02
Epilepsy status	Active epilepsy	3.74	1.19 to 11.8	0.02
	Inactive epilepsy	*	-	-
Age	7 years	1.33	0.55 to 3.21	0.77
	8 years	1.37	0.52 to 3.57	
	9 years	0.99	0.33 to 2.97	
Sex	Female	0.5	0.25 to 1.0	0.05
Schooling status	Nursery	0.74	0.35 to 1.6	0.16
	Standard 1	0.11	0.01 to 0.87	
	Standard 2	0.52	0.1 to 2.65	
Nutritional status	Weight/height	1.41	0.46 to 4.29	0.54
	Height/age	1.9	0.72 to 4.98	0.19
	Weight/age	0.92	0.27 to 3.17	0.9
SES status	Mother's education	1.04	0.49 to 2.24	0.91
	Father's occupation	0.85	0.42 to 1.73	0.65

Table 14. 10: Estimated odds ratio in pragmatics assessment scores between the exposed and unexposed groups

* dropped: inactive epilepsy predicts success perfectly

14.9 Phonological assessment

The maximum score for the phonological assessment was 100%. Due to the nature of the assessment (see section 11.2.7), some of the children did not produce all of the target words and by extension, all of the phonemes. The majority of children presented with no phonological errors: the median score in each exposure group was 100, resulting in a highly skewed distribution of scores (figure 14.11). There were more outliers in the CM and M/S groups relative to the unexposed group.

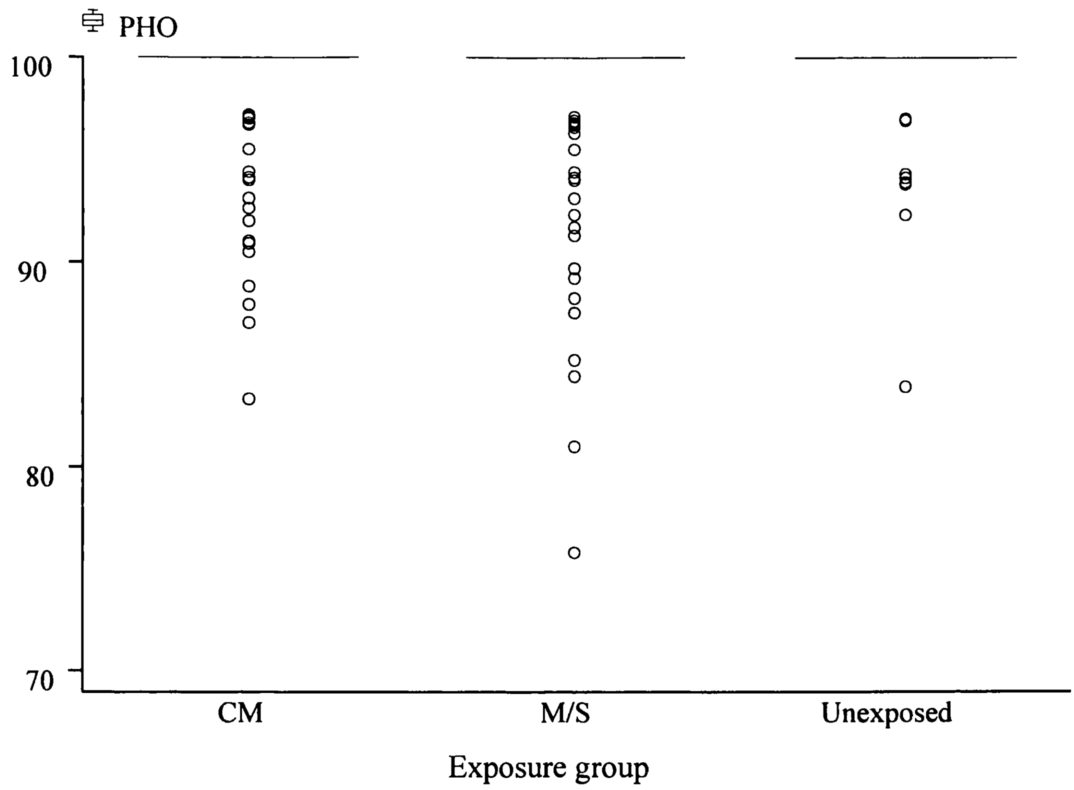

Figure 14. 11: Distribution of phonological assessment (PHO) scores by exposure group

As so many children achieved the maximum score, the range of scores was too narrow to attempt a transformation of the data. Therefore, a binary variable for logistic regression analysis with a cut-off of 99 was selected. There was a significant difference in the estimated odds of poorer performance between the M/S and unexposed groups but no evidence of a significant difference between the CM and unexposed groups or the epilepsy and no epilepsy groups (table 14.11). However, the direction of the association between the CM and unexposed groups suggested a poorer performance in the former group. This effect was also seen, although to a lesser extent, in the association between the active and no epilepsy groups, suggesting poorer performance in the active epilepsy group.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	2.03	0.91 to 4.53	0.09
	M/S	2.74	1.26 to 5.95	0.01
Epilepsy status	Active epilepsy	1.32	0.37 to 4.69	0.67
	Inactive epilepsy	0.9	0.18 to 4.38	0.89
Age	7 years	0.46	0.22 to 0.96	0.03
	8 years	0.35	0.14 to 0.84	
	9 years	0.37	0.15 to 0.91	
Sex	Female	1.17	0.65 to 2.08	0.6
Schooling status	Nursery	0.73	0.38 to 1.4	0.33
	Standard 1	0.33	0.09 to 1.18	
	Standard 2	0.5	0.1 to 2.44	
Nutritional status	Weight/height	0.51	0.15 to 1.77	0.29
	Height/age	3.62	1.68 to 7.77	0.001
	Weight/age	0.93	0.33 to 2.63	0.9
SES status	Mother's education	0.96	0.51 to 1.79	0.89
	Father's occupation	1.03	0.57 to 1.86	0.91

Table 14. 11: Estimated odds ratio of phonological assessment scores between the exposed and unexposed groups

A qualitative assessment of the errors produced by the 63 children with scores less than 100% indicated that the most common error was the substitution of the phoneme /l/ for /r/ (table 14.12). This and all other errors occurred in both initial and medial positions, where applicable. Mother tongue Kigiryama speakers among the assessment team noted that /r/ → /l/ is a common developmental error in Kigiryama acquisition and is colloquially known as 'talking baby language' when it occurs in children older than about 5 years. However, there is no information on the sequence of acquisition of Kigiryama phonemes, therefore it is not possible to ascertain whether processes that occur during normal development in English, such as fronting (/k/ → /t/; /g/ → /d/) are also developmental processes in children acquiring Kigiryama.

Phonological error/s	CM	M/S	Unexposed
	(Single error/One of multiple errors)		
/r/ → /l/	21 (14/7)	22 (11/11)	8 (7/1)
/r/ → /j/	2 (1/1)	5 (3/2)	1 (1/0)
/l/ → /j/	2 (0/2)	3 (0/3)	1 (0/1)
/ʃ/ → /ʧ/	0	4 (0/4)	3 (1/2)
/ʃ/ → /s/	0	1 (0/1)	1 (1/0)
/s/ → /ʃ/	7 (0/7)	3 (0/3)	0
/z/ → /ʤ/	1 (0/1)	1 (0/1)	1 (0/1)
/b/ → /p/	0	1 (0/1)	0
/k/ → /t/	0	2 (0/2)	0
/g/ → /d/	0	2 (0/2)	0
/g/ → /k/	0	1 (0/1)	0
/ʤ/ → /d/	1 (0/1)	0	0

Table 14. 12: Patterns of errors in the phonological assessment

Six of the 63 children were judged to have a reduced level of intelligibility at the time of assessment. Level of intelligibility was a subjective judgement made by the assessor, based on whether he/she was able to understand the child during the play and assessment sessions and whether other children participating in the play session exhibited difficulties in understanding the child. Two-thirds of these children were from the M/S group (table 14.13).

ID	Group	Errors
096	Unexposed	/l/, /r/ → /j/; /s/ → /ʃ/; /z/ → /ʤ/
103	M/S	/r/ → /l/; /k/ → /t/; /b/ → /p/; /g/ → /d/
396	M/S	/r/ → /l/; /s/ → /ʃ/; /z/ → /ʤ/
411	CM	/r/ → /l/; /s/ → /ʃ/; /z/ → /ʤ/
416	M/S	/r/ → /l/; /k/ → /t/; /g/ → /d/
472	M/S	/r/ → /l/; /ʃ/ → /ʧ/

Table 14. 13: Patterns of errors in children with reduced intelligibility

14.10 Word finding assessment

Three children (2 CM; 1 M/S) were not able to complete the word finding assessment because of limited speech and one child (unexposed) did not complete it because of a visual impairment. The word finding assessment comprised 40 items and generated two scores: an accuracy score and a delay score, the former measuring how many pictures were named correctly and the latter, how many pictures were named after a delay.

14.10.1 Accuracy score

The accuracy results were skewed with median scores of 35, 36 and 37 in the CM, M/S and unexposed groups respectively (figure 14.12). The distributions of the CM and M/S group scores were broader than that of the unexposed group. The minimum score in both exposed groups was 0 compared to 15 in the unexposed group.

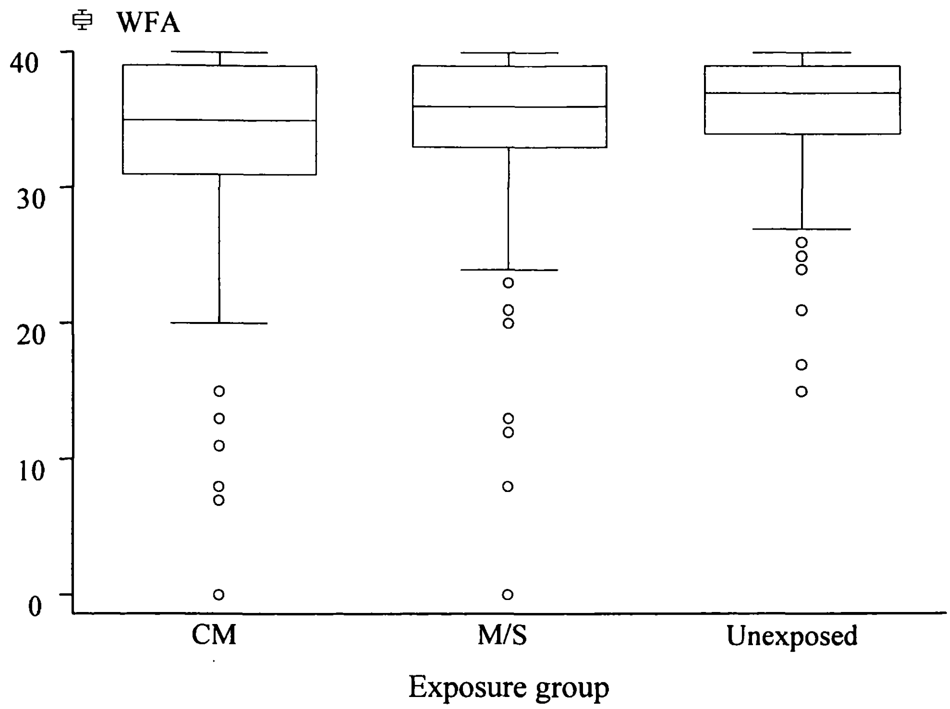

Figure 14. 12: Distribution of word finding assessment accuracy (WFA) scores by exposure group

A transformation could not be found that produced a normal distribution of these data, therefore they were analysed as a binary outcome. A logistic regression analysis (cut-off at 34) of the results showed no evidence of a difference in the estimated odds of a poorer performance between either of the exposed groups and the unexposed group (table 14.14). However, the direction of the association between the CM and unexposed groups was indicative of a poorer performance amongst the CM group. Children with active epilepsy had significantly higher odds of a lower accuracy score than children who didn't have epilepsy. This effect was not seen in the inactive epilepsy group, although the direction of the association suggested that they had a poorer group performance than the no epilepsy group.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	1.55	0.87 to 2.78	0.14
	M/S	0.88	0.48 to 1.6	0.67
Epilepsy status	Active epilepsy	4.23	1.27 to 14.07	0.02
	Inactive epilepsy	2.21	0.59 to 8.3	0.24
Age	7 years	0.42	0.23 to 0.77	<0.001
	8 years	0.28	0.14 to 0.54	
	9 years	0.12	0.06 to 0.25	
Sex	Female	1.11	0.69 to 1.79	0.66
Schooling	Attends school *	0.18	0.11 to 0.29	<0.001
Nutritional status	Weight/height	0.79	0.32 to 1.94	0.61
	Height/age	1.99	0.95 to 4.16	0.07
	Weight/age	2.05	0.75 to 5.63	0.16
SES status	Mother's education	1.22	0.72 to 2.09	0.46
	Father's occupation	0.48	0.29 to 0.8	0.01

Table 14. 14: Estimated odds of a poor accuracy score on the word finding assessment between the exposed and unexposed groups

* Used because Standard 2 predicts success perfectly

14.10.2 Delay score

The distribution of the delay scores was skewed (figure 14.13). The median score for the M/S and unexposed groups was 3 and for the CM group, 4. The maximum score (equivalent to the poorest score) was similar in each group (26 for the CM and M/S groups; 27 for the unexposed group), although the interquartile ranges were larger in the exposed groups.

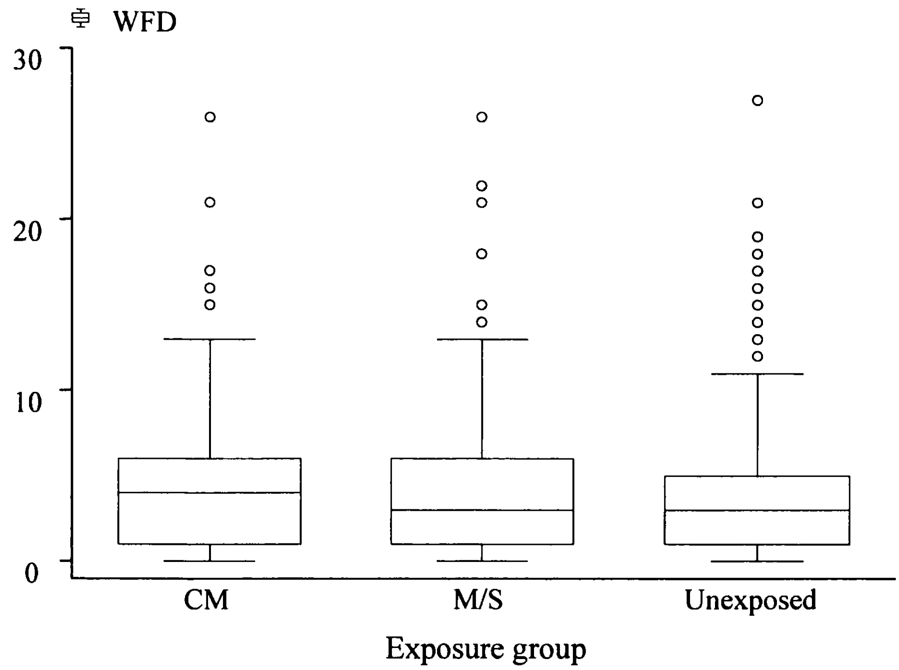

Figure 14. 13: Distribution of word finding assessment delayed response (WFD) scores by exposure group

As with the accuracy score, a binary outcome was used for analysis as none of the transformations applied resulted in a normal distribution of the data. A logistic regression analysis (cut-off at 10) showed no evidence of a difference between the exposed and unexposed groups or the epilepsy and no epilepsy groups (table 14.15). The direction of the association between the exposure groups suggested poorer performance in the unexposed group whereas the association between the epilepsy and no epilepsy groups was indicative of poorer performance amongst children with epilepsy, particularly in its active form.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	0.68	0.32 to 1.45	0.32
	M/S	0.57	0.26 to 1.27	0.17
Epilepsy status	Active epilepsy	3.08	0.92 to 10.29	0.07
	Inactive epilepsy	1.73	0.33 to 9.08	0.52
Age	7 years	0.92	0.42 to 1.99	0.69
	8 years	0.53	0.21 to 1.34	
	9 years	0.48	0.19 to 1.2	
Sex	Female	1.11	0.6 to 2.06	0.74
Schooling	Attends school *	0.37	0.18 to 0.75	0.01
Nutritional status	Weight/height	0.79	0.27 to 2.29	0.66
	Height/age	2.36	1.01 to 5.55	0.05
	Weight/age	1.38	0.46 to 4.1	0.56
SES status	Mother's education	0.81	0.39 to 1.67	0.56
	Father's occupation	0.54	0.27 to 1.06	0.07

Table 14. 15: Estimated odds of poorer performance in word finding assessment delayed response scores between the exposed and unexposed groups

* Used because Standard 2 predicts failure perfectly

14.11 Summary and discussion

14.11.1 Overview

The direction of the association between the CM and unexposed groups suggested a poorer performance among children with CM on all of the assessments, with the exception of the receptive grammar and syntax assessments and the word finding delay score. These differences were significant on the assessments of higher level language, lexical semantics (content words) and pragmatics. Few of the children in this group had been identified as having gross neurological impairments on hospital discharge so there is likely to be a continuum of deficits within the group, with a large proportion of children with mild or subtle impairments and a minority more severely affected. However, on the pragmatics assessment, the distribution of scores was skewed. Although there was a broader distribution of scores among the children with previous CM relative to the unexposed group, the similar median scores suggest that the larger number of outliers in that group may have been partly responsible for the group difference.

In contrast to the trend in the CM group, there was no evidence of a difference in performance between the M/S and unexposed groups on many of the assessments and the group performed significantly better than the unexposed group on the syntax assessment. The direction of the association on the tests of lexical semantics (function words), pragmatics and phonology was indicative of a poorer performance among children with previous M/S. The areas of reduced functioning for the M/S group were concentrated on the phonology and pragmatics assessments, in which there were significant differences in performance. The distribution of scores on these assessments was skewed, showing similar median scores across the three exposure groups and large numbers of outliers. There was a broader distribution of M/S scores relative to unexposed group scores on the pragmatics assessment but the phonological assessment scores were condensed into a majority group who attained the maximum score and a minority group of outliers. As discussed above, this pattern may indicate an influence from the outliers on the group differences found.

Significant differences in performance were detected in the pilot study between children exposed to severe malaria (an inclusive term used in the pilot study, encompassing CM and severe malaria with prostration, multiple seizures or severe anaemia) and a group unexposed to severe malaria on assessments of receptive language, syntax and lexical semantics (section 10.4.2). The disparity in pilot study and main study findings for groups exposed to severe malaria may be explained by factors in the design of each respective study. All of the assessments, except lexical semantics (the only assessment with immediately comparable findings), were altered or replaced following analysis of item- and test-level performance in the pilot study (Chapter Eleven). The pilot study was intended as a preliminary investigation into the occurrence of persisting speech and language impairments following severe malaria and did not adjust for many of the variables considered in the main study. Variables such as schooling status and active epilepsy (described below) were found to account for much of the variance in main study assessment scores.

The performance of the active epilepsy group was significantly poorer than that of the group without epilepsy on the tests of receptive grammar, receptive vocabulary, syntax, pragmatics and word finding (accuracy score). The direction of the association was lower on the remaining assessments, with the exception of the function word element of lexical semantics. These findings indicate that active epilepsy in the context of a previous episode of severe malaria is associated with a general depression of language skills. Difficulties in language content and use were apparent but there were also group differences in the more basic functions of language form. Performance on both the receptive and expressive grammar assessments, which measure aspects of syntax and morphology, were affected.

Children with inactive epilepsy did not have the same level of poor performance as children with active epilepsy. They had lower estimated scores than children without epilepsy on the receptive grammar, lexical semantics (content words) and word finding assessments, although none of the differences were significant.

These findings are discussed in more detail in the following sections.

14.11.2 The CM group

A broad framework based upon the universal aspects of content, form and use, as described by Bloom and Lahey (1978), was postulated in Chapter Eight. Significant differences in estimated scores between the CM and unexposed groups were confined to the 'content' and 'use' aspects of language described in this model. Both aspects of language content – vocabulary and higher level aspects of word meaning – were affected, although group differences were restricted to expressive vocabulary. This may reflect a genuine discrepancy between expressive and receptive semantic abilities or may be partly due to the difference in assessment techniques between the lexical semantics and receptive vocabulary assessments. The former utilised a profiling technique to measure the breadth of vocabulary demonstrated in a spontaneous language sample, whereas the latter assessed the child's knowledge of a pre-selected set of 25 words.

The findings suggest that both aspects of language use – social functions and contexts – are affected in the CM group. Significant differences between the CM and unexposed groups were found in socially-mediated functions such as directing another person's attention and giving information. Children with previous CM were also reported to demonstrate significantly poorer skills in determining the context of utterances, both in terms of linguistic (presupposition) and nonlinguistic (conversational repair) rules.

This pattern is indicative of problems in higher level discourse functions and suggests that persisting impairments in language associated with CM do not involve basic-level dysfunction in aspects of language form. The results also indicate the presence of an outlier group on assessments in which group differences were not found: the presence of a subgroup of 'impaired' children will be investigated further in Chapter Sixteen.

The finding of semantic (lexical semantics and higher level language) and pragmatic impairments is redolent of the category 'semantic pragmatic deficit syndrome' (SPDS), described in Rapin and Allen's (1987) model or 'semantic pragmatic disorder' described in Bishop and Rosenbloom's (1987) model. Rapin and Allen conceived the term 'SPDS' to describe a subtype of language deficits observed in a group of preschool children with developmental language disorders. SPDS was one of two subtypes (the other being 'lexical syntactic deficit disorder') encompassing children with higher level deficits, 'those whose basic deficiency was at the discourse level, not at the levels of phonology and syntax' (Rapin and Allen, 1998 p82). The characteristics of SPDS are verbosity, poor turn-taking skills, word finding problems, difficulties in topic maintenance and formulation of discourse, inordinate use of scripts and deficits in abstract comprehension (Adams, 2001; Rapin and Allen, 1998). The direction of the association between the CM and unexposed groups on the word finding assessment suggested poorer performance among children with CM and there were a number of outliers in this group. Parental reports of pragmatic skills indicated verbosity, difficulties in conversational skills and deficits in the comprehension of humour.

The current study, the first detailed investigation of language impairments associated with severe malaria, is not able to advance beyond speculation on these issues. Boucher (1998) comments that the term SPDS is variously used as a clinical description, merely summarising the essentials of a child's problems or as a means of integrating the child into a taxonomy of communication disorders within which SPDS is a recognised diagnostic entity. Speculation in this context evidently falls into the former category for several reasons other than the novelty of the data. First, impairments associated with malaria would probably fall under the category of 'acquired', whereas SPDS is primarily used in the taxonomy of developmental disorders. In her study of appropriate models for the description of acquired language disorders, Lees (1993) cautions against reliance on models designed to classify other phenomena. This may be a particularly pertinent point in the context of a classification that is still evolving and hitherto lacks clear criteria for the developmental disorders which it was designed to describe. Secondly, there is not necessarily a direct link between the semantic and pragmatic elements of the differences in performance observed. Pragmatic impairments may occur secondary to linguistic deficits: some communicative goals are closely linked to linguistic ability. McTear and Conti-Ramsden (1992) comment that this relationship should be investigated in terms of the correspondence between a particular linguistic structure and a particular pragmatic function, giving the example of the use of the definite article in English to mark information mutually shared between listener and speaker. A related factor is that poor language abilities may affect peer relationships, in that previously unsuccessful attempts at communication may inhibit further attempts at interaction and result in problems with language use that are a secondary consequence of lack of social experience (Bishop, 2000).

14.11.3 The M/S group

These findings represent the first indication that other complications of falciparum malaria may be associated with subsequent speech and language impairments. Whereas the direction of the association between the CM and unexposed groups was indicative of poorer general performance amongst children with CM, the association between the M/S and unexposed groups suggests that the majority of children do not experience a persistent reduction in general language performance after an episode of M/S. However, reduced functioning relative to the unexposed group is found in language use and to a lesser extent, the phonological aspect of language form. An outlier group is also indicated on all assessments in which group differences were not found, with the exception of the semantic measures (lexical semantics and higher level language), and will be discussed in Chapter Sixteen.

A qualitative analysis of responses on the phonological assessment showed that only four of the twenty-eight children with previous M/S who produced errors were judged to have a consequent reduction in intelligibility. Thirty-nine percent (n=11) of M/S children with errors produced a single error type (/r/ → /l/), which is considered to be a normal developmental process in younger Giryama children (section 14.9). A further 39% of the group produced this error as one of multiple error types. Although any conclusions on the nature of other errors are limited by the fact that very little is known about the acquisition of Kigiryama, it may be postulated that a proportion are the result of developmental delay rather than phonological disorder, which would imply a qualitative abnormality.

On the basis of these findings, it may be proposed that the focus of the disorder found in the M/S group is the aspect of language use. In common with the pattern seen in the CM group, pragmatic functions and contexts are both affected, the former evidenced by poor skills in requesting clarification and the latter by deficits in the use of conversational devices such as appropriate termination of a conversation. Both M/S and CM groups were reported to display deficits in metalinguistic awareness and the use of and response to humour.

As discussed above, pragmatic impairments may occur secondary to language impairments: it is not possible to know whether the M/S group experienced more obvious linguistic deficits after discharge that have since improved but left residual pragmatic impairment. McTear and Conti-Ramsden (1992) comment that pragmatic impairment is not a unitary phenomenon and propose other underlying causes of problems in language use such as general cognitive impairment and affective and emotional difficulties. They describe the concept of 'world knowledge', the ability to assimilate and communicate coherent information by making predictions based on knowledge of objects, events and people. Deficiencies in such knowledge may result in problems with socially- and culturally-appropriate behaviours (greetings, polite forms) and an inability to progress beyond the surface characteristics of an utterance to its underlying significance, impacting on skills such as making inferences or appreciating humour. Affective aspects of language use may impact upon pragmatic ability because the purpose of communication is more than the simple exchange of information but is for the development of relationships and the sharing of experiences. Positive experiences provide emotional rewards and motivation to engage in further interaction and children who receive persistently negative feedback, for example because of the stigma of having certain impairments, may withdraw from social contact.

As an extension of the continuing debate on SPDS, Bishop (2000) suggested the term 'pragmatic language impairment' (PLI) to describe children with pragmatic impairments that are not secondary to linguistic problems. The term implies that deficits in semantics and pragmatics will not necessarily co-occur. Again, given the context of the debate on PLI and SPDS, this only warrants a speculative discussion in the current study but it is an interesting concept as it implies that the linguistic deficits observed in CM and M/S may lie on the same continuum of language disorders.

Other studies of children with deficits in semantics and pragmatics have found that standardised assessments do not identify language impairments, whereas reports from people who know the child highlight communicative problems (Conti-Ramsden, 1997). Although it is possible that the problems of the M/S group were primarily confined to language use, the fact that subtle problems were also detected on the phonological assessment may suggest that the group has subtle language impairments that were not detected by the current assessments but are apparent to the parents (who responded to the pragmatics questionnaire).

McTear and Conti-Ramsden (1992) comment that a criticism of parental reports of pragmatics is that they may over- or under-estimate the child's abilities, as the parent may be unaware of developmental norms or which aspects of communication are important to report. However, as Bishop (2000) comments in the light of the results Conti-Ramsden's study, a person who interacts with the child regularly may be better able to evaluate the child's communicative abilities than an assessor who sees them once. Pragmatics can be a difficult aspect of language to assess – for instance, the use of observational checklists relies on the observer's intuitions about the appropriateness of each behaviour – even more so in a cross-cultural situation in which parents are likely to know more about the appropriateness of certain behaviours than the assessors or certainly the candidate. These problems were highlighted in the pilot study (section 11.2.6), which prompted the use of the pragmatics questionnaire as an alternative to observational techniques.

14.11.4 The active epilepsy group

The speech and language assessment findings indicate that active epilepsy in the context of a previous episode of severe malaria is associated with a general depression of language skills. Other studies have confirmed the association between speech and language impairments and epilepsy (Caplan, et al., 2002; Hermann, et al., 2001; Robinson, 1991). There is no one impairment pattern characteristic of epilepsy (Lebrun and Fabbro, 2002) and current descriptions are unclear due to methodological variations between studies, resulting from the clinical heterogeneity of the population and different approaches to measuring language functions (Hermann, et al., 2001; Metz-Lutz and Massa, 1999).

Language deficits have been particularly associated with temporal lobe epilepsy (TLE), resulting in more detailed studies and characterisation of the impairments. Word finding difficulties are the most commonly cited problem (Hamberger and Tamny, 1999; Mayeux, et al., 1980; Shulman, 2000), although syntactic (Schoenfeld, et al., 1999) and pragmatic (Caplan, et al., 2001; Caplan, et al., 1993) impairments have also been described. Deficits in social communication have also been associated with generalised epilepsy syndromes (Caplan, et al., 2002). This pattern corresponds to that found in the active epilepsy group, despite the fact that there was only one child with complex partial seizures. This may simply reflect the fact that this is a broad pattern that may correspond to different epilepsy syndromes. The significant difference in performance on the word finding assessment is interesting in the light of the TLE evidence, although anomia is generally considered to be a nonlocalising symptom (Love and Webb, 2001) and does not necessarily indicate a temporal lobe focus.

The picture of impairments across different aspects of language is reflected in another childhood epilepsy syndrome in which language impairment is increasingly a recognised part of the disorder. Deonna and colleagues (2000) and Yung and colleagues (2000) describe children with BECRS presenting with generalised aphasic impairments, although other studies have documented more isolated problems in semantics (D'Alessandro, et al., 1990), word finding, phonology and oromotor functions (Deonna, et al., 1993). In one of the most detailed studies of language function in BECRS, children were found to have particular problems with reading/spelling single words, auditory verbal learning, expressive grammar and auditory discrimination with background noise (Staden, et al., 1998). Direct comparison is not possible because BECRS is associated with high rates of epileptiform discharge and with the exception of expressive grammar, none of these functions was specifically tested in the current study. However, the notion of widespread impairment is also reflected in Staden and colleagues' findings as 62% of the 13 children with language impairments had difficulties in up to eight different measures of speech and language.

A multiplicity of associated factors may be implicated in the cognitive and language impairments seen in children with epilepsy, including the extent of the underlying brain damage or dysfunction; age of brain insult and onset of seizures; nature of the epilepsy syndrome and frequency of epileptic activity (Niemann, et al., 1985). In children exposed to CM, all language assessments in which there were significant differences between the epilepsy and non-epilepsy groups had lower but not significantly different mean scores between the CM and unexposed groups, indicating an association between epilepsy and CM. This suggests that CM may be associated with baseline performance in certain language skills, whereas epilepsy may affect functions spared by malaria.

14.11.5 The inactive epilepsy group

The findings suggest that in the context of severe malaria, inactive epilepsy is not sufficient to have a negative impact on the language functions of the group as a whole. This contrasts with 'malignant' epilepsy syndromes in which it is common for children to be left with residual language impairments after seizure remission. For example, in LKS, less than 20% of children make a complete language recovery (Robinson, et al., 2001; Rossi, et al., 1999) and in ESES, most children are left with persisting discrepancies between performance and verbal IQs (Ballaban-Gil and Tuchman, 2000). The discrepancy between the findings of the active and inactive epilepsy groups may suggest that the language impairments in the former group are caused by epileptic discharges directly interfering with cognitive processes rather than the epilepsy and language impairments both being epiphenomena of underlying brain damage. This may indicate that malaria-related and epilepsy-related impairments co-occur in some children but are not linked. Residual language impairments may be present among children with inactive epilepsy but not in sufficient numbers to effect a group difference. This possibility will be investigated further in Chapter Sixteen.

14.11.6 Other effects on performance

As anticipated, much of the variance in scores on the speech and language assessments was related to schooling status and age. Low height/age scores were associated with poor performance on the syntax, phonology and word finding (delay score) assessments. This corresponds with previous data suggesting that stunting, a marker of chronic malnutrition during infancy, is associated with poor performance on cognitive assessments (Berkman, et al., 2002), although it is unclear why these particular assessments were affected more than others. Low SES, as measured by low-income occupations in fathers, was associated with reduced odds of a poor performance on the word finding assessment (accuracy score) but not with performance on any other assessments. This is suggestive of a chance finding due to the number of language and cognitive assessments. Gender also had little effect on the variance: girls had a significantly better reported performance on the pragmatics assessment, which may reflect parental attitudes and expectations of boys and girls (Serpell, 1993), and significantly worse performance on the syntax assessment.

In summary, the results of the speech and language assessments suggest a general depression of language functions among children with previous CM. There were significant differences in performance between the CM and unexposed groups in language content and use, with relative sparing of aspects of language form. Areas of reduced functioning among children with previous M/S were more circumscribed, with findings suggestive of delayed phonological development and difficulties in language use. Analysis of the results by epilepsy group indicated that active epilepsy in the context of a previous episode of severe malaria is associated with widespread reductions in performance across the aspects of content, form and use. There were no significant differences in performance in the inactive epilepsy group.

Chapter Fifteen: Cognitive and Behavioural Results

15.1 Introduction

In the context of febrile seizures, complicated seizures (prolonged, focal or repetitive seizures) are associated with neurological damage, particularly to the temporal lobe (Annegers, et al., 1987; Maher and McLachlan, 1995) and the subsequent development of epilepsy (Verity and Golding, 1991), particularly complex partial seizures. Studies using invasive EEG monitoring of temporal lobe seizures have indicated that they are predominantly mesial temporal/hippocampal in origin (Hermann, et al., 1992), thus children are at risk of deficits in memory, particularly episodic memory (Vargha-Khadem, et al., 1997). In consequence, the major part of the cognitive assessment comprised the Kilifi Creek Behavioural Memory Test (KCBMT), based upon the Rivermead Behavioural Memory Test for Children (RBMTC) (Wilson, et al., 1991). The cognitive assessment also included measures of non-verbal functioning and attention. The behaviour questionnaire was administered to the parents. The results for each assessment will be presented, summarising the comparative performance of each group and analysing differences in performance by exposure group and epilepsy status.

15.2 Kilifi Creek Behavioural Memory Assessment

All children completed the KCBMT, although the scores of younger children on certain tasks were not included in the final score (Appendix 27) and individual tasks were occasionally refused by a minority of children. In such instances, the task was assigned a score of '0' and the child's data was included in the analysis. This will be detailed in each task section. The KCBMT comprised 12 individual tasks, generating 12 item scores and one total score. Following the RBMTC procedure, all raw scores were converted to scaled scores before calculation of the total score, to ensure that unequal weight was not given to one particular task. Each scaled score ranged from 0 to 2: a score of 0 represented 'impaired' performance; 1, 'borderline' performance and 2, 'normal' performance. The maximum scaled score was dependent on age and ranged from 10 to 18 (table 15.1). The raw scores of the unexposed group were stratified by age and analysed to generate age-specific scaled scores. This procedure is described in Appendix 27 and the resulting scaled scores are presented in table 15.1.

Age	Items completed	Normal	Borderline	Impaired
6	3, 4, 6, 7, 8, 9	10-12	6-9	0-5
7	3, 4, 6, 7, 8, 9	10-12	6-9	0-5
8	all items	16-18	12-15	0-11
9	all items	16-18	12-15	0-11

Table 15. 1: Age-specific scaled scores relating to KCBMT outcomes

Key to items:

1= Remembering a name
2= Picture recognition
3= Immediate story recall
4= Delayed story recall
5= Face recognition
6= Immediate route recall
7= Delayed route recall
8= Message recall
9= Orientation questions

The distribution of scores was skewed (figure 15.1) with median scores of 12 and 13 in the exposed and unexposed groups respectively. The spread of scores in the CM group was much broader than that in the unexposed group. The distribution of M/S and unexposed scores was similar, although there were outliers among the former group.

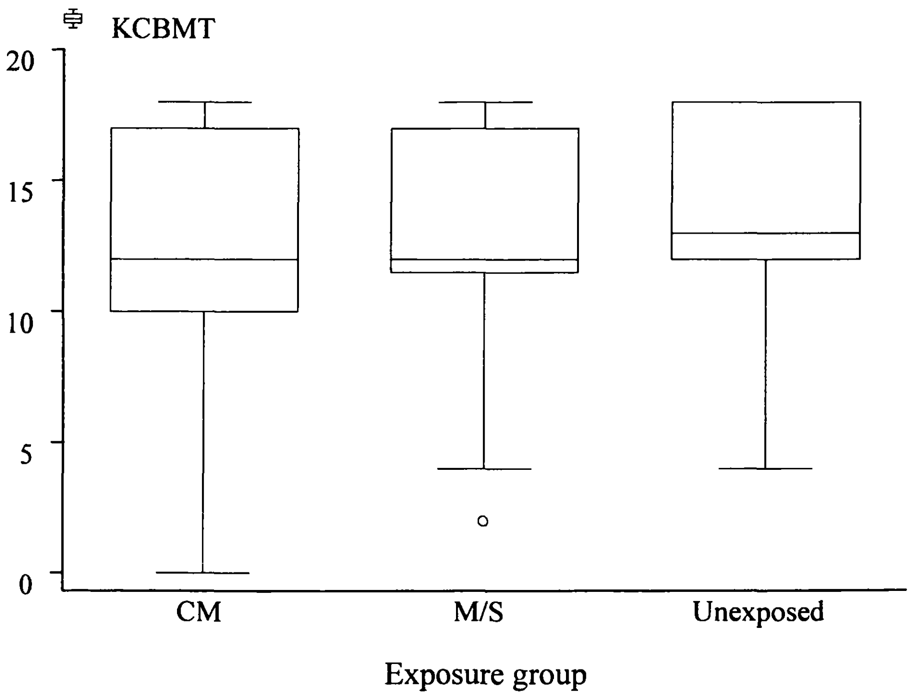

Figure 15. 1: Distribution of KCBMT scores by exposure group

15.2.1 'Impaired' group

The proportion of children assigned an 'impaired' score was highest in the CM group (figure 15.2). 'Impaired' children from the unexposed groups were concentrated in the 8 and 9 year age groups, in which their proportions generally equalled or exceeded those of the exposed groups. This effect may be partly explained by the scaling procedure, an issue that will be discussed further in section 15.2.3.

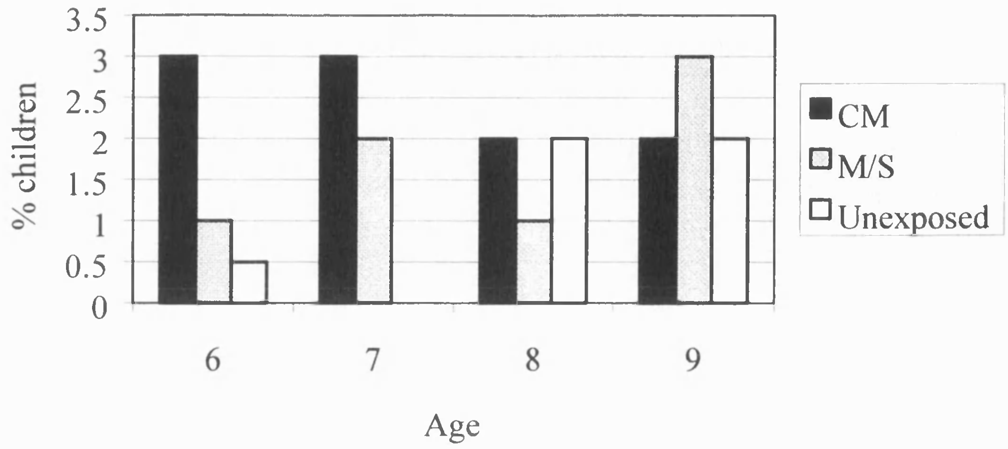

Figure 15. 2: Proportion of children in each exposure group with a diagnosis of 'impaired' on the KCBMT, stratified by age

RBMTC scores are subject to a univariate analysis (although age has been accounted for in the scaling process). When the total KCBMT scores were analysed according to the RBMTC manual, the difference in the proportion of children with 'impaired' scores in the CM (10.5%) and unexposed groups (5%) approached significance (χ^2 = 3.56 p=0.06). The proportion of the M/S group with an 'impaired' score (7.1%) was greater than that of the unexposed group but there was no evidence of a difference between the groups (χ^2 = 0.61 p=0.44). A logistic regression model, including epilepsy status and other potential covariates, indicates that much of the variance is due to the active epilepsy group (table 15.2). There was a significant difference between the active and no epilepsy groups, whereas there was no evidence of a difference in the odds of an impaired score between the exposed and unexposed groups or the inactive and no epilepsy groups. Age was not included in the model because the scores were scaled: to confirm that age did not alter the results, the variable was added to a second model but resulted in no significant changes to the odds presented in table 15.2.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	1.44	0.57 – 3.62	0.43
	M/S	0.97	0.36 – 2.59	0.94
Epilepsy status	Active epilepsy	5.77	1.74 – 19.11	0.004
	Inactive epilepsy	0.8	0.11 – 1.7	0.23
Sex	Female	1.2	0.57 – 2.52	0.62
Schooling	Attends school *	0.44	0.19 – 1.02	0.06
Nutritional status	Weight/height	0.44	0.11 – 1.7	0.23
	Height/age	2.65	0.99 – 7.06	0.05
	Weight/age	2.63	0.83 – 8.33	0.1
SES status	Mother's education	0.79	0.33 – 1.87	0.59
	Father's occupation	0.87	0.4 – 1.89	0.72

Table 15. 2: Estimated odds of an 'impaired' KCBMT score in exposure and epilepsy groups

* Used because Standard 2 predicts success perfectly

15.2.2 'Borderline' group

The proportion of children with a 'borderline' KCBMT score was higher in the CM group relative to the M/S and unexposed groups, with a concentration in the younger age groups (figure 15.3). The proportion of 'borderline' scores was similar in the unexposed and M/S groups.

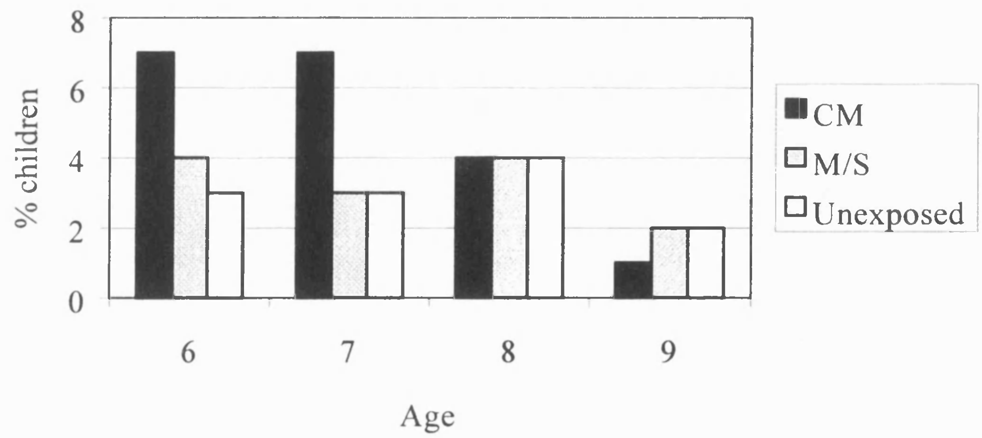

Figure 15. 3: Proportion of children in each exposure group with a diagnosis of 'borderline' on the KCBMT, stratified by age

Analysed according to the RBMTC manual, there was no evidence of a difference between the unexposed group and the CM (χ^2 = 1.96 p=0.16) or M/S (χ^2 = 0.03 p=0.85) groups. This pattern was repeated in a logistic regression model of the data (table 15.3). There was also no evidence of a difference between the active and no epilepsy groups. None of the inactive epilepsy group had a 'borderline' score so the variable was dropped from the model.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	1.33	0.7 – 2.53	0.38
	M/S	0.85	0.43 – 1.68	0.64
Epilepsy status	Active epilepsy	0.23	0.03 – 1.83	0.17
	Inactive epilepsy	*	-	-
Sex	Female	1.4	0.81 – 2.4	0.23
Schooling status	Nursery	0.44	0.24 – 0.82	<0.001
	Standard 1	0.14	0.04 – 0.48	
	Standard 2	0.16	0.04 – 0.73	
Nutritional status	Weight/height	0.86	0.32 – 2.33	0.76
	Height/age	1.19	0.54 – 2.64	0.67
	Weight/age	0.82	0.28 – 2.43	0.72
SES status	Mother's education	0.62	0.33 – 1.18	0.15
	Father's occupation	1.03	0.59 – 1.81	0.92

Table 15. 3: Estimated odds of a 'borderline' KCBMT score in exposure and epilepsy groups

* Dropped because variable predicts success perfectly

15.2.3 Individual task analysis

There was a general trend towards poorer performance in the unexposed group relative to the performance of UK children on the RBMTC (Appendix 27). Alterations to the scaling process to take account of these discrepancies may have resulted in a bias towards lower scores in the 8-9 year age group.

Younger children (6 to 7 years of age) were excluded from the 'remembering a name' task by the RBMTC convention of omitting younger age groups from items showing a clear developmental pattern, with particularly poor scores in these age groups (Wilson, et al., 1993). This convention was followed and extended to the picture and face recognition tasks of the KCBMT because of the poor performance of the younger children on these tasks. Twenty-six percent of 6 year olds and 22% of 7 year olds attained scores of four or less on the picture recognition task, which was equal to an 'impaired' scaled score. Similarly, 39% of 6 year olds and 31% of 7 year olds obtained a score of 0 or less (minus scores were possible) on the face recognition task, again equal to an 'impaired' score.

Although the performance of the older children was comparatively better on these tasks, cut-offs for a 'normal' scaled score still had to be lowered for the Kenyan children in order to reach a level of 90%, the operational definition of a 'normal' score on the RBMTC (Wilson, et al., 1993). In extreme cases, such as the 'remembering a hidden object' and 'remembering an appointment' items, the tasks were excluded from the final scaled score because of the difficulties of achieving this level. On other tasks, such as 'remembering a name', a 90% cut-off could not be achieved if the 0,1,2 scoring pattern was maintained and a lower cut-off (in this case, 75%) was used. Lower cut-offs also had to be used on the other tasks omitting the scores of younger children,: 89% on the face recognition task, compared to 96% on the RBMTC task and 93% on the picture recognition task relative to 97% on the RBMTC task. In consequence, the scaling process may have resulted in an artificial inflation of 'impaired' scores in the 8-9 year age group, producing the patterns seen in figures 15.2 and 15.3.

The problems inherent in the scaling process were difficult to avoid because raw scores could not be used to generate a total score due to the discrepancies in maximum scores for each task (for example, a maximum score of 4 on the 'remembering a name' task compared to 31 on the story recall task). This would have resulted in unequal weighting of tasks in the final score. To investigate whether the scaling process masked poor performance in the exposed or epilepsy groups, analyses of individual tasks was carried out, comparing raw scores with no omissions by age or task. The process and combination of tasks reflected the method of Isaacs and colleagues (2000), who carried out a similar analysis in children with low birth weights using the RBMTC. The results are summarised below and presented in detail in Appendix 27.

15.2.3.1 Remembering a name

One child (M/S) refused the remembering a name task and one child (CM; active epilepsy) did not complete it. The whole cohort was included in the analysis for this task, although 6 and 7 year olds were omitted from the scaled score analysis, following the RBMTC convention. A logistic regression analysis showed no evidence of a difference between either of the exposed groups and the unexposed group, or the epilepsy groups relative to the no epilepsy group (table 15.4).

Group	Odds Ratio	95% C.I.	p-value
CM	0.88	0.54 – 1.43	0.6
M/S	0.73	0.45 – 1.2	0.21
Active epilepsy	1.69	0.62 – 4.58	0.3
Inactive epilepsy	1.21	0.41 – 3.54	0.73

Table 15. 4: Estimated odds of a poorer performance on the remembering a name task, by exposure group and epilepsy status

15.2.3.2 Prospective items

The three tasks targeting prospective memory (remembering an appointment, a hidden object and a message) were grouped together for analysis in Isaacs and colleagues' (2000) study. The appointment and hidden object tasks were omitted from the scaling process because only 60% of children from the unexposed group attained a 'normal' score but were amalgamated with the remembering a message score for the this analysis. The results of a multiple regression analysis showed that children from the CM or active epilepsy groups had significantly lower scores than children from the unexposed and no epilepsy groups respectively (table 15.5). There was no evidence of a difference between the M/S and unexposed or inactive and no epilepsy groups.

Group	Estimated difference	95% C.I.	p-value
CM	-0.53	-1.01 to –0.05	0.03
M/S	-0.02	-0.49 to 0.46	0.94
Active epilepsy	-1.2	-2.27 to –0.12	0.03
Inactive epilepsy	0.33	-0.71 to 1.37	0.53

Table 15. 5: Estimated differences in prospective task scores, by exposure group and epilepsy status

15.2.3.3 Picture recognition

Children of 6 and 7 years were omitted from the scaled score analysis but included in the individual task analysis. The odds of a low score were significantly lower in the M/S group relative to the unexposed group (table 15.6). There was no evidence of a difference in performance between the CM and unexposed groups or the epilepsy and no epilepsy groups.

Group	Odds Ratio	95% C.I.	p-value
CM	0.73	0.36 to 1.46	0.37
M/S	0.23	0.1 to 0.56	0.001
Active epilepsy	2.17	0.59 to 7.98	0.24
Inactive epilepsy	1.28	0.23 to 7.11	0.78

Table 15. 6: Estimated odds of a poorer performance on the picture recognition task, by exposure group and epilepsy status

15.2.3.4 Story recall

Seven children (5 CM; 2 M/S) were unable to complete either the immediate or delayed story recall tasks: three of these children had inactive epilepsy (1 CM; 2 M/S) and two others (CM) had very limited language and had been unable to complete many of the speech and language assessments. The same children were also unable to complete the route recall and orientation questions tasks. The immediate and delayed components of this task were combined to make one score for the analysis of story recall. There was no evidence of a difference in performance between the exposed and unexposed groups or the epilepsy and no epilepsy groups (table 15.7).

Group	Estimated difference	95% C.I.	p-value
CM	-0.61	-3.14 to 1.93	0.64
M/S	1.31	-1.19 to 3.81	0.3
Active epilepsy	-4.71	-10.41 to 0.99	0.11
Inactive epilepsy	0.86	-4.65 to 6.37	0.76

Table 15. 7: Estimated differences in story recall scores, by exposure group and epilepsy status

15.2.3.5 Face recognition

As with the picture recognition task, only 8 and 9 year olds were assigned a scaled score for this task but children from the younger age groups were included in this analysis. The M/S group had significantly decreased odds of a low score compared to the unexposed group (table 15.8). There was no evidence of a difference in performance between the CM and unexposed groups or the epilepsy and no epilepsy groups.

Group	Odds Ratio	95% C.I.	p-value
CM	1.06	0.58 to 1.91	0.86
M/S	0.31	0.15 to 0.63	0.001
Active epilepsy	2.02	0.64 to 6.43	0.23
Inactive epilepsy	0.57	0.1 to 3.11	0.51

Table 15. 8: Estimated odds of a poorer performance on the face recognition task, by exposure group and epilepsy status

15.2.3.6 Route recall

Fourteen children (4 CM; 6 M/S; 4 unexposed) refused the route recall task. Analysis of the comments recorded by the cognitive assessors at the time of assessment suggested that the high rate of refusals was due to particular reluctance to perform 'action' tasks in these children. The immediate and delayed recall scores were combined to make one score for analysis of this task. There was no evidence of a difference between any of the groups of interest (table 15.9).

Group	Odds Ratio	95% C.I.	p-value
CM	1.19	0.51 to 2.79	0.69
M/S	0.74	0.3 to 1.83	0.52
Active epilepsy	3.03	0.71 to 12.89	0.13
Inactive epilepsy	1.36	0.26 to 6.97	0.72

Table 15. 9: Estimated odds of a poorer performance on the route recall task, by exposure group and epilepsy status

15.2.3.7 Orientation questions

One child (unexposed) refused to answer any of the orientation questions. There was a significant difference in performance between the CM and unexposed groups on this task (table 15.10) but no evidence of a difference between the M/S and unexposed groups or the active and no epilepsy groups.

Group	Odds Ratio	95% C.I.	p-value
CM	3.36	1.61 to 7.0	0.001
M/S	0.99	0.43 to 2.26	0.98
Active epilepsy	0.16	0.02 to 1.35	0.09
Inactive epilepsy	0.28	0.03 to 2.61	0.26

Table 15. 10: Estimated odds of a poorer performance on the orientation questions task, by exposure group and epilepsy status

In addition to the analyses suggested by Isaacs and colleagues (2000), differences in performance across immediate and delayed recall tasks was examined.

15.2.3.8 Immediate recall

The immediate story recall and route recall tasks were combined to generate an 'immediate score'. Performance was similar between the exposed and unexposed groups and the epilepsy and no epilepsy groups (table 15.11).

Group	Estimated difference	95% C.I.	p-value
CM	-0.5	-1.89 to 0.89	0.48
M/S	0.95	-0.42 to 2.32	0.17
Active epilepsy	-2.93	-6.05 to 0.19	0.07
Inactive epilepsy	-0.25	-3.27 to 2.76	0.87

Table 15. 11: Estimated differences in immediate story and route recall scores, by exposure group and epilepsy status

15.2.3.9 Delayed recall

The delayed story recall and route recall tasks were combined to generate a 'delayed score'. There was a significant difference between the scores of the active and no epilepsy groups (table 15.12) but no evidence of a difference between the exposed and unexposed groups or the inactive epilepsy and no epilepsy groups.

Group	Estimated difference	95% C.I.	p-value
CM	-0.03	-1.47 to 1.4	0.96
M/S	0.75	-0.67 to 2.16	0.3
Active epilepsy	-3.31	-6.53 to –0.09	0.04
Inactive epilepsy	0.99	-2.12 to 4.1	0.53

Table 15. 12: Estimated differences in delayed story and route recall scores, by exposure group and epilepsy status

15.2.3.10 Summary

In summary, there were significant differences between the CM and unexposed groups on the prospective memory and orientation questions tasks of the KCBMT, possibly indicative of specific hippocampal damage in this group. Low birthweight infants with reduced hippocampal volume, assessed with the RBMTC, have been found to have deficits in route recall, prospective memory and orientation (Isaacs, et al., 2000). Performance on the route recall task in the current cohort was similar in all groups.

Children with previous M/S had a significantly better performance than those from the unexposed group on tasks involving recognition memory (face recognition and picture recognition). This is thought to be mediated by the parahippocampal cortices and is often preserved in children with developmental amnesia due to hypoxic-ischaemic damage (Baddeley, et al., 2001; Vargha-Khadem, et al., 2001). Children with M/S did not have significantly poorer performance relative to the unexposed group on any of the tasks.

Epilepsy status also had a limited effect on individual task performance. Children with active epilepsy performed significantly worse than those without epilepsy on the prospective and delayed recall tasks whereas there was no evidence of any group differences in the inactive epilepsy group.

Age and schooling were responsible for much of the variance in task scores (Appendix 27). Poor nutritional status (particularly as measured by weight/age and height/age ratios) resulted in poorer performance on the prospective, picture recognition, story recall and immediate recall tasks. The effects of other covariates were more erratic: female gender significantly improved performance on the remembering a name tasks but resulted in significantly worse scores on the story recall task and higher levels of maternal education significantly improved performance on the route recall, prospective items and orientation tasks.

15.3 Non-verbal functioning results

Non-verbal functioning was assessed with a construction test, which comprised six levels, each with three tasks. Five children were unable to complete the test, four (3 CM; 1 M/S) of whom were unable to understand the task requirements and one (unexposed) who had a visual impairment. Two (1 CM; 1 M/S) of the four had active epilepsy and two (CM) had limited language skills.

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	-0.33	-0.61 – -0.06	0.02
	M/S	-0.04	-0.31 – 0.24	0.8
Epilepsy status	Active epilepsy	-0.17	-0.78 – 0.44	0.58
	Inactive epilepsy	-0.63	-1.21 – -0.04	0.04
Age	7 years	0.38	0.07 – 0.69	<0.001
	8 years	1.03	0.7 – 1.36	
	9 years	1.23	0.88 – 1.58	
Sex	Female	-0.79	-1.02 – -0.57	<0.001
Schooling status	Nursery	0.84	0.57 – 1.1	<0.001
	Standard 1	1.6	1.24 – 1.95	
	Standard 2	2.21	1.76 – 2.66	
Nutritional status	Weight/height	-0.25	-0.16 – 0.65	0.23
	Height/age	-0.6	-0.97 – -0.23	0.001
	Weight/age	0.01	-0.49 – 0.5	0.98
SES status	Mother's education	0.12	-0.12 – 0.36	0.32
	Father's occupation	0.02	-0.21 – 0.25	0.84

Table 15. 13: Estimated differences in construction task scores in the exposed and epilepsy groups

15.4 Attention test

A visual search task measured speed of information processing, spatial processing, planning, impulsivity and sustained and selective attention. The task generated two error scores – errors of omission and errors of commission – and a measure of the time taken to complete the task. Eight children were unable to complete the task, seven (5 CM; 2 M/S) of whom were unable to understand the task requirements and one (unexposed) who had a visual impairment. Two (M/S) of the group of seven had active epilepsy and two (CM) had limited language skills.

15.4.1 Errors of omission

The omission scores had a skewed distribution with a median score of 3 in each group (figure 15.5). The outliers in the M/S group had higher scores (equating to poorer performance) than the CM or unexposed groups.

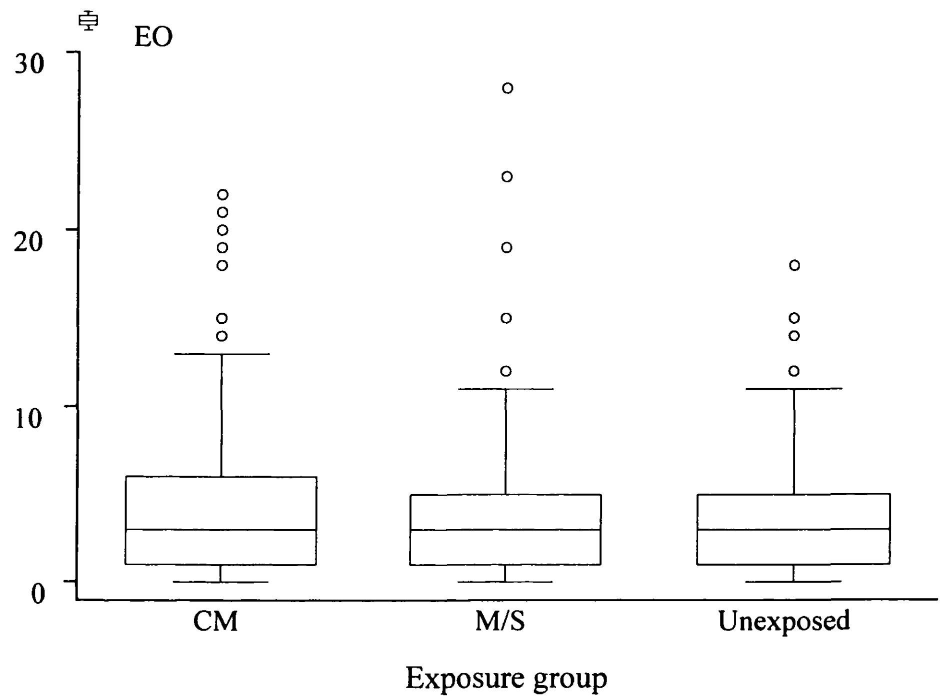

Figure 15. 5: Distribution of visual search – errors of omission (EO) scores by exposure group

15.4.2 Errors of commission

Fewer errors of commission than omission were made by each group. The median score in each group was 0, resulting in a highly skewed distribution of scores (figure 15.6). Both the CM and M/S groups had small numbers of extreme outliers.

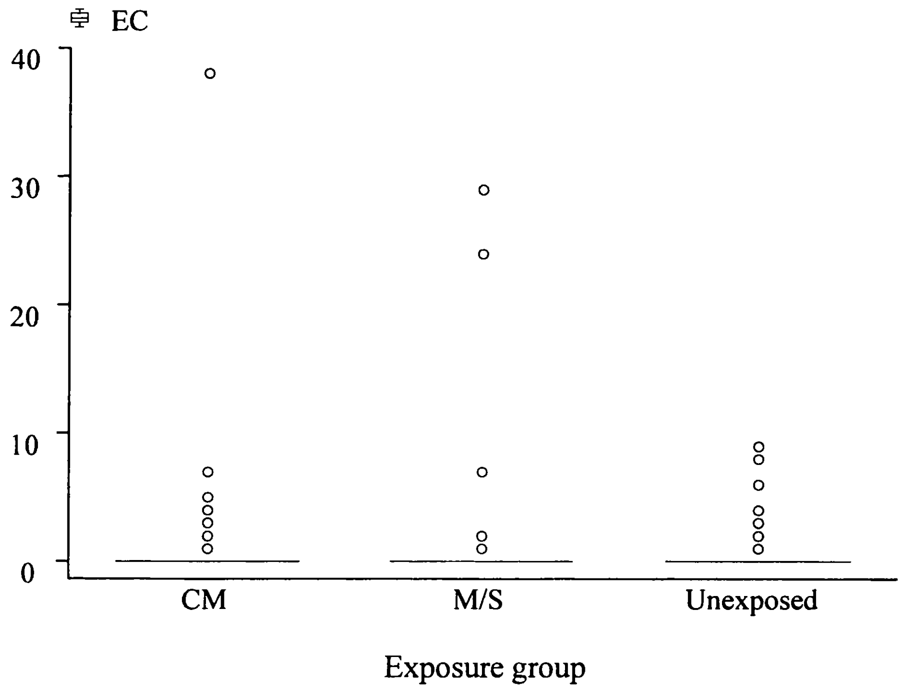

Figure 15. 6: Distribution of visual search – errors of commission (EC) scores by exposure group

15.4.3 Total error score

Errors of omission and commission were combined to generate one error score, which was analysed using a logistic regression model (cut-off=9). Performance was similar in the exposed and unexposed groups (table 15.14). There was a significant difference in performance between the active and no epilepsy groups. This effect was not replicated in the inactive epilepsy group, although the direction of the association with the no epilepsy group suggested poorer performance among children with inactive epilepsy.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	1.31	0.6 – 2.87	0.5
	M/S	0.86	0.37 – 1.99	0.72
Epilepsy status	Active epilepsy	5.55	1.66 – 18.52	0.01
	Inactive epilepsy	1.79	0.34 – 9.45	0.49
Age	7 years	0.66	0.31 – 1.4	0.004
	8 years	0.25	0.09 – 0.7	
	9 years	0.16	0.05 – 0.5	
Sex	Female	0.68	0.36 – 1.29	0.24
Schooling status	Nursery	1.05	0.52 – 2.12	0.44
	Standard 1	0.3	0.06 – 1.43	
	Standard 2	0.53	0.06 – 4.57	
Nutritional status	Weight/height	2.08	0.78 – 5.56	0.14
	Height/age	3.85	1.67 – 8.89	0.002
	Weight/age	1.3	0.46 – 3.7	0.62
SES status	Mother's education	0.68	0.33 – 1.42	0.31
	Father's occupation	1.04	0.55 – 1.99	0.9

Table 15. 14: Estimated odds of more errors on the visual search by exposure and epilepsy groups

15.4.4 Time taken

The time taken to complete the visual search was measured in seconds and expressed as minutes and seconds. The results approximated a normal distribution (figure 15.7). The mean scores were similar across the three groups, although the exposed groups had higher maximum scores (equating to poorer performance) than the unexposed group.

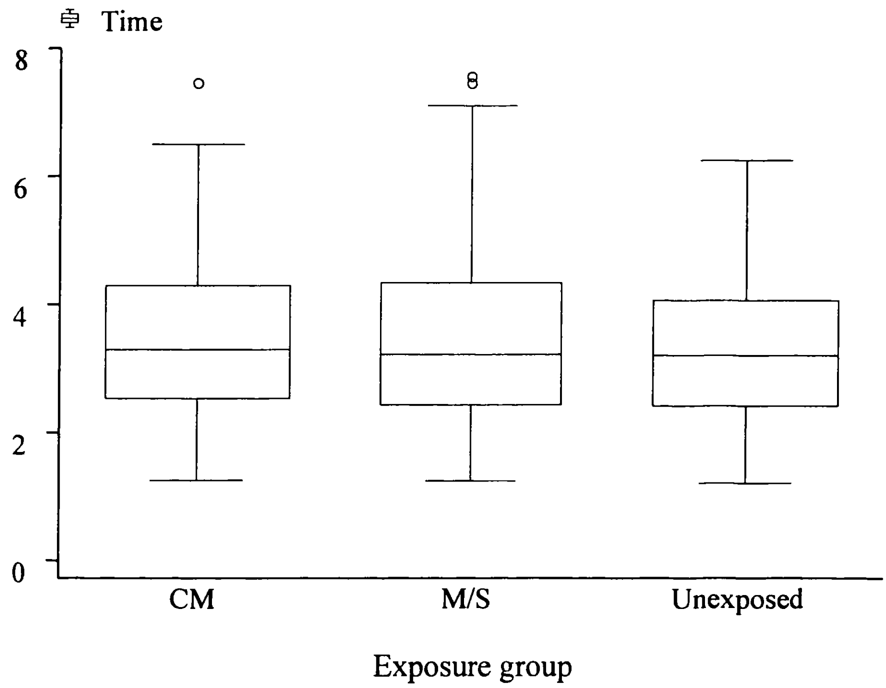

Figure 15. 7: Distribution of visual search – time taken (in minutes) by exposure group

There was no evidence of a difference in time taken between the exposed and unexposed groups or the epilepsy and no epilepsy groups (table 15.15).

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	0.04	-0.19 – 0.27	0.75
	M/S	0.08	-0.14 – 0.31	0.48
Epilepsy status	Active epilepsy	0.25	-0.25 – 0.76	0.32
	Inactive epilepsy	-0.26	-0.74 – 0.23	0.3
Age	7 years	-0.24	-0.5 – 0.03	<0.001
	8 years	-0.6	-0.87 – -0.32	
	9 years	-0.83	-1.12 – -0.54	
Sex	Female	-0.12	-0.31 – 0.06	0.2
Schooling status	Nursery	-0.29	-0.52 – -0.07	<0.001
	Standard 1	-0.78	-1.07 – -0.48	
	Standard 2	-1.24	-1.61 – -0.86	
Nutritional status	Weight/height	0.06	-0.28 – 0.39	0.75
	Height/age	0.4	0.09 – 0.71	0.01
	Weight/age	0.01	-0.41 – 0.43	0.95
SES status	Mother's education	-0.18	-0.38 – 0.02	0.08
	Father's occupation	0.02	-0.17 – 0.21	0.81

Table 15. 15: Estimated differences in time taken to complete the visual search between exposed and epilepsy groups

15.5 Behaviour questionnaire

The behaviour questionnaire comprised 15 questions scored from 0 to 2 (0=never exhibits the behaviour; 1=sometimes; 2=often). The results of the questionnaire had a skewed distribution with median scores of 4 in the CM and unexposed groups and 5 in the M/S group (figure 15.8). The exposed groups had broader distributions of scores and more extreme outliers than the unexposed group.

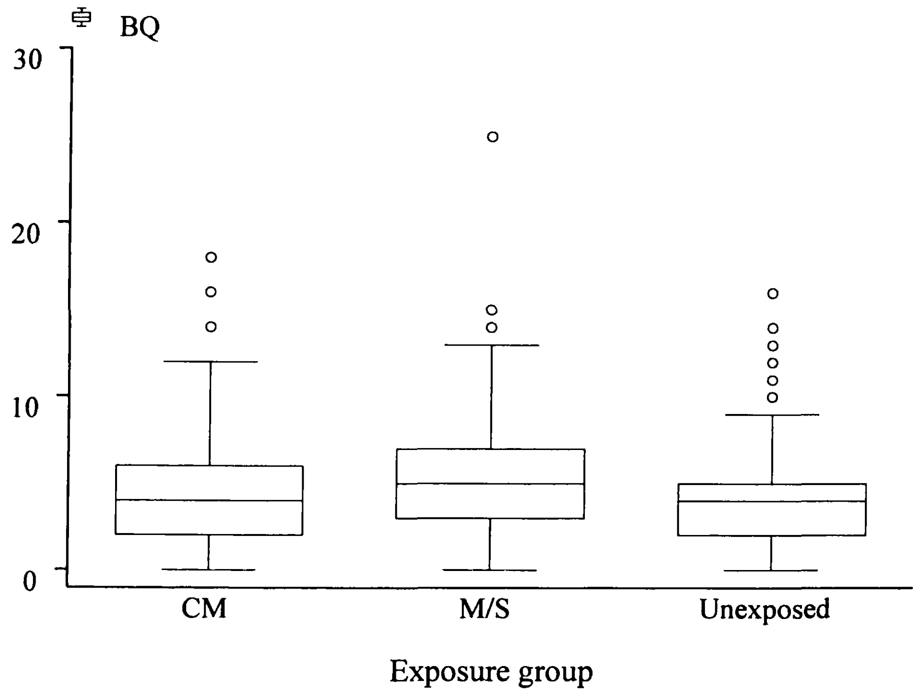

Figure 15. 8: Distribution of behaviour questionnaire scores by exposure group

A classification of problem behaviour was based on the system used by Holding and colleagues (1999), whereby the scores are divided into thirds, reflecting the three-point item-level scale, the top third indicating 'impaired behaviour', the middle third, 'borderline behaviour' and the bottom third, 'normal behaviour'. Following this system, the scores were divided into thirds (omitting the outlier with a score of 25 from the construction of the scale, although the child with this score was included in the 'impaired' group). Children from the M/S group had the highest proportion of 'impaired' and 'borderline' scores (table 15.16). Children from the CM group had an increased prevalence of such scores relative to the unexposed group.

Category	Scores	CM	M/S	Unexposed
Normal	**0-6**	118 (77.7)	115 (73.7)	154 (86)
Borderline	**7-12**	30 (19.7)	32 (20.5)	22 (12.3)
Impaired	**13-18**	4 (2.6)	9 (5.8)	3 (1.7)

Table 15. 16: Scoring categories in the behaviour questionnaire

'Impaired' and 'borderline' scores were amalgamated for comparison with 'normal' scores in a logistic regression analysis. The results showed significant differences in reported performance between the M/S and unexposed groups and the active and no epilepsy groups (table 15.17). There was no evidence of a difference between the CM and unexposed groups or the inactive and no epilepsy groups.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	1.24	0.67 – 2.3	0.49
	M/S	1.8	1.0 – 3.23	0.05
Epilepsy status	Active epilepsy	2.76	1.0 – 7.56	0.05
	Inactive epilepsy	1.08	0.33 – 3.56	0.9
Age	7 years	0.8	0.44 – 1.45	0.03
	8 years	0.31	0.14 – 0.66	
	9 years	0.67	0.33 – 1.37	
Sex	Female	0.55	0.34 – 0.88	0.01
Schooling status	Nursery	0.6	0.35 – 1.04	0.02
	Standard 1	0.3	0.12 – 0.73	
	Standard 2	0.28	0.09 – 0.92	
Nutritional status	Weight/height	0.97	0.41 – 2.31	0.94
	Height/age	0.8	0.36 – 1.75	0.57
	Weight/age	1.71	0.63 – 4.67	0.29
SES status	Mother's education	1.18	0.58 – 2.4	0.66
	Father's occupation	1.19	0.6 – 2.35	0.61

Table 15. 17: Estimated odds of a poorer performance in the behaviour questionnaire between exposure groups and epilepsy groups

15.5.1 Individual item analysis: exposure status

Individual item performance, measured by the percentage of the maximum score assigned to each group, indicated that the main areas of reported problems for the cohort were level of independence (wetting/soiling and self-care), repetitive habits, fears and mood (temper tantrums) (figure 15.9). The main area of difference between the CM and unexposed groups was number of habits (proportion of '2' scores: χ^2=4.7 p=0.03) and between the M/S and unexposed groups, frequency of wetting and soiling (proportion of '2' scores: χ^2=5.8 p=0.02). The M/S group had a higher proportion of the maximum score relative to the CM or unexposed groups on the majority of questionnaire items. Only on the affect, separation, dependency and concentration questions did the CM group equal or exceed the proportion attained by the M/S group.

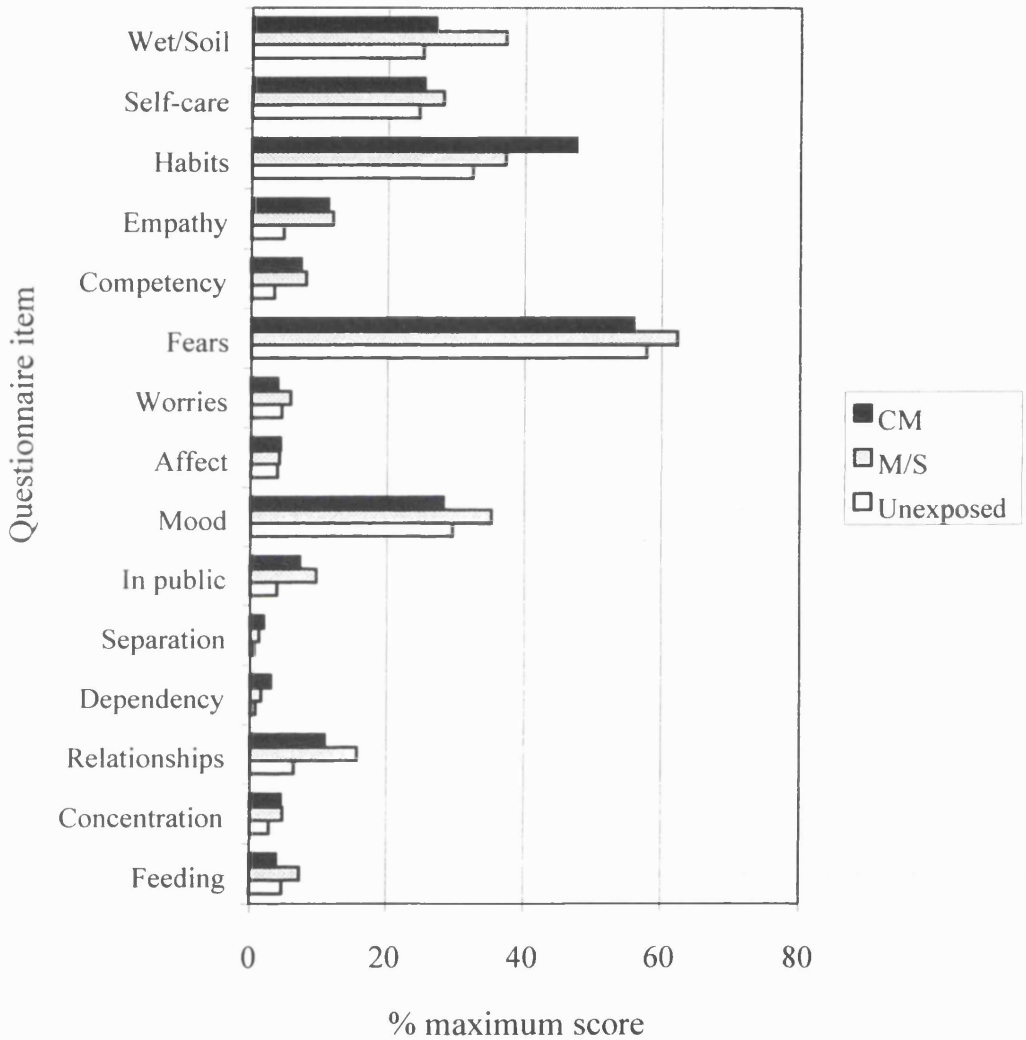

Figure 15. 9: Individual item analysis expressed as the proportion of the maximum score attained by each exposure group

Key:

Feeding: feeding and eating

Concentration: concentration span

Relationships: social relationships

Separation: separation from parents or close family

In public: behaviour in public

Mood: mood/temper

Competency: Social competency

Wet/Soil: Wetting and soiling

15.5.2 Individual item analysis: epilepsy status

Individual item performance was also analysed by epilepsy status because of the particular link between epilepsy and behavioural difficulties reported in the literature (section 8.3.3).

The active epilepsy group had a higher proportion of the maximum score relative to the inactive or no epilepsy groups on all questionnaire items except the social competency, separation from parents or family, social relationships and feeding questions (figure 15.10). The primary areas of difference between the active and no epilepsy groups were wetting/soiling (proportion of '2' scores: χ^2=4.02 p=0.05) and ability to empathise (χ^2=7.49 p=0.01), on which children with active epilepsy were reported to have more problems. In most aspects of behaviour, the inactive epilepsy group was reported to have a similar level of performance to the no epilepsy group. The only significant difference was in number of fears, in which the no epilepsy group had a higher proportion of the maximum item score (χ^2=3.99 p=0.05).

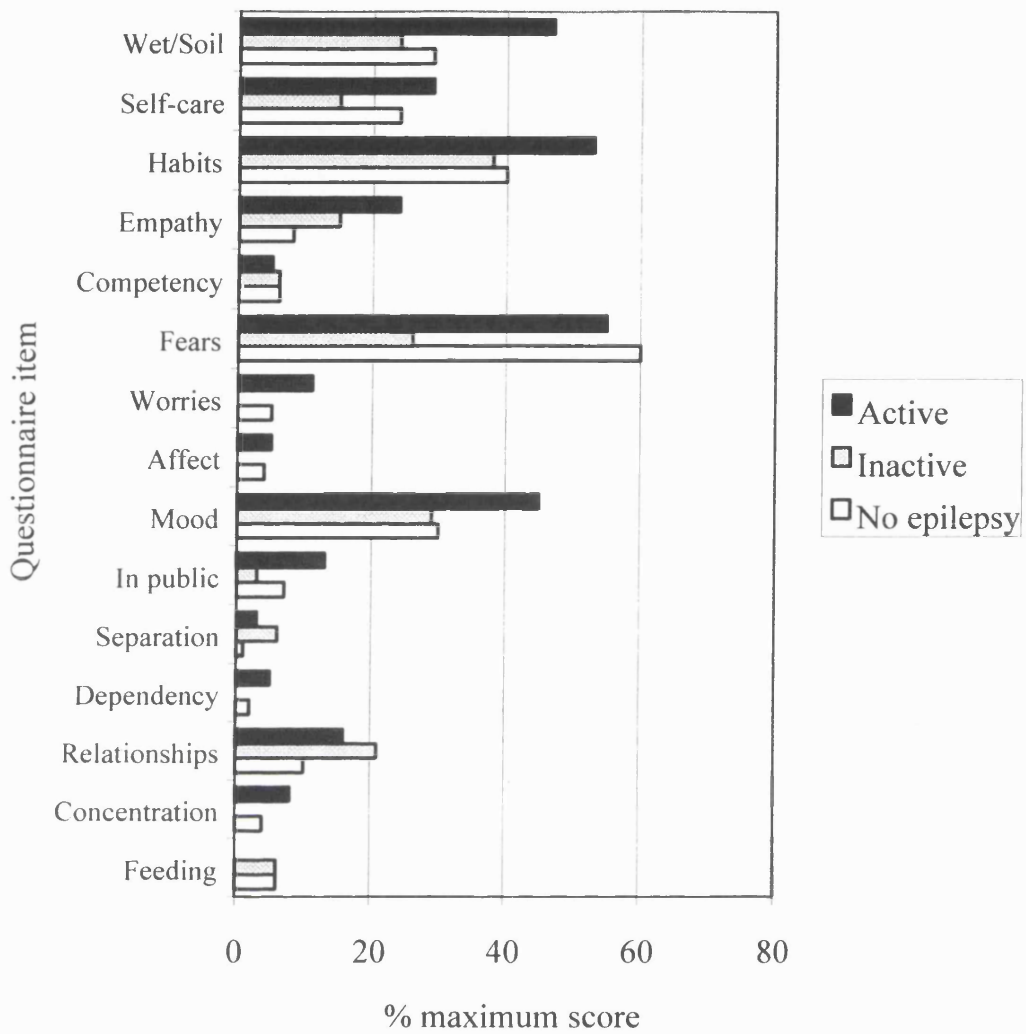

Figure 15. 10: Individual item analysis expressed as the proportion of the maximum score attained by each epilepsy group

Key same as Table ** except:

Active: active epilepsy

Inactive: inactive epilepsy

15.6 Summary and discussion

15.6.1 Overview

The direction of the association between the CM and unexposed groups suggested poorer performance among children with previous CM on all of the cognitive assessments. However, the only significant difference between the groups was found on the non-verbal functioning (construction) task.

There was no evidence of a difference in performance between the M/S and unexposed groups on the assessments of non-verbal functioning, memory or attention, although the direction of the association on the non-verbal functioning task suggested poorer performance in the former group. There was a significant difference between the groups in reported behaviour.

The performance of the active epilepsy group was significantly poorer than that of the group without epilepsy on the measures of attention (number of errors) and behaviour, specifically wetting/soiling and ability to empathise. The estimated odds of an 'impaired' memory score were also significantly higher among children with active epilepsy. The direction of the association between the two groups was suggestive of poorer non-verbal functioning performance in the active epilepsy group.

There was a significant difference between the scores of children with inactive and no epilepsy on the measure of non-verbal functioning. The pattern of disparate results between the active and inactive epilepsy groups reflects that found in the results of the speech and language battery, on which children with inactive epilepsy did not have the same level of poor performance as children with active epilepsy.

15.6.2 The CM group

The findings in the CM group suggest that although there is a trend towards poorer performance, when active epilepsy is taken into account the presumed insult is not sufficient to cause persisting impairments in the cognitive facets measured in the current study. In the context of previous results in a similar population (Holding, et al., 1999), it may be that the children have recovered from an original level of impairment in some areas, although recovery is not universal to cognitive functions, as difficulties remain in non-verbal functioning.

The measures of non-verbal functioning, attention and behaviour were taken from a previous study carried out in the same geographical area (Holding, et al., 1999). Holding and colleagues found significant differences in performance on the behaviour questionnaire and attention assessment (time taken) between a group of 6-year-old children at least 42 months after severe malaria with impaired consciousness and a group of controls. There was no evidence of a difference in performance on the non-verbal functioning task, although the direction of the association suggested poorer performance among children with a history of severe malaria. Holding concluded that the nature of the difficulties she identified could be attributed to developmental immaturity. Qualitative analysis of attention task performance in the severe malaria group indicated that their difficulties could be explained by inefficient planning rather than impaired attention and group differences in reported behaviour focussed on immature behaviours (independence/self care and habits/repetitive actions), as opposed to issues of control or developmental problems (Holding, 1998). If such an immaturity was due to irreversible brain damage or dysfunction, differences in group performance would be exacerbated by advancing age, as the cognitive requirements of tasks increase in complexity. Alternatively, if the effects of any damage are reversible in the majority of children after a period of recovery, group differences would be expected to diminish over time. Following this line of reasoning, it could be argued that the discrepancy in behaviour and attention results may be partly explained by the fact that the current study included older age groups, after a longer post-admission period (median 64 months in the CM group): group-level impairments in these functions may have attenuated over time, thus supporting the latter hypothesis. The direction of the association between the CM and unexposed groups indicated poorer performance among the children with CM and there were outliers on both the attention and behaviour measures, which suggests that the level of group performance has improved but that there may still be a subgroup of children with impairments. This possibility will be discussed in Chapter Sixteen.

Evidently, this line of reasoning does not apply to the non-verbal functioning findings. The construction task had been altered since Holding and colleagues' study (section 8.3.2.2): the new version proved problematic in several ways, suggesting that the results may have been influenced by the response of the group to difficulties with the assessment. The task had been extended from the original test format and developed into a learning task (a teach-test format), in which the child received prompts and verbal feedback for each item. In addition, stick drawings replaced the stick templates used in the original study and some children reported finding the stick drawings difficult to interpret because the joins between the sticks were not visible on the pictures. The assessors reported that the test was very long and many children complained of boredom. As the findings of Holding and colleagues' study were approaching significance, an alternative hypothesis is that the current study had greater power to detect a difference because of the larger numbers of participants. Finally, children participating in the current study were assessed on the KEMRI site whereas the assessments were administered at home to the participants in Holding and colleagues' study: the possibility of differences in performance with study site has not yet been measured (Dr P Holding, personal communication).

Other studies of neuropsychological functioning after CM or severe malaria with impaired consciousness have reported conflicting results. Muntendam and colleagues (1996) found no impairments in Gambian children assessed an average of 3.4 years after hospitalisation, except in the balance task of a sensory-motor development test. Boivin (in press) administered an adapted version of the Kaufman Assessment Battery for Children but found contrasting results to Holding and colleagues (1999) (who also used an adapted version of this battery) in that they found group differences in performance on aspects of sequential and simultaneous processing and non-verbal performance.

Methodological variations in studies, for example heterogeneous assessment procedures and populations, make comparisons difficult, either with the current study or between other studies. The current study is one of the first (the other being that of van Hensbroek and colleagues (1997)) to follow-up all children in the target age group with a recorded history of CM, rather than employing selection procedures. Another difference in the current study is that it was not designed to investigate general cognitive impairments following severe forms of malaria but to focus on specific temporal lobe deficits, therefore, the bulk of the cognitive battery was the KCBMT. In consequence, the assessments were not necessarily specific to the cognitive impairments associated with CM. Considering the trend for lower mean scores in the CM group, it is possible that subtle impairments exist but that the assessments were not sensitive enough to identify them. In addition, the criteria for a diagnosis of CM differs between studies. For example, Boivin (in press) did not provide information on the depth of coma, while one of the accepted criteria for CM is a deep level of unconsciousness, defined as the inability to localise a painful stimulus (Newton, et al., 2000). Holding and colleagues (1999), while meeting this criterion, chose a Blantyre coma score cut-off of ≤4 (resulting in the label of 'severe malaria with impaired consciousness, as opposed to 'CM') whereas the current study used a cut-off of ≤2.

The current study aimed to investigate the link between epilepsy and developmental impairments, thus epilepsy status was included as one of the covariates, in contrast to previous studies. The results suggested an association between active epilepsy and CM. Attempting to explain the disparate results from studies of neuropsychological impairment following CM, Boivin (in press) hypothesised that the multiple pathogenetic subtypes in CM, as discussed by Marsh and colleagues (1996), may result in different impairment profiles at follow-up (section 2.3.2). This was not investigated in the current study but the data could be used for a subsequent analysis of this hypothesis.

The largest proportion of 'impaired' scores on the KCBMT were found in the CM group, although the group difference was not significant after adjustment for other covariates. Individual KCBMT task analysis indicated the possibility of hippocampal or mesial temporal damage in this group, although this assessment is a screening tool, therefore more evidence would be required to investigate this possibility further.

15.6.3 The M/S group

The hypothesis of an association between complex partial seizures in malaria and temporal lobe damage was not supported by the findings of the cognitive assessment battery, namely those of the KCBMT. The association between complex febrile seizures and later mesial temporal sclerosis (MTS) is contentious and has mainly been construed from retrospective studies of surgically-treated temporal lobe epilepsy and animal work. Several population-based and prospective studies have failed to find an association (Lado, et al., 2000; Shinnar and Glauser, 2002), although hippocampal changes have been reported using magnetic resonance techniques (Scott, et al., 1998). Selective temporal lobe effects on cognition have only been reported in those with clear evidence of MTS and active epilepsy originating in that region and not in those who have been exposed to the primary risk (complex seizures) but who do not have subsequent epilepsy. The main problem in looking at these associations in the UK context has been that MTS is likely to be an uncommon sequela to complex febrile seizures, possibly affecting only those with seizures over 90 to 100 minutes in length (Maher and McLachlan, 1995). Seizures of such length are relatively common, possibly occurring in 1% of the 3-4% of the UK population who have febrile seizures (Berg and Shinnar, 1996) but it would still be difficult to recruit sufficient children to establish an association that would be significant at group level. A similar situation may occur in this context, indicating the need for a larger study and longer follow-up, with more sensitive neuropsychological assessment of hippocampal function or magnetic resonance studies.

Several studies have reported an association between pragmatic, emotional and behavioural disorders (McTear and Conti-Ramsden, 1992), so the combination of behavioural and pragmatic impairments (the latter discussed in Chapter Sixteen) is not unexpected. The distribution of behavioural scores was skewed. Although there was a broader distribution of scores among the children with previous M/S relative to the unexposed group, the similar median scores suggest that the larger number of outliers in that group may have been partly responsible for the group difference. However, as a group, children with previous M/S had a higher proportion of maximum scores compared to either the CM or unexposed groups on 11 of the 15 items on the questionnaire. This indicates poorer reported performance across behavioural domains rather than one or two isolated areas of difficulty. However, level of independence as represented by wetting and soiling, fears and mood (temper tantrums) were the main areas of difference between the M/S and unexposed groups, suggesting that immature behaviour and issues of control were the focus of problems.

Behaviour problems suggestive of difficulties with separation and fearfulness have been associated with hospitalisation (Perrin, 1999), although this is an unlikely interpretation of these results because the experience of hospitalisation was not recent. In addition, there was no evidence of significant difficulties among children with previous CM, who would arguably have been hospitalised for a more prolonged period. However, the fact that the main sources of group differences between the M/S and unexposed groups were both parental questionnaires suggests a number of possibilities to account for the differences. First, in contrast to the assessors, parents were not blind to the exposure status of their child, which may have introduced bias.

Parents were aware that the purpose of the study was to identify children with developmental impairments: continued research work in the community has created expectations among some of the local population that participation in research projects will lead to improved health care (as the unit is attached to the district hospital) or conceivably in this case, educational benefits (Dr S Molyneux, personal communication). Alternatively, the experience of having nursed their child through a potentially life-threatening illness may have engendered a particular sensitivity to the child's subsequent development. This creates the possibility that parents are directly influencing the differences in behaviour identified (Campbell, 1995). However, these explanations for differences found on parental questionnaires are again unlikely because of the lack of evidence for a group difference in the CM group, whose parents are in the same situation as described above. The possibility is also raised, as in the previous chapter, that these results may suggest that the group has subtle cognitive impairments that are not detected by the current assessments but are apparent to parents.

15.6.4 The active epilepsy group

The pattern of results is similar to that found in the speech and language battery, with a trend of poorer performance across the range of cognitive and behavioural assessments. In addition, there was again a pattern of assessments in which there were significant differences between the epilepsy and no epilepsy groups to have lower but not significantly different mean scores between the CM and unexposed groups. As discussed in section 14.11.4, this suggests a link between CM and active epilepsy, in that the former is associated with baseline performance in certain cognitive facets whereas the latter affects functions spared by malaria.

The level of cognitive and behavioural performance among children with active epilepsy in the context of previous malaria is not surprising: between 15 and 30% of childhood-onset epilepsies are associated with learning difficulties (Shinnar and Pellock, 2002) and symptomatic epilepsy is more likely to result in cognitive and behavioural deficits than idiopathic epilepsy (Cull, 1988). Children with epilepsy are at increased risk of cognitive and behavioural problems, exposed both to the risk associated with chronic illness and that engendered by a neurological disorder (Dunn and Austin, 1999). In an epidemiological study of childhood behaviour problems, the prevalence of problems was highest in children with seizures and CNS damage (58.3%), compared to children with CNS damage (37.5%) or seizures (28.6%) alone (Rutter, et al., 1970). Even in childhood epilepsy syndromes in which language deficits are the dominant feature, such as LKS, impairments in memory (Robinson, et al., 2001) and behaviour (Neville, et al., 2000) have been reported. Children with benign epilepsy with centrotemporal or Rolandic spikes (BECRS) have generally been found to have intelligence within the normal range but with specific weaknesses in various domains such as memory (Croona, et al., 1999; Deonna, et al., 2000; Weglage, et al., 1997); attention (D'Alessandro, et al., 1990) and behaviour (Weglage, et al., 1997). The experience of BECRS suggests that paroxysmal activity alone may be sufficient to disrupt cognitive processes, even in the absence of conditions that may be present in this situation: organic brain damage and adverse sociocultural conditions.

The cognitive and behavioural difficulties identified in the current study may be a direct consequence of central nervous system dysfunction. Using parental behaviour ratings, Dunn and colleagues (1997) found a greater prevalence of reported behaviour problems in children up to six weeks after a first non-febrile seizure (24%) than in the same cohort four months after the initial interview (12%). Although parental anxiety relating to the initial seizure episode may have biased the first interview, Dunn and colleagues suggested that the reported improvement in behaviour may indicate that the effects of recurrent seizures, anti-epileptic medication or social stigma were less of a contributory factor to behaviour problems than central nervous system dysfunction. Alternatively, the presence of early and prolonged epileptic activity at a time of active learning may affect the development of neuronal networks and lead to permanent damage. The latter would suggest that the prognosis for the active epilepsy group is poor and that impairments may become more apparent as the social and educational demands placed on the child increase (Cross and Ozanne, 1990).

15.6.5 The inactive epilepsy group

As with the speech and language results, children with inactive epilepsy did not have the same level of poor performance as children with active epilepsy. There was a significant difference between the scores of children with inactive and no epilepsy on the measure of non-verbal functioning. This may have been a chance finding due to the number of assessments in the cognitive and speech and language batteries.

A recent study investigating seizure control and educational outcome produced findings supportive of the current results. Fifteen percent of children who had been seizure-free for at least one year after the cessation of therapy required special educational provision compared to 89% with active secondary generalised epilepsy and 46% with active partial epilepsy (Zelnik, et al., 2001). Studies of the cognitive impact of 'inactive epilepsy' often refer to children who are seizure-free as a result of effective treatment with anticonvulsant medication. Although not immediately comparable to the current inactive epilepsy group, none of whom were receiving treatment, a study of children with cerebral palsy and well-controlled epilepsy indicated that children with a history of seizures were impaired on measures of verbal and non-verbal IQ and memory (Vargha-Khadem, et al., 1992), which is in contrast to the findings of Zelnik and colleagues and those of the current study.

15.6.6 Other effects on performance

Age and schooling had a consistently positive effect on performance on the cognitive assessments. Low height/age scores were associated with significantly poorer performance on the memory, non-verbal and attention assessments. Gender was also a factor in explaining the variance in scores. Girls had a significantly poorer performance than boys on the non-verbal functioning assessment and a significantly better reported performance on the behaviour questionnaire. The latter finding may be influenced by different parental expectations of boys and girls: greater compliance is often expect and enforced in girls than boys in many rural African communities (Serpell, 1993). Despite the effects of these covariates, exposure status and epilepsy status both had an effect on performance on the cognitive battery.

In summary, there was a trend towards poor performance in children with previous CM, although the only significant different between the CM and unexposed groups was on the non-verbal functioning assessment. Interpreted in the light of Holding and colleagues' study, which assessed younger children after a shorter follow-up, these results may indicate that the level of group performance has improved over time but that there may still be a subgroup of children with impairments in cognition and behaviour. As with the speech and language battery, areas of reduced functioning among children with previous M/S were more circumscribed, focussing on reported behaviour, in which the M/S group had significantly increased odds of difficulties. There was no evidence of specific hippocampal damage or dysfunction in the M/S group on KCBMT subtests, although the scores of the CM group were significantly poorer than those of the unexposed group on several subtests linked to hippocampal functioning. Cognitive and behavioural functions were generally depressed in children with active epilepsy: a similar level of poor performance was not seen in the inactive epilepsy group.

Chapter Sixteen: Summary of Results and Description of the Impaired Group

16.1 Summary of the results

There was a significant increase in the prevalence of epilepsy in children who had previously been admitted with CM (OR=4.4 95%C.I.=1.42 – 13.69 p=0.01) or M/S (OR=6.1 95%C.I.=2.02 – 18.25 p=0.001) compared to the unexposed group. The most commonly reported active seizure types were tonic-clonic (42%), partial becoming secondary generalised (16%) and a combination of the two (21%). Only two instances of other seizure types – one each of complex partial seizures and tonic seizures, both in children from the M/S group – were reported. The EEG focal features categories included both epileptiform abnormalities and non-specific focal slow wave abnormalities: both were uncommon.

The direction of the association with CM suggested a poorer performance on all of the assessments with the exception of the receptive vocabulary and syntax assessments from the language battery. These differences were significant on the assessments of higher level language, lexical semantics (content words), pragmatics and non-verbal functioning (construction task). The scores of the CM group were significantly poorer than those of the unexposed group on several KCBMT subtests linked to hippocampal functioning

In contrast, there was no evidence of a difference in performance between the M/S group and the unexposed group on many of the assessments, although their performance on the tests of lexical semantics, pragmatics, phonology, non-verbal functioning, behaviour and motor skills was poorer than that of the unexposed group. The areas of reduced functioning for the M/S group were concentrated on phonology, pragmatics and behaviour, in which there were significant differences in performance. There was no evidence of specific hippocampal damage or dysfunction in the M/S group on KCBMT subtests.

The performance of the active epilepsy group was significantly lower than that of the group without epilepsy on the tests of receptive grammar, receptive vocabulary, syntax, pragmatics, word finding, 'impaired' memory, attention errors, behaviour and motor skills. The direction of the association suggested poorer performance in the active epilepsy group on the remaining assessments, with the exception of the function word element of lexical semantics and the 'borderline' category of the memory test.

Children with inactive epilepsy did not have the same level of poor performance as children with active epilepsy. They had lower estimated scores than children without epilepsy on several language assessments – receptive grammar, lexical semantics (content words) and word finding – as well as attention and behaviour. Their performance was significantly lower than that of the no epilepsy group on the measure of non-verbal functioning.

Neither the CM or M/S groups had an increased prevalence of visual or hearing problems. Twelve children were diagnosed as having hearing problems on the audiometric screening test, eleven mild and one moderate. Five of these children were from the unexposed group.

Despite the fact that there was no evidence of a difference between the exposed and unexposed groups in performance on some of the assessments, there was a trend towards lower mean/median and minimum scores in the exposed groups (particularly the CM group) relative to the unexposed group. This may indicate the existence of a group of outliers with poor performance, in the context of average group performance. To investigate this possibility, an 'impairment' group was defined by the process described in the next section.

16.2 The 'impaired' group

There is no universally-accepted system for defining impairment on non-standardised neuro-cognitive assessments (Anderson, 2001). However, a commonly accepted classification of ability levels is described by Lezak (1995) and reproduced in table 16.1.

Classification	z-score	Percent included	Lower limit of percentile range
Very superior	+2.0 and above	2.2	98
Superior	+1.3 to 2.0	6.7	91
High average	+0.6 to 1.3	16.1	75
Average	+/-0.6	50	25
Low average	-0.6 to -1.3	16.1	9
Borderline	-1.3 to -2.0	6.7	2
Impaired (retarded*)	-2.0 and below	2.2	-

Table 16. 1: Classification of ability levels from Lezak (1995, p159)

* the term 'impaired' will be used in place of 'retarded'

In the current study, several of the assessments – the KCBMT, behaviour, neurological, hearing and vision assessments – indicated 'impairment' levels. For the remaining assessments, an estimate of more than 2SDs below the age-specific unexposed group mean or below the 2.0 centile of the unexposed group results was adopted for normally-distributed and skewed data respectively.

16.3 Low functioning children

Through the course of the study, a group of eight children emerged who were unable to attempt some of the assessments because they were functioning at such a low level. All of these children were able to attempt at least some of the assessments, therefore it was possible to ascertain their performance to a degree and they are included in further descriptions of the 'impaired' group in sections 16.4 and 16.5. However, because of their low ability level, they stood out from the rest of this group and merit further description.

None of these children were able to complete the visual screening and all except one (ID 415) were unable to complete the hearing test. Four (ID 034, 184, 253, 285) could not do the non-verbal functioning assessment and all except one (ID 034) were unable to complete the attention test. Most were able to attempt the speech and language battery, although five (ID 253, 285, 428, 451, 471) were unable to produce enough language for the lexical semantics assessment and three (ID 184, 285, 428) could not complete the syntax assessment. In most cases, the notes made by the assessors indicate that the reasons for non-completion were lack of understanding of the task demands, poor attentional skills and limited expressive language. Three children (ID 184, 285 and 428) produced very little expressive language, limited only used to single words.

Six of the eight children in this subgroup were from the CM group and two were from the M/S group (table 16.2), representing 3.9% and 1.3% of the CM and M/S groups respectively. All of the children were females and most were in the younger age groups. None were attending school. One child was reported to have a possible birth injury and had delayed speech and language development at the time of admission to hospital for CM, which may account for the impairments detected in this study. Three of the children, including both children from the M/S group, had active epilepsy. Both of the children with previous M/S and four of the children with previous CM were above the median ages of admission in the respective groups (CM group=2:4; M/S group=1:11).

In terms of impairments detected on the assessments the children were able to complete, all children had impairments on at least four of the speech and language assessments (the number in brackets indicating the number of assessments on which an impairment was detected). As indicated in Appendix 28, all of the children were at the severe end of the speech and language impairment spectrum, as defined by the number of assessments on which there were impairment-level scores. Seven of the eight children were described as impaired on the KCBMT and the neurological examination. Two children were assigned an impairment score on the behaviour questionnaire, according to the method described in section 8.3.3.

ID	034	184	253	285	415	428	451	471
Diagnosis	CM	CM	M/S	CM	CM	M/S	CM	CM
Age (years)	9	7	7	7	7	6	6	6
Age of insult (y:m)	2:10	2:2	3:0	2:7	2:3	2:1	3:1	3:3
Pre- or peri-natal problems	N	N	N	N	N	N	Y*	N
Developmental problems pre-malaria	N	N	no info	N	N	no info	Y*	N
Epilepsy	Y**	N	Y**	N	N	Y**	N	N
Impairments on study assessments	S/L(5) Mem Neuro	S/L(4) Mem Behav Neuro	S/L(4) Mem Neuro	S/L(5) Mem Behav	S/L(4) Neuro	S/L(5) Mem Neuro	S/L(4) Mem Neuro	S/L(7) Mem Neuro

Table 16. 2: Demographic, developmental and performance characteristics of the low functioning group

* Problems breathing after birth; admitted to hospital for one week. Mother reported speech was delayed at the time of hospital admission

** All cases are active epilepsy

Key

S/L speech/language	Mem KCBMT
Behav behaviour	Neuro neurological

16.4 Patterns of impairment and epilepsy

To determine levels and trends in impairments across the domains tested in the study, the core assessments were selected and performance across the groups analysed. Detailed individual data are presented in Appendix 28. The proportion of children with impairments in the CM (23.7%) and M/S groups (23.7%) was higher than in the unexposed group (10.1%) (figure 16.1). The proportion of children with impairments in the unexposed group is comparable to levels found in other resource-poor countries: 7% of 2-9 year old Bangladeshi children have been found to have developmental impairments (Khan and Durkin, 1995) and 8.4% of children in a recent survey of 6-9 year olds in Kilifi have been found to have impairments (Mr V Mung'ala-Odera, personal communication).

The speech and language battery was the most common locus of impairment in both groups exposed to severe malaria. Neurological and memory impairments were the most common impairment in the unexposed group and this group had more impairments in hearing and vision than the CM or M/S groups. There were more impaired children in the CM group in each of the other domains except behaviour, in which there was a markedly increased number of M/S group children with impairments compared to the other groups.

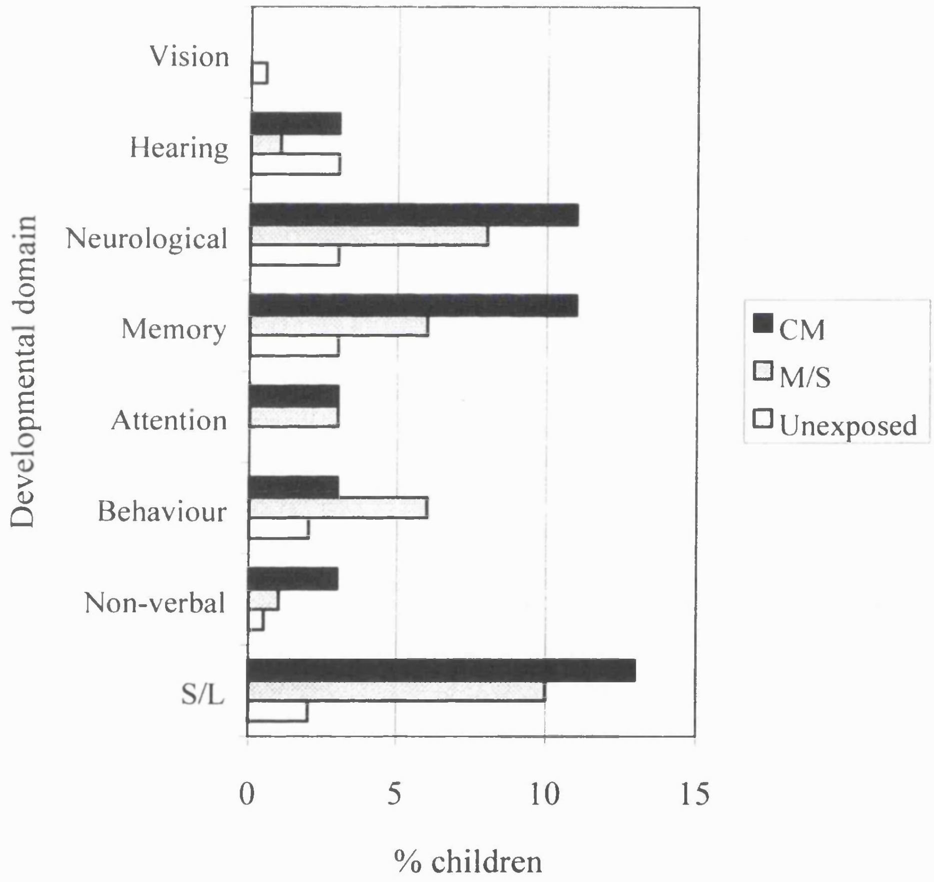

Figure 16. 1: Proportion of children with impairments in each developmental domain by exposure group

A previous diagnosis of CM or M/S increased the adjusted odds of an impairment in any domain assessed relative to the unexposed group (table 16.3). The estimated odds of an impairment-level score was significantly higher in the active epilepsy group compared to the no epilepsy group. There was no evidence of a difference between the inactive and no epilepsy groups, although the direction of the association suggested poorer performance among the children with inactive epilepsy.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	2.27	1.18 – 4.38	0.02
	M/S	2.44	1.27 – 4.7	0.01
Epilepsy status	Active epilepsy	3.05	1.06 – 8.77	0.04
	Inactive epilepsy	1.16	0.34 – 4.03	0.81
Age	7 years	1.82	0.92 – 3.6	0.06
	8 years	2.59	1.27 – 5.3	
	9 years	2.2	1.01 – 4.78	
Sex	Female	1.12	0.68 – 1.85	0.65
Schooling status	Nursery	0.53	0.31 – 0.93	<0.001
	Standard 1	0.1	0.03 – 0.32	
	Standard 2	0.15	0.04 – 0.55	
Nutritional status	Weight/height	1.06	0.43 – 2.61	0.89
	Height/age	1.14	0.53 – 2.46	0.74
	Weight/age	2.06	0.79 – 5.42	0.14
SES status	Mother's education	1.16	0.68 – 2.0	0.59
	Father's occupation	1.34	0.8 – 2.22	0.26

Table 16. 3: Estimated odds of impairment in any domain by exposure group

Despite the fact that the odds of an impairment in any domain were slightly increased in the M/S group (OR=2.35; 95%C.I.=1.22 – 4.56) compared to the CM group (OR=2.21; 95%C.I.=1.14 – 4.28), there were larger numbers of children with previous CM who had more extensive impairments, as measured by the number of domains in which an impairment-level score was assigned (figure 16.2). The proportion of the CM impaired group with two or more impaired domains was 41.6% compared to 29.7% and 22.2% of the M/S and unexposed impaired groups respectively. The numbers were too small for further statistical analysis.

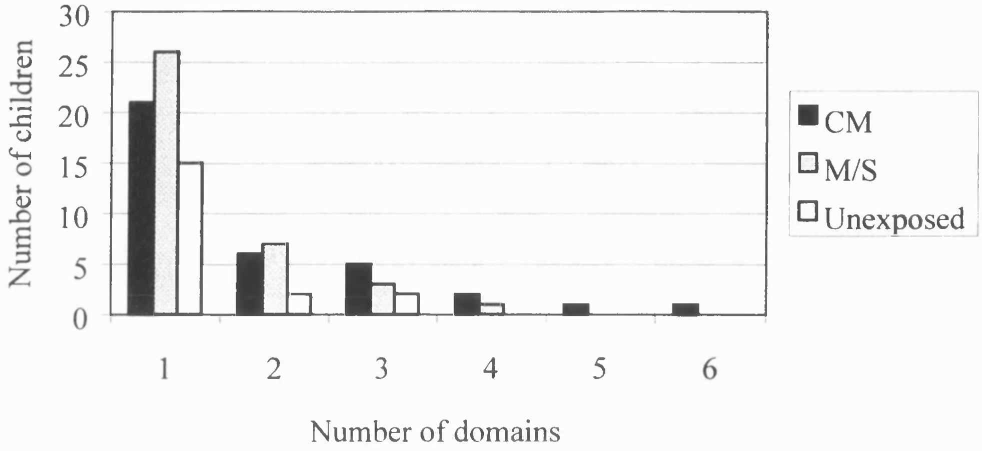

Figure 16. 2: Number of domains with impairment-level scores by exposure group

16.5 Speech and language battery

Forty-three (28.3%) of the CM group, 44 (28.2%) of the M/S group and 14 (7.8%) of the unexposed group had an impairment level score on one or more of the eight speech and language assessments. For children without a lexical semantics score, the MLU score was used.

'Impairment' on the speech and language battery was based on an impairment level score on two or more of the assessments. Although impairments on individual components of the speech and language battery may be valid, it was thought that the novelty of the assessments and the population's unfamiliarity with such assessment techniques advocated caution in the designation of impairment labels. Sixty-two percent (56% CM; 66% M/S; 71% unexposed) of the children with impairment level scores had such a score on only one assessment. In the CM group, single impairment scores were concentrated on the lexical semantics (n=7), receptive vocabulary (n=5) and phonological (n=8) assessments. The predominance of single impairments in the M/S group was in the phonological (n=10) and pragmatics (n=11) assessments. Single scores were distributed across the assessments in the unexposed group, producing no patterns.

For children classified as impaired in speech and language, there was a discrepancy in the patterns of impairments across the three groups (figure 16.3). There was no clear focus of impairment in the unexposed group: relatively small proportions of children in the group were impaired in assessments across the speech and language domain. The locus of impairment in the M/S group was clearly in the phonology and pragmatics assessments. The locus was less clear in the CM group but the two measures of vocabulary – receptive vocabulary and lexical semantics – had the largest proportions of children with impairments. Measures of grammatical ability – receptive grammar and syntax – had the smallest proportions of impairments in the CM group.

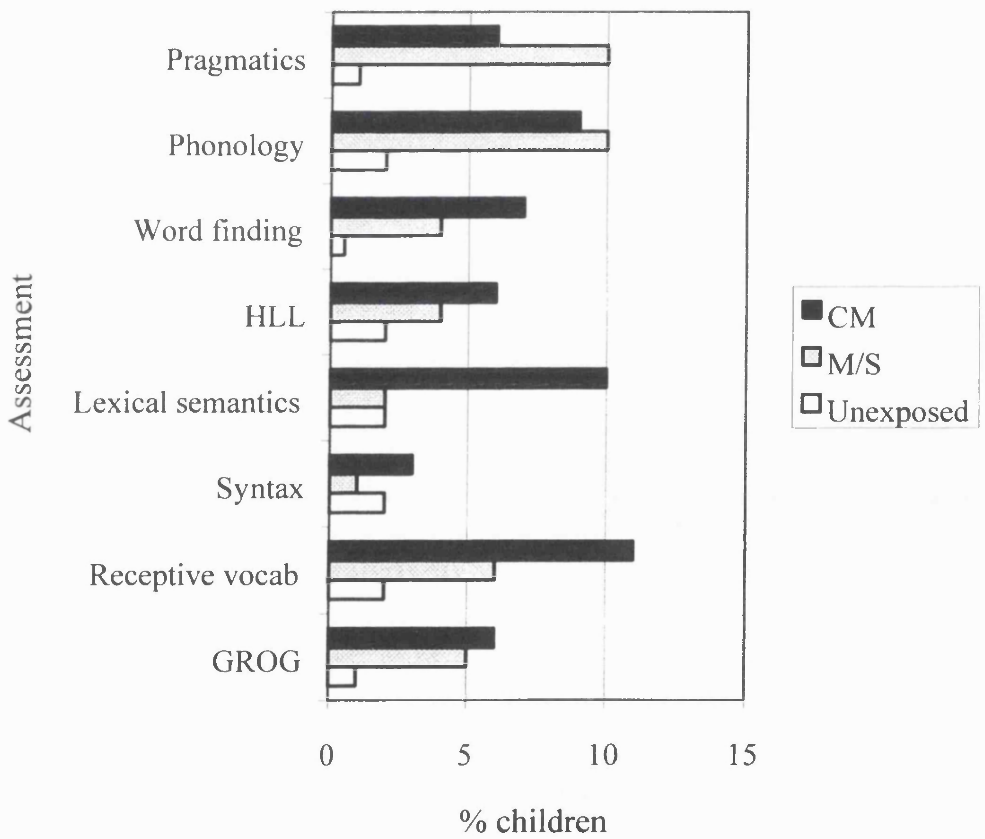

Figure 16. 3: Proportion of children with speech and language impairments by exposure group

Key:

GROG receptive grammar

HLL higher level language

Children from the CM group had more extensive impairments, defined as a greater number of assessments on which performance was designated as impaired, than either the M/S or unexposed groups (figure 16.4). The majority (71%) of children with previous M/S had impaired performance on two assessments whereas over 50% of the CM group had at least three assessments with impairments.

Four children from the unexposed group had impairments, two of which were in more than two assessment domains. Three of these children had previous hospital admissions (section 12.4.1) and two had been diagnosed with hearing impairment (one moderate with three impaired scores; one mild with two impaired scores). The child with impairment level scores on four assessments had previously been admitted with LRTI, which may conceivably result in neurological damage in two ways: first, due to hypoxia and second, due to the increased likelihood of aspiration if there is pre-existing neurological damage. One of the children with two impaired scores had previously been admitted with malaria, in addition to having a mild hearing impairment. The other child was reported by the mother to have been admitted to another hospital with CM but as this could not be verified with official records, the child remained in the unexposed group.

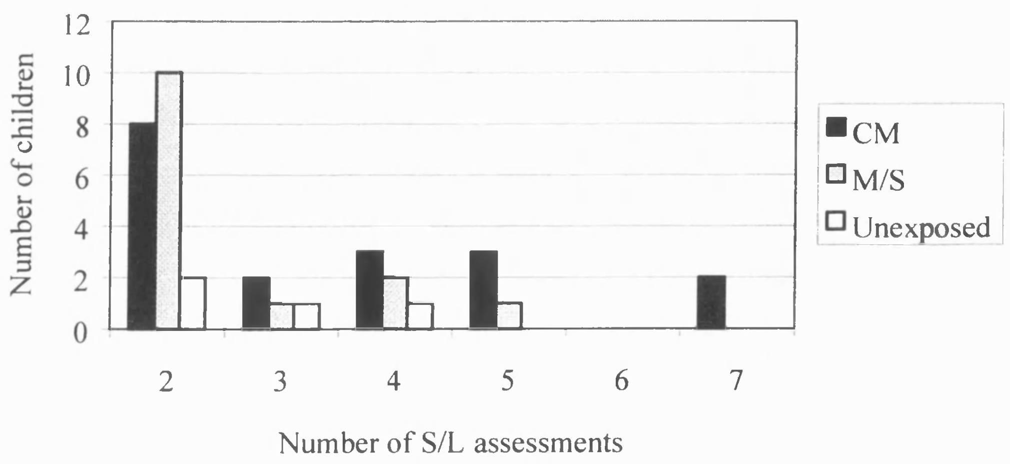

Figure 16. 4: Number of speech and language assessments with impaired performance by exposure group

As highlighted in previous results, school attendance has a positive effect on assessment performance and reduces the odds of impairment on the speech and language battery (table 16.4). However, despite this finding, a previous diagnosis of CM results in significantly increased odds of impairment. The direction of the association between the M/S and unexposed groups suggests poorer performance in the former, with a difference approaching the level of significance.

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	3.68	1.09 – 12.4	0.04
	M/S	3.12	0.9 – 10.8	0.07
Epilepsy status	Active epilepsy	2.66	0.73 – 9.63	0.14
	Inactive epilepsy	*	-	-
Age	7 years	1.61	0.58 – 4.43	0.69
	8 years	1.74	0.58 – 5.28	
	9 years	1.06	0.3 – 3.69	
Sex	Female	1.21	0.55 – 2.68	0.63
Schooling status	Attends school **	0.04	0.01 – 0.2	<0.001
Nutritional status	Weight/height	1.01	0.26 – 3.94	0.99
	Height/age	3.81	1.39 – 10.46	0.01
	Weight/age	1.3	0.37 – 4.59	0.68
SES status	Mother's education	1.74	0.73 – 4.17	0.21
	Father's occupation	1.29	0.57 – 2.9	0.54

Table 16. 4: Estimated odds of a speech and language impairment by exposure group

* Variable dropped – predicts the no-impairment group perfectly

** Used because Standards 1 and 2 predict the no-impairment group perfectly

Analysis of individual children's data for trends or groupings in impairment patterns suggested that the more extensive (2+) impairments among the CM group involved the receptive (grammar and vocabulary) and word finding assessments (Appendix 28). Two of the children from the low functioning group (ID 184, 285) were unable to produce any sample at all for the lexical semantics/MLU language sample: if they were also classified as impaired in this domain, this may indicate that vocabulary (receptive vocabulary and lexical semantics) should be included in this pattern. There were no apparent impairment patterns in children from the M/S group and too few children in the unexposed group to determine any trends.

Of the ten children from the CM group with impairment-level performance on the word finding assessment, seven showed signs of perseveration, five used lexical paraphasias, four used neologisms, one displayed delayed appearance of the target and one showed evidence of circumlocution (Appendix 29). Four of the five children from the M/S group showed signs of perseveration, two used lexical paraphasias, one used circumlocution but none used neologisms. One child from the unexposed group was impaired on the word finding assessment: he used perseverations and circumlocution but no neologisms.

16.6 Impairments on hospital discharge

A neurological assessment was carried out with 51% (n=157; 80% of the CM group and 22% of the M/S group) of the children from the exposed groups at the time of discharge from hospital. The occurrence of the assessment depended on the clinical protocol employed during the year of discharge and the ward the child had been admitted to (children with CM were more likely to be admitted to the high dependency unit, where neurological discharge assessments were used), rather than any child or clinician characteristics.

Seventeen percent (n=21) of those from the CM group who underwent assessment had at least one impairment on discharge, as did 20% (n=7) of the M/S group (table 16.5). Motor impairments were the most prevalent, although this may reflect the method of assessment adopted. Most were isolated impairments.

Domain	Impairment (as reported in discharge record)	No. children (single/multiple impairments)	
		CM	M/S
Speech/language	Limited speech	3 (3/0)	2 (1/1)
Motor	Cannot sit	3 (3/0)	1 (0/1)
	Cannot stand	1 (0/1)	1 (1/0)
	Cannot walk unsupported	2 (2/0)	1 (1/0)
	Unsteady	1 (1/0)	0
	Unspecified motor	1 (1/0)	1 (1/0)
	Hemiplegia	2 (1/1)	0
Special senses	Cortical blindness	1 (0/1)	0
Epilepsy	Epilepsy	1 (1/0)	0
Behaviour	Hallucinations	1 (1/0)	0
	Violent behaviour	1 (0/1)	0
Unspecified	Unspecified	6 (6/0)	2 (2/0)

Table 16. 5: Impairments detected at hospital discharge

Thirty-eight percent of children identified with impairments on discharge after CM and 29% after M/S exhibited impairment level scores on one or more assessments in the current study (table 16.6). There was little association between the nature of the impairments detected at discharge and those found in the current study. The child discharged with cortical blindness and hemiplegia (ID 023) was one of the few children discharged with severe, multiple impairments and also displayed the most extensive pattern of impairments in assessment performance in the current study (Appendix 28), possibly suggesting an association between severity of discharge and current deficits. Another child (ID 285) was part of the low functioning group (section 16.3) but as no detail about impairment characteristics was provided in her discharge report, it is not possible to speculate further on the basis of the current data.

ID	Group	Impairments detected at discharge	Impairments detected in current study
023	CM	Cortical blindness, R hemiplegia	S/L, Non-verbal, Behaviour, Memory, Attention, Neurological
037	CM	Unspecified	Memory
054	CM	Cannot walk unsupported	S/L, Memory
118	M/S	Unspecified	S/L
285	CM	Unspecified	S/L, Behaviour, Memory (low functioning group)
333	CM	Unsteady	Non-verbal, Memory, Attention, Inactive epilepsy
408	CM	L hemiplegia	Neurological
421	M/S	Cannot stand	Attention, Neurological
455	CM	Cannot sit	Hearing
487	CM	Epilepsy	S/L, Neurological, Active epilepsy

Table 16. 6: Impairments detected on discharge and in the current study

16.7 Summary and discussion

Both CM (OR=2.15 95%C.I.=1.07-4.3 p=0.03) and M/S (OR=2.46 95%C.I.=1.24-4.9 p=0.01) were associated with significantly increased odds of an impairment-level score on any of the major domains assessed in the study (motor skills, memory, behaviour, attention, non-verbal functioning, hearing, vision, speech and language). Children from the CM group also had significantly increased odds of impairment on the speech and language battery compared to children from the unexposed group (OR=3.62 95%C.I.=1.11-11.8 p=0.03). The direction of the association between the M/S and unexposed groups suggested poorer performance in the former, although the difference was not significant (OR=2.96 95%C.I.=0.88-10.02 p=0.08). Children with previous CM had more extensive impairments, with 50% of the impaired group attaining impairment-level scores on three or more assessments, with a locus of impairment in measures of vocabulary. In contrast, 29% of the M/S group displayed impaired performance on three or more assessments with a locus of impairment in phonology and pragmatics.

Twenty-four percent of the CM group had at least one impairment. A wide range of levels of impairments has been found in previous studies of CM that have followed children up for at least 6 months, from 3% (Meremikwu, et al., 1997) and 9.7% (Bondi, 1992) to 26% (Brewster, et al., 1990) and 31% (Carme, et al., 1993). However, most of these studies did not investigate the spectrum of developmental domains tested in the current study. The only previous study to have done so found that 4.4% of survivors still had impairments at 6 months (van Hensbroek, et al., 1997). Despite the apparent difference between these results and the current findings, a level of congruence is suggested by the fact that van Hensbroek and colleagues used a neurological examination to detect impairments and were thus likely to identify only gross deficits. In the current study, the group of children described as the 'low functioning group', who represented 3.9% of the CM group, may be comparable to this group. Further support for the accuracy of the level of impairment identified by this study is that the proportion of cognitive (excluding memory) and language impairments (13.8%) is comparable to that found in a previous study of cognitive impairments following severe malaria with impaired consciousness in Kilifi, which also used detailed assessments, as opposed to a neurological examination (14%) (Holding, et al., 1999).

The pattern of mortality and morbidity in CM compared to acute bacterial meningitis (ABM) identified in Chapter Two was of high mortality in both infections but differing levels of morbidity, with ABM resulting in higher levels of impairments. However, the impairment level identified in this study is comparable to those seen in the three ABM studies investigating the spectrum of developmental domains, which found that between 24.6% and 30% of survivors were left with impairments (Grimwood, et al., 1995; Pikis, et al., 1996; Salih, et al., 1991). The pattern of deficits is, unsurprisingly, very different with large numbers of children with sensori-neural hearing loss among the ABM groups.

Twenty-four percent of the M/S group also had impairments, suggesting that although there were not as many differences in group performance between these and the unexposed children as occurred in the CM group, the number of children performing at the lower end of the spectrum was similar. However, a larger proportion (42.4%) of children with previous CM had impairments in two or more domains compared to children from the M/S (27.8%) or unexposed (20%) groups, indicating a pattern of more extensive impairments in the CM group. Levine (1999) comments that impairments in neurodevelopmental functions manifest differently depending on the pattern of weaknesses in other areas. This suggests that although the proportion of children with impairments was the same in the CM and M/S groups, the latter may be more likely to be able to compensate for deficits in the absence of extensive concomitant impairments in the majority of children.

A subgroup of six children from the CM group and two from the M/S group seemed to be performing at a particularly low level, unable to complete many of the assessments and scoring at a level indicative of impairment on many of the assessments they attempted. Membership of this subgroup was associated with active epilepsy in three of the children including both of the children with previous M/S.

Of children with impairments, 19% of the CM group, 16% of the M/S group and 6% of the unexposed group had epilepsy (inactive in 6%, 5% and 6% of the groups respectively). These findings do not suggest that impairments are more extensive in children with epilepsy (Appendix 28) but indicate that CM and M/S alone are sufficient for an association with impairment. However, severe impairments (defined as membership of the low functioning group) are particularly associated with epilepsy in the M/S group, postulating that children with previous M/S may only suffer severe impairment with concomitant epilepsy. Thirty-nine percent of the children with epilepsy had at least one impaired domain. This level was highest in the epileptic children from the CM group (50% compared to 33% and 25% in the M/S and unexposed groups), which may suggest that the combination of previous CM and epilepsy is more virulent or that the children with previous CM had more severe forms of epilepsy. There was also a significant difference in the odds of impairment between the active and no epilepsy groups (OR=3.72 95%C.I.=1.3-10.68 p=0.02). This effect was not seen in the inactive epilepsy group.

These speech and language results suggest that the language difficulties observed in the impaired group may be defined as acquired childhood aphasia (ACA). Although definitions of ACA have varied, two main criteria have consistently been identified:

first that the onset of the disorder is precipitated by a cerebral insult and secondly, that it follows a period of normal language acquisition. The minimum age for a diagnosis of ACA also varies in the literature. Some reports use a cut-off of one year, based on Woods and Carey's (1979) report that lesions incurred after this age are associated with more severe language deficits than those sustained earlier (Paquier and Van Dongen, 1998). Others use 2 years, as this is the mean age of acquisition of first sentences (van Hout, 1997), although there is no data on whether this is applicable to Kigiryama. Early reports of ACA described a nonfluent aphasia characterised mainly by 'negative symptoms' such as mutism, telegraphic speech and reduction in phrase length. Later reports have confirmed the presence of fluent aphasic patterns in children (Paquier and Van Dongen, 1996) and attempted to establish equivalent ACA syndromes for most of the aphasias encountered in adults (van Hout, 1997).

The children constituting the impaired group fulfil the diagnostic criteria for ACA in that the language impairment is associated, and is presumed in most cases to have been precipitated, by a cerebral insult and the median age of insult was 2:4 and 1:11 in the CM and M/S groups respectively. Due to the length of time since the presumed insult, it can be assumed that these children are past the acute stage of ACA, although three of the low functioning group presented with symptoms of telegraphic speech and the other five had extensive language impairments between 2 years 9 months and 6 years 2 months after presumed onset. In most cases, there is no available data providing evidence of post-illness arrest of language: there is no information on impairments noted while the child was on the ward and only five of the 157 who were assessed were noted to have gross language deficits on discharge. None of these children received impairment level scores in the current study. The occurrence of anomic symptoms is indicative of an acquired disorder. Mutism may occur immediately after recovery from CM (Dr C. Newton, personal communication) but as in the case of other forms of ACA, usually resolves rapidly. Further investigation of the occurrence of language arrest following the acute episode would provide further evidence to support the proposition that the disorder is acquired.

Residual deficits in word retrieval, syntax/morphology, verbal reasoning, understanding linguistically-based humour and sarcasm, monitoring discourse and understanding figurative language have been noted following apparent recovery from

ACA (Cooper and Flowers, 1987; Ozanne and Murdoch, 1990; Woods and Carey, 1979). Ozanne and Murdoch (1990) comment that residual or long-term linguistic deficits in ACA resemble developmental impairments, falling into three categories. First, the nature of most linguistic deficits is a developmental immaturity; second, in some facets of language, a specific impairment is evident and third, deficits may be due to cognitive factors, rather than specifically linguistic in nature. This pattern is reflected in the CM and M/S groups. Parental reports of pragmatic skills and behaviour and performance on the phonological assessment indicated immaturities in these facets of language. Detailed qualitative evaluation was not performed on the other language assessments, thus further conclusions about other language skills cannot be drawn. Specific impairments occurred in both groups in word finding, including children with 'positive' aphasic symptoms such as neologisms, paraphasias and perseveration. Sixty-one percent of the speech and language impairments in the CM group and 57% of those in the M/S group co-occurred with impairments in cognition (non-verbal functioning, memory or attention) compared to 25% of those in the unexposed group (Appendix 28). This suggests that the majority of speech and language impairments were not specific in nature.

The contribution of the epileptic disturbance to the language impairments seen in some of the children is unclear: the findings do not suggest that the impairments in these children are invariably worse, although 22% and 14% of the CM and M/S language-impaired groups respectively had epilepsy. Epileptic disorders may produce ictal or post-ictal language disturbances, the nature of which depends on the location of the epileptogenic focus (Paquier and Van Dongen, 1998). In these cases, the aphasia usually fluctuates along with the electroencephalographic manifestations. As speech and language functions were only assessed on one occasion in the current study, it is not possible to reach any conclusions about the possibility of transient ictal or post-ictal phenomena, except that parents did not report obvious fluctuations in language performance in questionnaire responses. Another possible effect of epilepsy is that seizures secondary to cerebral lesions may impede the recovery of a language disorder, possibly due to the spread of abnormal bioelectrical activity beyond the original lesion (Paquier and Van Dongen, 1993).

Early hypotheses about prognostic factors in ACA suggested an inverse relationship between age of lesion and degree of language recovery (Woods and Carey, 1979), although a systematic relationship between these factors is not reported in the literature (Paquier and Van Dongen, 1998), possibly due to other prognostic variables such as the underlying aetiology and the size and site of the lesion. Infectious aetiologies have been found to have a poorer prognosis than traumatic aetiologies (Loonen and van Dongen, 1991), although most of these reports have concerned herpes simplex virus, which has a particular tropism for the temporal lobes and a different mechanism of damage to severe malaria. Lees and Neville (1990) found that children who did not reach the normal range of performance (defined as z-scores of –1 to +1) within 6 months post-onset never did so, which suggests a poor prognosis for the current impaired group, all of whom are after this point. Other studies indicate that even small levels of impairment can affect the child's schooling and be a significant handicap for future life (Lees, 1997; van Hout, 1997).

The findings of the pilot study indicated that children discharged from hospital with impairments achieved scores on speech and language assessments that were not significantly different to those of children discharged without impairments (section 10.4.2). The results presented in this chapter similarly suggest that the detection of neurological impairments on hospital discharge does not always equate with current impaired performance, as measured by the neuro-cognitive assessments used in the current study. As proposed in section 10.4.3, these findings may indicate that the current assessment battery is more sensitive to brain damage associated with severe malaria than the screening assessment performed on hospital discharge. Alternatively, the concept of a continuum of deficits within each group was proposed in section 14.11.1, with a minority of children with moderate to severe impairments and a large proportion of children with mild or subtle impairments, which have a minor effect on performance at a young age but become increasingly apparent with the child's advancing age, as the cognitive requirements of tasks increase in complexity.

In summary, 24% of the CM and M/S groups were impaired in at least one of the domains assessed in the study. This suggests that although there were fewer differences in group performance in the M/S group than in the CM group, the number of children performing at the lower end of the spectrum was similar. However, children with previous CM presented with a more extensive pattern of impairments. Nineteen percent of the CM impairment group, 16% of the M/S impairment group and 6% of the unexposed impairment group had epilepsy. The findings do not suggest that impairments are more extensive in children with epilepsy, although membership of the low functioning group was associated with epilepsy among children with M/S. The prevalence of speech and language impairments was higher among children with a history of CM or M/S. The age at presumed injury and the pattern of impairments are suggestive of ACA in this subgroup of children.

Chapter Seventeen: Discussion and Implications of the Study

17.1 Introduction

This study aimed to explore epilepsy and developmental impairments following severe falciparum malaria, in particular their prevalence, relationships, clues to pathogenesis and service requirements. The study is the first to show that epilepsy is associated with severe forms of malaria and that active epilepsy in the context of previous malaria is associated with neuro-cognitive impairments. The current findings represent the longest follow-up of an unselected group of children with previous CM investigating the full spectrum of developmental domains and the first indication that neurological impairments are associated with forms of severe malaria other than CM. The results also represent the most detailed report to date of speech and language deficits associated with malaria.

This chapter will discuss the implications of the study's findings for children and communities in malaria-endemic regions, discuss the limitations of the study and evaluate the validity of the assessment tools and by extension, its findings. Finally, possible directions for future work will be considered.

17.2 Implications of results

Murphy and Breman (2001) estimate that each year in Africa, between 9,000 and 19,000 children under 5 years of age have persistent neurological problems following CM for more than 6 months after discharge from hospital. The current findings suggest that the impact of malaria on child development is more extensive. Epilepsy was reported in 9.2% of the CM group and 11.5% of the M/S group, representing odds of 4.4 (95%C.I.=1.42-13.69) and 6.1 (95%C.I.=2.02-18.25) respectively of developing epilepsy relative to the unexposed group.

Twenty-four percent of children exposed to severe malaria had an impairment-level score on one or more of the major domains assessed in the study. There is no universally-accepted system for defining impairment on non-standardised neuro-cognitive assessments: Anderson (2001), reviewing neuropsychological studies, comments that investigators have variously used scores equal to or in excess of 1 or 2 SDs below the control mean to indicate impairment. A conservative estimate of more than 2SDs below the unexposed group mean on assessments that did not already indicate an 'impairment' level was adopted in the current study. These estimates are likely to be minimal, as children with complex seizures who recover probably never attend hospital. The minimum community incidence of CM and complex seizures not associated with CM in this area is 1.5 (Snow, et al., 1997) and 5.8 (Waruiru, et al., 1996) respectively per 1000 per year. Thus, a minimum estimate of children acquiring impairments from severe falciparum malaria (accounting for 16.8% mortality in CM and 6.8% in M/S (Marsh, et al., 1995)) is 319, 200 children per year. This estimation does not include children with severe neurological impairments following CM, who often die within the first year after discharge (Dr C Newton, personal communication).

This is the first study to estimate the prevalence of epilepsy following severe forms of malaria and to show the effect of malaria-associated epilepsy on other domains of impairment. Previous studies have found neurological sequelae and cognitive impairment following CM but not investigated the spectrum of developmental domains using domain-specific assessment tools and none have examined the other complications of falciparum malaria.

Significant differences in CM group performance relative to the unexposed group were concentrated on the higher level language, lexical semantics (content words), pragmatics and non-verbal functioning assessments. Phonology, pragmatics and behaviour were the areas of significantly reduced functioning in the M/S group. Significant differences in performance were found between the active and no epilepsy groups on a number of assessments: receptive grammar, receptive vocabulary, syntax, pragmatics, word finding, 'impaired' KCBMT performance, attention errors, behaviour and motor skills (neurological examination). In comparison, the only significant difference between the inactive and no epilepsy groups was found on the non-verbal functioning task.

The validity of conclusions drawn from these findings is dependent on the reliability, validity and sensitivity of the assessment methods and tools employed. Parental questionnaires are a common method of determining the prevalence of epilepsy in resource-poor countries (Placencia, et al., 1992) and have been used in previous studies in Kilifi (Snow, et al., 1994; Waruiru, et al., 1996), where it has been established that seizures are recalled with a high degree of accuracy over time, particularly generalised convulsions (Snow, et al., 1993a). Focal seizures may not be recognised to the same degree (Senanayake and Roman, 1992) and complex partial seizures may have been under-reported in the current study, although the EEG data gave little evidence of epileptiform activity in the temporal lobe. In addition, there were discrepancies in parental recollection of early seizures (occurring before hospital admission), suggesting that recall of seizures in the first few years of life may not have been as accurate as recall of recent episodes.

The sensitivity of the EEG recordings may have been increased with the use of more electrodes, repeated recordings or recordings during sleep. Sleep recordings, in particular, increase the possibility of recording epileptiform activity, usually reduce movement artefacts and are particularly useful when partial seizures are suspected (Commission, 2002). Limitations in time and equipment precluded these procedures. There is only one EEG machine, with a 21-lead capacity, at Kilifi District Hospital, used for clinical and research purposes, thus there was no time for repeated recordings, awake or asleep, on the 487 participants in the study.

Speech and language assessments were specifically developed for the study by the candidate. The development process was carried out following the principles of content validation and preliminary measures of construct validity, including age differentiation and principal components analysis, suggested that the theoretical assumptions behind the construction of the assessments were appropriate. Evidently, further use of the battery will depend on a continuing process of validation and a detailed evaluation of the current findings to identify and improve weaker test items and methods. The assessments attained an acceptable re-test and inter-rater reliability, although further studies will provide more evidence on the clinical acceptability of test-related variance.

Many of the assessments in the cognitive battery had been specifically designed for this population and had been used previously in Kilifi (Holding, et al., 1999). The exception was the Kilifi Creek Behavioural Memory Test (KCBMT), which was adapted from a UK-based screening test for memory, the Rivermead Behavioural Memory Test for Children (RBMTC) (Wilson, et al., 1991) and had never been used in this context prior to the current study. Analysis of the results indicated discrepancies in the attainment of the Kilifi cohort relative to that of UK children on similar tasks (Appendix 27), which may suggest that the assessment in its current form is an inappropriate measure of memory function in this community. Further study may require more sensitive neuropsychological assessment of hippocampal function or magnetic resonance studies. Nevertheless, the finding that neurological assessments may not identify the majority of cognitive and language impairments on discharge or currently (sections 16.6 and 13.4 respectively), highlights the necessity for continued development and refinement of specific cognitive and language assessments if children with deficits are to be identified and treated.

Losses to follow-up (30%) were greater than those recommended in the systematic review conducted in Chapter Two (≤20%). These children were reported to no longer be at the same address as cited in the database record. Economic migration is a common phenomenon in Kilifi District, as families have to move where employment opportunities lead them. Chapter Twelve indicated a high level of socioeconomic homogeneity among the cohort, which presumably extends to other people in Kilifi District, thus suggesting that the necessity of migration for economic reasons is similar across the community. This implies that losses to follow-up for this reason would not have biased the composition of the cohort.

17.2.1 Exposure status

The CM group had significantly poorer performance relative to the unexposed group in language content, language use and non-verbal functioning, in addition to a trend of generally lower scores in all of the domains assessed in the study, apart from hearing and vision. These findings suggest that the language impairments are likely to be one part of a generalised impairment that is perhaps more conspicuous in the language domain. Alternatively, the prevalence of language deficits may simply reflect the fact that this domain was subject to more detailed assessment than others, for example cognition in which assessments were targeted towards specific skills. In contrast to the CM group results, there was little evidence of a trend towards poorer group performance in the M/S group, rather deficits in group performance in specific domains and a subgroup of children with generalised impairments.

Children with epileptic disorders may face stigma, anecdotal evidence of which was discussed in Chapter Thirteen. Using the impairment/ disability/ handicap classification outlined in Chapter Four, Fayyad and colleagues (2001) comment that attitudes towards impairments such as epilepsy may result in disabilities in the social sphere. Studies carried out in resource-poor settings have found that children with epilepsy may face teasing from peers and isolation from the family unit (Debruyn, 1990), fewer prospects of school attendance (Pal, 1998; Rwiza, et al., 1993) and greater likelihood of removal from school to prevent family embarrassment (Birbeck, 2000). Fifty-nine percent of the inactive epilepsy group attended school, the same proportion as those without epilepsy. In contrast, 26% of the active epilepsy group attended school, indicating that children who experienced at least one seizure in the last year were less likely to attend school. This issue was not directly investigated: a complex web of social and economic factors determines school attendance, a situation made even more complex in the current study by the influence of exposure status.

A second implication of these findings for the children with epilepsy is the seizure treatment gap identified in the study (Meinardi, et al., 2001). Only two of the 19 children (10.5%) with active epilepsy were receiving anti-epileptic medication at the time of assessment, which is similar to other studies indicating that 90% of people in resource-poor countries are not receiving appropriate treatment for epilepsy (Scott, et al., 2001). The remaining 17 were referred to the Kilifi District Hospital neurology clinic for appropriate treatment, representing a potential immediate benefit for those participating in the study. Currently, there is no data to indicate whether well-controlled epilepsy would result in improvements in the functioning of other domains in these children. Scott and colleagues (2001) emphasise that addressing the issue of the seizure treatment gap entails more than drug treatment but the education of health workers, patients and the wider community to reduce the social and economic burden that often accompanies epilepsy.

The implications of developmental impairments are more difficult to specify. The eight children in the low functioning group were unable to complete many of the assessments and displayed limited ability to engage with the assessors at any level. Their level of performance suggests that these children would have difficulties in an educational environment without specific support, which is rarely available in Kilifi District. None were attending school, although the reasons for this were not investigated. Stigma and reduced opportunities in education, marriage and employment have been described for children with impairments (Kisanji, 1995). The negative consequences of impairments may also extend to the child's family, who rely on each family member for help in the home: for example, in most African homes, girls cook, clean the house and look after younger siblings as early as 7 to 8 years of age. On the other hand, Kisanji (1995) argues that children with impairments and their families experience fewer problems in subsistence economies compared to technologically more sophisticated societies, particularly in the extended family situation in which responsibility for care can be shared amongst family members.

In general, children who have suffered a brain injury may display a wide spectrum of concomitant sequelae, impeding subsequent cognitive, social and family functioning. Language deficits may result in particular difficulties at school, as much as what is taught is encoded in literate language and most basic academic skills are conveyed through verbal expression (Levine, 1999). The evidence from other studies documenting the types of impairments suggested by the findings of the current study indicates that even residual problems can have a negative impact on performance. Persisting linguistic deficits following ACA have consistently been found to impede academic performance, particularly in the form of problems relating to the integration of new information (Paquier and Van Dongen, 1998), orthography and calculation, even resulting in dyslexia or dyscalculia (van Hout, 1991b). In addition, difficulties may only become apparent as children progress and face more complex cognitive and linguistic demands both socially and educationally (Cross and Ozanne, 1990), raising the possibility that the number of children with poor performance may increase over time.

Speculation in Chapter Fourteen about the similarities between the findings in the exposed groups and the patterns of deficit seen in semantic pragmatic deficit syndrome (SPDS) and pragmatic language impairment (PLI) may also give some indication of the implications of these difficulties. SPDS may be handicapping in its subtle social impairments because the child's behaviour initially appears insignificant but becomes progressively unusual over time, in ways that may be difficult for friends and family to specify (Bowler and Brook, 1998). Although it is difficult to anticipate how similar behaviours would manifest and be interpreted in a cross-cultural situation, the ramifications in an environment in which such impairments are currently unlikely to be identified, even by professionals, are that similar difficulties would remain undiagnosed and untreated.

17.2.2 Epilepsy status

The findings of the study suggest that children with active epilepsy are at additional risk of developmental impairments, possibly with a specific target in domains unaffected by or recovered from deficits associated with severe malaria. Alternatively, epilepsy may simply be a manifestation of more extensive damage associated with malaria or other factors. Many interrelated factors are involved in cognitive impairments associated with epilepsy including seizure type; underlying pathophysiology; possible cerebral pathology; anti-epileptic medication; social stigma; educational deprivation; genetic factors; disruption of sleep by seizures and subclinical discharges causing transient cognitive impairments (Binnie, 2001). Without further investigation and characterisation of the active epilepsy group, it is difficult to evaluate the relative influence of these factors and the prognosis of the developmental problems. Fifty percent of children with previous CM and active epilepsy had at least one impairment compared to 33% of children with epilepsy and previous M/S and 25% of children with epilepsy from the unexposed group. This indicates that the combination of a previous diagnosis of CM and active epilepsy confers the poorest prognosis but also that epilepsy in the context of severe malaria does not automatically engender impairments. Again, this highlights the need for further evaluation of the active epilepsy group to investigate the determinants of impairment in this group.

Despite the fact that active epilepsy was associated with more extensive impairments than either form of severe malaria, the prognosis may be more positive because of the potential for treatment. In contrast, the current potential for rehabilitation in Kilifi is limited.

17.3 The context of the impairments

Boivin (in press) suggests that the outcome of severe malaria is enmeshed with other health and development factors affecting children in resource-poor countries that constitute a complex web of poverty. Nutritional and socioeconomic indicators implied that the majority of children in the study lived in conditions of economic deprivation: some of these indicators, particularly those of long-term nutritional status, were associated with poor performance on cognitive and speech and language assessments. Levine (1999) comments that mild to moderate neurodevelopmental dysfunction exerts more negative influence in contexts of environmental turmoil or deprivation. This suggests that similar levels of impairment may have more detrimental effects in this context compared to that of resource-rich settings. Children such as those participating in the current study encounter more risks to normal development than their counterparts in richer countries: this is evidenced by the fact that the prevalence of impairments in the unexposed group was higher than that usually reported in resource-rich countries.

The comparatively high level of impairments found in the unexposed group may have moderated the odds of impairment associated with CM or M/S, possibly masking the true impact of malaria on development. However, as Boivin states, the effect of malaria cannot be separated from the impact of other detrimental factors in the sub-Saharan context, if an accurate picture of child development and the factors influencing it is to emerge and influence clinical and educational practice. The unexposed group were drawn randomly from community surveillance databases, rather than selected in the community or from a hospital reference group. The latter would be difficult to establish in this context because most in-patients, other than those admitted with severe malaria, have conditions with a potential impact on brain function such as meningitis, encephalitis or malnutrition.

Educational status was an elemental context to the study because of its dual role as a covariate and an outcome. The regression models adjusted for schooling status as it was assumed that education would have a positive effect on assessment performance in all exposure groups. School attendance was associated with significantly better performance on assessments of language, cognition and behaviour. However, the proportion of children from the exposed groups attending school was lower than in the unexposed group. It is unclear whether children at school performed better because of the positive effect of education or whether schooling status is actually a consequence of malaria and children with impairments were simply less likely to be attending school. As discussed in section 12.3, a complex web of social and economic factors determines school attendance: the contribution of exposure or epilepsy status to parent and teacher views on schooling has not previously been investigated and should be a focus of further study.

17.4 Further study

Many of the study's findings are novel, therefore replication in further studies and population groups is necessary to provide further evidence of their validity. Similar studies in areas of different malaria endemicity would elucidate the distribution of the burden of impairment, thus influence the targeting of scarce resources. As mentioned above, further studies will also provide more data on the reliability and validity of new assessment instruments and possibly allow the design of more complex frameworks for the study of language disorders in Kigiryama (section 9.6). This study aimed to provide a broad overview of impairments associated with malaria across the spectrum of developmental domains. In consequence, the level of detailed analysis possible in a more focussed study was not performed: however, the current study has provided the basis on which further studies could utilise the assessment tools to provide in-depth analysis of the characteristics and course of these impairments.

The current findings suggest that malaria-associated epilepsy is a potential risk factor for developmental impairments. As this is a novel finding, the impact of anti-epileptic treatment on concomitant impairments, particularly cognitive functions, is unknown but will be an essential element of further studies if the full benefit of allocating resources to this condition is to be effectively communicated to service providers.

Further studies with a longitudinal design would enable conclusions to be drawn on development and recovery over time. This would address the possibility suggested by the findings of other encephalopathies (Annegers, et al., 1988), that the prevalence of epilepsy increases over time and would provide evidence on the course of impairments identified in the current study. An important issue for the future educational, career, economic and social prospects of children with impairments is whether deficits recover or, as hypothesised earlier, whether increased social and scholastic demands result in greater numbers of children experiencing difficulties over time. A prospective study, following children from the onset of the disease would provide valuable information on the natural history of impairment and recovery, which would aid the development of rehabilitative programmes, particularly those based in the community, which are more feasible, sustainable and arguably more effective than those provided by professionals.

The current study is the first to provide evidence of neuro-cognitive impairments following other manifestations of severe falciparum malaria. In addition, although the small numbers in the speech and language pilot study precluded investigation of specific subgroups, poor performance was found in the non-CM severe malaria group, which included children with severe malarial anaemia and malaria with prostration. These findings suggest that the current methodology should be extended to include children with any features of severe malaria to investigate whether some impairments are a function of severity of illness.

As mentioned in section 15.6.3, the findings of the KCBMT suggested the need for further investigation of hippocampal functioning with more detailed and sensitive neuropsychological assessments. Although the technology is not currently available in coastal Kenya, magnetic resonance studies of the mesial temporal lobe would provide valuable evidence of the effects of malaria on the structures supporting memory functions.

The current research has raised questions regarding the nature of the support required by children post-malaria, their families and communities and the protective or risk factors affecting the outcome of the disease. Due to the current lack of rehabilitative provision, the efficacy of secondary prevention could be improved by investigation of the factors associated with subsequent poor outcome. Neurological impairment following CM has been associated with prolonged or focal seizures (Bondi, 1992; Brewster, et al., 1990; Meremikwu, et al., 1997; van Hensbroek, et al., 1997); deep coma (van Hensbroek, et al., 1997); prolonged coma (Bondi, 1992; Brewster, et al., 1990; Meremikwu, et al., 1997; van Hensbroek, et al., 1997); raised intracranial pressure (Newton, et al., 1997); hypoglycaemia (Bondi, 1992; Brewster, et al., 1990) and severe anaemia (Brewster, et al., 1990). Holding and colleagues (1999) identified hypoglycaemia and multiple seizures as potential targets for alteration or improvement in clinical management, which may result in a reduction in the risk of cognitive impairments.

17.5 Conclusions

CM and M/S are frequent causes of admission to hospital in malaria-endemic areas. These results suggest that both forms of malaria are associated with an increased prevalence of epilepsy and neuro-cognitive impairments. These findings highlight the fact that falciparum malaria may represent a major public health problem in terms of education and development in malaria-endemic areas. Epilepsy is under-recognised and often poorly managed but can be controlled with drugs. The integration of rehabilitation into community-level services, as advocated in the community-based rehabilitation model, is an inexpensive and effective means of providing remedial services in resource-poor countries. The associations between malaria, epilepsy and developmental impairments suggested by this study should provide an even greater impetus for identifying such children and making provision for follow-up after malaria.

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Appendix 1: Neurological Assessment

Child's Name: [________] [________] [________]

Study Number: [ ][ ][ ][ ][ ]

Date of assessment: [ ][ ]/ [ ][ ]/ [ ][ ][ ][ ]

Assessor: [ ][ ]

Was the child co-operative? **Yes/ No** [ ] **(CC)**

Was there any neurological deficit noted? **Yes/ No** [ ] **(ND)**

Problems

1:________________________ |__|__|__|. |__|

2:________________________ |__|__|__|. |__|

3:________________________ |__|__|__|. |__|

4:________________________ |__|__|__|. |__|

5:________________________ |__|__|__|. |__|

Disabilities

Motor	None (0)	Mild (1,2)	Intermediate (3,4)	Severe (5)	|__|
Visual	None	Mild	Intermediate	Severe	|__|
Hearing	None	Mild	Intermediate	Severe	|__|
Cognitive	None	Mild	Intermediate	Severe	|__|
Epilepsy	None	Mild	Intermediate	Severe	|__|

EPILEPSY RECORD

Answer **Yes (Y)** or **No (N)** or **Unknown (U)**

Has the child ever had a fit	[ ] **(CF)**
Has the child ever had episodes when s/he loses consciousness	[ ]**(CLC)**
Has the child ever fallen to the ground without a reason	[ ]**(CFG)**
and the arms or legs twitch/shake	[ ]**(ALT)**
and bites the tongue	[ ] **(BT)**
and wets him/herself	[ ] **(WH)**
Have you ever noticed that the child has episodes of	
shaking, trembling of one arm or one leg or the face	[ ] **(ST)**
becoming stiff	[ ] **(BS)**
loses contact with the surroundings	[ ]**(LCS)**
Has the child had episodes when s/he appears dazed	[ ] **(CD)**
complains of tummy aches	[ ] **(TA)**
smells an odd smell	[ ] **(OS)**
sees something strange	[ ] **(SS)**
Have you ever been told that the child has had a fit	[ ]**(TCF)**
When does the child have seizures? **Daytime** / **Sleeping**/ **Both**	[ ] **(WS)**
How many seizures has the child ever had? **0 – 9** or **Frequent** (>9)	[ ] **(NS)**
How many times per month? **0 – 9** or **Frequent** (>9)	[ ] **(PM)**
How many times per week? **0 – 9** or **Frequent** (>9)	[ ] **(PW)**
How many times per day? **0 – 9** or **Frequent** (>9)	[ ] **(PD)**

If response to any of the above questions is Yes, please fill in table on the next page:

Date of onset of seizures: [ ][ ]/[ ][ ]/[ ][ ][ ][ ] **(DOS)**

Number of different seizure types: [ ] **(NST)**

Description of seizure types:	1st		2nd	
Before the episode				
Does s/he knows it is going to occur eg. goes to an adult		(KO1)		(KO2)
Abnormal behaviour		(AB1)		(AB2)
During the episode				
Becomes unresponsive (not answer questions, disobey commands)		(BU1)		(BU2)
Fall to the ground		(FG1)		(FG2)
Talks nonsense		(TN1)		(TN2)
Does not know where s/he is		(DW1)		(DW2)
Hallucinations; paraesthesiae		(HP1)		(HP2)
Automatisms: swallowing/grimacing/fiddling/gestures/vocalisations/walking		(AM1)		(AM2)
Other phenomena: fear/weeping/abdominal/déjà vu,		(OP1)		(OP2)
Convulsive movements				
Which side: Both; Right; Left; one Side (unsure which)		(CS1)		(CS2)
Which limb: Both; Arms; Legs		(CM1)		(CM2)
Partial: Face; Lips; Hand		(CP1)		(CP2)
Eyes involved:				
Blank look		(BK1)		(BK2)
Stares ahead		(SA1)		(SA2)
Deviate: Upwards; Right; Left; Deviate (unsure to which side)		(ED1)		(ED2)
Jerking movements		(JM1)		(JM2)
Lips involved: No, Smacking, Licking		(LI1)		(LI2)
Bites tongue		(BG1)		(BG2)
Wets self		(WE1)		(WE2)
Soils self		(SO1)		(SO2)
Duration (minutes)		(DU1)		(DU2)
After the episode				
Drowsy		(DY1)		(DY2)
Sleeps		(SP1)		(SP2)
Headache		(HE1)		(HE2)
Abnormal behaviour		(AN1)		(AN2)
Paralysis		(PA1)		(PA2)
Disturbance of sleep		(DS1)		(DS2)
Speech and language difficulties (aphasia)		(SL1)		(SL2)
Does s/he remember the episode		(RE1)		(RE2)
Number per day		(NU1)		(NU2)
per month		(NM1)		(NM2)
Age when started (months)		(AS1)		(AS2)
Age of last seizure (months)		(ALS1)		(ALS2)
Seizure in the last year? (Y/N)		(SLY1)		(SLY2)

Description of seizures:

Type of seizures:

Simple Partial (**SP**); Complex Partial (**CP**); Generalised Absence (**GA**); Secondary Generalisation (**SG**); Tonic–Clonic/grand mal (**TC**); Myoclonic Seizures (**MS**); Atonic Attacks (**AA**); Tonic Attacks (**TA**); Unclassifiable Seizure (**US**)

	ST1		**ST2**		**ST3**		**ST4**	
Type of seizure		**(TS1)**		**(TS2)**		**(TS3)**		**(TS4)**
Duration <5 min = **1** 5-30 min = **2** >30 min = **3**		**(DT1)**		**(DT2)**		**(DT3)**		**(DT1)**
Unprovoked **Y/N**		**(UP1)**		**(UP2)**		**(UP3)**		**(UP4)**
Provoked by febrile illness **Y/N**		**(FI1)**		**(FI2)**		**(FI3)**		**(FI4)**
Provoked by non-febrile illness **Y/N**		**(NF1)**		**(NF2)**		**(NF3)**		**(NF4)**

Current anti-epileptic drugs:

Phenobarbitone (**PB**); Phenytoin (**PH**); Carbamazepine (**CB**); Sodium valproate (**NN**)

First drug taken: [ ][ ] **(AE1)** Second drug taken: [ ][ ] **(AE2)**

Drug		Dose (mg)	Times daily	Total daily dose (mg/kg/day)
1:____________	|__|__|__|	|__|__|__|	|__|	|__|__|__|
2:____________	|__|__|__|	|__|__|__|	|__|	|__|__|__|

Previous anti-epileptic drug history:

Drugs		From	To	Max Dose (mg/kg/day)
1:____________	|__|__|__|	|__|__|/|__|__|	|__|__|/|__|__|	|__|__|__|
2:____________	|__|__|__|	|__|__|/|__|__|	|__|__|/|__|__|	|__|__|__|

Drug reactions or unacceptable side effects from anti-epileptic drugs (Y/N) ......[ ]

Drug	Date	Nature of reaction or side-effect
__________	________	______________________
__________	________	______________________

Family history:

Does anyone else have a similar problem to this in the family (Y/N) ....[ ]**(SPF)**
Does anyone have seizures (fits) in the family (Y/N) .... [ ] **(SF)**
If so, who? ....
Do any of the brothers or sisters have seizures (Y/N)...........................[ ]**(BSS)**
Do any of the parents have seizures (Y/N)...................................... [ ] **(PS)**
Does anyone else have seizures associated with fever (Y/N)...................[ ]**(SAF)**

Obstetric and Perinatal history:

Pregnancy: Normal Abnormal [ ] **(NP)**

If abnormal what was the problem: ______________________________

Delivery at **Nyumbani; Hospatilini; Clinic** [ ] **(DL)**

Delivery: Normal Abnormal [ ]

(NAD)

If abnormal what was the problem: ______________________________

Did the baby cry after delivery (Y/N) [ ] **(BC)**

Were there any problems with the baby after the delivery (Y/N) [ ] **(PA)**

If so what: ______________________________

Did the child breast feed well on the first day (Y/N) [ ] **(BF)**

Other significant medical history

EXAMINATION

Weight |__|__| . |__| Kg **(WT)**
OFC |__|__| . |__| cm **(HC)**
Height |__|__|__| . |__| cm **(HT)**

Skull shape; Normal/ Abnormal [ ] **(SSN)**

Facial Appearance: Normal; Dysmorphic [ ] **(FA)**
Dysmorphic features (examine ears, tongue, face, hands, feet)

____

____

____

Skin: Normal; Abnormal [ ] **(SN)**
Any features of neurocutaneous syndromes (Y/N) [ ]**(NCS)**
Abnormality____________________________________

____

Hands and feet: Normal; Abnormal [ ] **(HF)**

General Examination

Cardiovascular:
Normal / Abnormal [ ] **(CV)**

Respiratory:
Normal / Abnormal [ ] **(RP)**

Gastrointestinal:
Normal / Abnormal [ ] **(GI)**

Other:

Examination of Cranial Nerves
Cranial Nerve II

Ptosis	Yes/ No		[ ] **(PT)**	
Pupils	Normal/ Abnormal		[ ] **(PU)**	
Reaction to light:				
			Right	Left
Direct	Yes/ No		[ ] **(DR)**	[ ] **(DL1)**
Consensual	Yes/ No		[ ] **(CR)**	[ ] **(CL)**
Accommodation	Yes/ No		[ ] **(MR)**	[ ] **(ML)**

Cranial Nerves III, IV and VI; V and VII
Eye movements **Cranial nerves III, IV and VI**

Squint?	Yes/ No	[ ] (SQ)
Which eye? **(SWE)**	Right /Left/ Both	[ ]
Nystagmus?	Yes/ No	[ ] (NY)
Direction of fast phase: Pendular, Jerk, Upbeat, Downbeat, Horizontal, Rotatory **(DFP)**		[ ]

The face **Cranial Nerves V and VII**

Muscles of mastication		
Jaw jerk: Brisk / Normal		[ ] (MM)
Muscles of facial expression		
Facial weakness?	Yes/ No	[ ] (FW)
Forehead stronger than lower face?	Yes/ No	[ ] (FS)

Cranial Nerves VIII; IX and X; XI; XII

The mouth, pharynx and larynx **Cranial Nerves IX, X, XII**

Pharynx and larynx			
Uvula:	Moves centrally	Yes/ No	[ ] (UMC)
	Deviates to:	Right/ Left	[ ] (UD)
Tongue			
Wasting?		Yes/ No	[ ] (TW)
Fasciculation?		Yes/ No	[ ] (TF)
Deviation?		Yes/ No	[ ] (TD)

Motor system:
Arms:

Wasting?	**Yes/ No**		[ ] **(AW)**
Where?________________________			
Fasciculation?	**Yes/ No**		[ ] **(AF)**
Where?________________________			
Tone	Normal **I**ncreased or **D**ecreased?		[ ] **(AT)**
Spasticity?	Right [ ] **(ASR)**	Left [ ] **(ASL)**	
Rigidity ?	Right [ ] **(ARR)**	Left [ ] **(ARL)**	
Clonus ?	Right [ ] **(ACR)**	Left [ ] **(ACL)**	
Contractures?	**Yes/ No**		[ ] **(AC)**
Where?____________________________			
Power (MRC 0-5)	Normal/ Abnormal/ **G**rossly Abnormal		[ ] **(AP)**
	Right		**Left**
Shoulder abduction	__		__
Shoulder adduction	__		__
Elbow flexion	__		__
Elbow extension	__		__
Wrist extension	__		__
Wrist flexion	__		__
Finger extension	__		__
Finger flexion	__		__
Finger abduction	__		__
Finger abduction	__		__
Thumb abduction	__		__

Legs:

Wasting?	**Yes/ No**		[ ] **(LW)**
Where?____________________________			
Fasciculation?	**Yes/ No**		[ ] **(LF)**
Where?____________________________			
Tone	Normal **I**ncreased or **D**ecreased?		[ ] **(LT)**
Spasticity?	Right [ ] **(LSR)**	Left [ ] **(LSL)**	
Rigidity?	Right [ ] **(LRR)**	Left [ ] **(LRL)**	
Clonus?	Right [ ] **(LCR)**	Left [ ] **(LCL)**	
Contractures?	**Yes/ No**		[ ] **(LC)**
Where?____________________________			
Power (MRC 0-5)	Normal/ Abnormal/ **G**rossly abnormal		[ ] **(LP)**
	Right		**Left**
Hip flexion	__		__
Hip extension	__		__
Hip adduction	__		__
Hip abduction	__		__
Knee flexion	__		__
Knee extension	__		__
Ankle dorsiflexion	__		__
Ankle plantarflexion	__		__
Ankle eversion	__		__
Big toe extension	__		__

Motor system - continued

Reflexes:

	Right	Left
Biceps	[ ] **(BR)**	[ ] **(BL)**
Knee	[ ] **(KR)**	[ ] **(KL)**
Ankle	[ ] **(AR)**	[ ] **(AL)**
Plantar	[ ] **(PR)**	[ ] **(PL)**

(Decreased Normal Increased)

Co-ordination:

Finger-nose	Normal/ Abnormal	[ ]**(FN)**
Heel-knee-shin	Normal/Abnormal	[ ]**(HKS)**
Piano-playing	Normal/Abnormal	[ ]**(PP)**
Dysdiadochokinesia?	Yes/ No	[ ]**(DD)**
Can the child imitate gestures?	Yes/No	[ ] **(IG)**

Gait:

Normal/ Abnormal [ ] **(GN)**

Describe gait abnormality________________________________

Fogg test	Normal/ Abnormal	[ ] **(FT)**
Heel-toe	Normal /Abnormal	[ ]**(HT)**

Spine:

Scoliosis?	Yes/No	[ ]**(SC)**
Describe________________________________		
Cutaneous abnormality?	Yes/No	[ ] **(CA)**
Describe________________________________		

Fundoscope examination	Right	Normal/Abnormal	[ ] **(FR)**
	Left	Normal/Abnormal	[ ] **(FL)**
Auroscope examination:	Right	Normal/Abnormal	[ ] **(UR)**
	Left	Normal/Abnormal	[ ] **(UL)**

Any additional notes?	**Yes/No**	[ ] **(AD)**

Appendix 2: Cognitive Assessment

Child's name: [ ] [ ][ ]

Study number: [ ][ ][ ][ ][ ]

Date of assessment: [ ][ ]/[ ][ ]/ [ ][ ][ ][ ]

Assessor: [ ][ ]

Comments/Observations

SETTLING DOWN QUESTIONS

What is your name?	**Q1**	
(Explain what you are about to do and get consent)		
How old are you?	**Q2**	
Where do you live?	**Q3**	
Where do you go to school?	**Q4(a)**	
What the name of your class teacher?	**Q4(b)**	
What class are you in?	**Q4(c)**	
Who is your school headmaster?	**Q4(d)**	
Where are you now?	**Q5**	
(Ask the child if he/she is ready to continue)		

CONSTRUCTION

Item	Drawing	S	O	TS	TIME
Sample					
	SECTION 1				
Con 1					
Con 2					
Con 3					
SECTION 2					
Con 4					
5					
6					
SECTION 3					
Con 7					
8					
9					
Page total					

Item	Drawing	S	O	TS	TIME
SECTION 4					
Con10					
11					
12					
SECTION 5					
Con13					
14					
15					
SECTION 6					
Con16					
Con17					
Con18					
Page total					
Total Construction Score (max. 36)				ConT	

KCBMT SCORING SHEET

1.STORY RECALL

IMMEDIATE	**ISR**	
DELAYED	**DSR**	

Max: 31

2.PICTURE RECOGNITION

1. Basket	N		11. Pot	Y	
2. Shoes	Y		12. Tree	N	
3. House	Y		13. Table	Y	
4. Car	N		14. Chair	N	
5. Trousers	N		15. Cow	Y	
6. Ball	N		16. Bicycle	Y	
7. Spoon	Y		17. Person	N	
8. Book	N		18. Goat	N	
9. Knife	N		19. Maize	Y	
10. Pencil	Y		20. Chicken	Y	

Y-Y		N-Y		
	-		**PR**	

Max: 10

STORY 1 (ISR)

Once there was a boy/ by the name of Khamis./ He was walking around the forest./ He went and sat/ under a tree./

1. What is the name of the person in this story?
2. Was he an old man or a boy?
3. Where was he?
4. In the beginning of the story, where did he go?

Khamis felt sleepy./ He was wearing a hat./ On a tree/ there was a monkey./ When he was asleep/ the monkey came down/ took the hat/ climbed with it on the tree/ and put it on./

5. What was on top of the tree?
6. What was Khamis doing when the monkey came down the tree?
7. What did the monkey take?
8. Where did the monkey go with the hat?

Khamis felt the wind blowing on his head./ He touched his head/ and realised that his hat was not there./ The monkey made a noise/ Khamis looked up/and saw the monkey/ wearing his hat/. He told the monkey to give him his hat/ The monkey didn't give it back./

9. What woke Khamis up?
10. Who made a noise?
11. What did Khamis tell the monkey?

Khamis took a stone/ and hit the monkey/. The monkey took off the hat/ and ran away into the forest./ Khamis took it/ put it on/ and went home/ whistling./

12. What Khamis do to get his hat back?
13. Where did the monkey run to?
14. Where did Khamis go after getting his hat back?

3.REMEMBERING A SHORT ROUTE

4.DELIVERING A MESSAGE

	IRR	DRR		IMR	DMR
1. Chair					
2. Door			Takes message 2		
3. Window			With prompt 1		
4. Table					
5. Back to chair			Leaves message 1		

Max: 5	**IRR**	
Max: 5	**DRR**	
Max. 3	**IMR**	
Max. 3	**DMR**	

5.FACE RECOGNITION

1. Y		6. N	
2. Y		7. N	
3. N		8. N	
4. Y		9. Y	
5. N		10.Y	

Y-Y N-Y

Max.5		-		**FR**	

STORY 2 (DSR)

Once there was a boy/ by the name of Khamis./ He was walking around the forest./ He went and sat/ under a tree./

1. What is the name of the person in this story?
2. Was he an old man or a boy?
3. Where was he?
4. In the beginning of the story, where did he go?

Khamis felt sleepy./ He was wearing a hat./ On a tree/ there was a monkey./ When he was asleep/ the monkey came down/ took the hat/ climbed with it on the tree/ and put it on./

5. What was on top of the tree?
6. What was Khamis doing when the monkey came down the tree?
7. What did the monkey take?
8. Where did the monkey go with the hat?

Khamis felt the wind blowing on his head/. He touched his head/ and realised that his hat was not there/. The monkey made a noise/ Khamis looked up/and saw the monkey/ wearing his hat/. He told the monkey to give him his hat/ The monkey didn't give it back./

9. What woke Khamis up?
10. Who made a noise?
11. What did Khamis tell the monkey?

Khamis took a stone/ and hit the monkey./ The monkey took off the hat/ and ran away into the forest./ Khamis took it/ put it on/ and went home/ whistling./

12. What Khamis do to get his hat back?
13. Where did the monkey run to?
14. Where did Khamis go after getting his hat back?

6. ORIENTATION QUESTIONS

Do you know what day it is today?	**Q6(a)**	
Which month?	**Q6(b)**	
Which year?	**Q6(c)**	
Do you know in which year you were born?	**Q7**	
What is your birth order?	**Q8**	
Who takes care of you?	**Q9(a)**	
What is your name?	**Q9(b)**	
What is your household name?	**Q10**	
Where do you get drinking water from?	**Q11**	
What is the name of our President?	**Q12**	

7. REMEMBERING AN APPOINTMENT

Ask without prompt	2
Ask with prompt	1
Remembers has to say something	1

RA	

Max: 2

8. REMEMBERING A NAME

	Correct	Correct with prompt
First name	2	1
Second name	2	1

RN	

Max: 4

9. REMEMBERING HIDDEN OBJECT

Item	Remembered without prompting	2	Remembered with prompt	1
Place	Remembered " "	2	Remembered " "	1

RHO	

Max: 4

RECEPTIVE VOCABULARY TEST

	Sample				
	Sample				
	1	2	3	4	
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
18					
19					

20					
21					
22					
23					
24					
25					
26					
27					
28					
29					
30					
Total (max. 25)				**PVT**	

VISUAL SEARCH

	Score	
Total time {sec}	.	**VSTT**
Errors of Omission		**VSEO**
Errors of Commission		**VSEC**

Appendix 3: Behaviour Questionnaire

NAME OF CHILD: [ ] [ ] [ ]

STUDY NUMBER:[ ][ ][ ][ ][ ] ASSESSOR:[ ][ ]

DATE OF ASSESSMENT:[ ][ ]/[ ][ ]/[2000/1]

RESPONDENT: Mother/Father/Other [ ]

BQ1	**<u>APPETITE</u>:** First, tell me about his/her eating habits. - How was his/her eating in the last month? - Does s/he eat everything or sometimes refuse to eat? - Do you think s/he eats enough? - Do you think his/her eating habits are a problem?
BQ2	**<u>CONCENTRATION SPAN</u>:** - Is s/he a child who doesn't want to sit and settle? - For how long does s/he concentrate, for example when listening to a story?
BQ3	**<u>SOCIAL RELATIONSHIPS</u>:** - Describe x's relationships with his/her siblings in the last month? - Does s/he argue or quarrel? - Does s/he play well with his/her siblings? - Are there other children nearby with whom s/he can play? - When s/he is with them, how does s/he play?

BQ4a	**<u>CONTROLLING HIS/HER CARETAKERS</u>:** - Does x want others to help him/her to do what s/he is also capable of, for example feeding or dressing? - Does x like staying with you more than playing with others?
BQ4b	**<u>ANXIETY/EASE</u>:** - Can x be left with others who are familiar with him/her? - With whom do you normally leave him/her? - Does s/he stay with you for the whole day?
BQ5	**<u>BEHAVIOUR IN PUBLIC/MANAGEMENT IN AND OUT OF HOME</u>:** Most children can be troublesome sometimes: how is x at home? - Can you take him/her out for a walk with no problem? - Is s/he destructive? - Is s/he difficult behaviourally, or do you have problems with discipline? - How long have you had this problem? - Is s/he the same with others?
BQ6	**<u>MOOD:TEMPER/TANTRUMS:</u>** When x is annoyed, what does s/he do? - Is s/he hot-tempered? - Does s/he shout, scream or kick? - How many times in the last month? - Do you know what annoys x? - When did s/he start having tantrums? - When s/he is annoyed, how long does s/he take to calm down?

BQ7	**MOOD: HAPPINESS/SADNESS:** Are there times when x is not happy? - How was s/he in the last month, was s/he happy or sad? - How frequently is s/he like that? - When did s/he start?
BQ8	**WORRIES:** Does x often appear worried? - What does s/he do if he has lost something? - Does s/he persistently think about the same thing? - Does s/he think about things like accidents, sickness and witchcraft?
BQ9	**FEARS:** Most children are afraid sometimes. What is x afraid of? dogs people he is not familiar with cats being away from home animals/insects vehicles water darkness hair cut/shave thunder stories corporal punishment doctors/hospitals What does s/he normally do when s/he is afraid?

BQ10	**SOCIAL INDEPENDENCE:** - How is x when s/he is left alone? - Can s/he be sent to do something alone, for example going to fetch water, going to the shop, going to play?
BQ11	**UNDERSTANDING FEELINGS OF OTHERS/EMPATHY:** - Does x help others? How? - What does s/he do when s/he sees another child crying - When s/he has food or a toy, does s/he share with others?
BQ12	**HABITS:** Many children have different habits or repetitive actions. What is x known to repeat daily or weekly? biting finger nails lying laughing aimlessly crying stealing sucking his/her thumb screaming other
BQ13	**INDEPENDENCE/SELF-CARE:** Some children are able to do many things for themselves but sometimes they need assistance. Which out of these is s/he able to do without any assistance? Drinking feeding himself Dressing washing him/herself

BQ14	**<u>WETTING/SOILING</u>**: - Does s/he soil him/herself? How frequently - Does s/he wet him/herself? - What about at night?
	A. B.
Comments:	

Appendix 4: Electroencephalography

EEG CLASSIFICATION

Name: [ ][ ][ ]

Study No.: [ ][ ][ ][ ][ ] **Assessor No:** [ ][ ]

I General background	[ ] **(GB)**
a) Normal	
b) Mild	
c) Moderate	
d) Severe	
II Asymmetry (Y/N)	[ ] **(AS)**
III Focal features (Y/N)	[ ] **(FF)**
If so, temporal (Y/N)	[ ] **(FC)**
parieto-occipital (Y/N)	[ ] **(FP)**
IV Epileptiform activity (Spikes, sharp waves, spike + wave, rhythmic runs) (Y/N)	[ ] **(EA)**
a) Focal temporal (Y/N)	[ ] **(FT)**
Focal extra-temporal (Y/N)	[ ] **(FE)**
b) Multifocal (Y/N)	[ ] **(MF)**
Involves temporal lobe (Y/N)	[ ] **(MT)**
c) Generalised (Y/N)	[ ] **(GN)**
V Photosensitivity: abnormal response (Y/N)	[ ]**(PH1)**
VI Hyperventilation: abnormal response (Y/N)	[ ]**(HY1)**

Appendix 5: Visual Screening

Sonksen-Silver Acuity System

Name: [ ] [ ] [ ]

Study number: [ ] [ ] [ ] [ ] [ ]

Date of assessment: [ ][ ]/ [ ][ ]/ [ ][ ][ ][ ]

Assessor: [ ] [ ]

Acuity at six metres:

Both Eyes Open: 6/[ ] (BEO)

Right Eye: 6/[ ] (RE)

Left Eye: 6/[ ] (LE)

Classification: [ ] (VS)

Comments:

Appendix 6: Hearing Screening

Name: [ ] [ ] [ ]
Study number: [ ] [ ] [ ] [ ] [ ]
Date of assessment: [ ][ ]/ [ ][ ]/ [ ][ ][ ][ ]
Assessor: [ ] [ ]

Right Ear: Air Conduction

Frequency:	250Hz	[ ] **(RA250)**
	500Hz	[ ] **(RA500)**
	1000Hz	[ ] **(RA1000)**
	2000Hz	[ ] **(RA2000)**
	4000Hz	[ ] **(RA4000)**
	8000Hz	[ ] **(RA8000)**

Left Ear: Air Conduction

Frequency:	250Hz	[ ] **(LA250)**
	500Hz	[ ] **(LA500)**
	1000Hz	[ ] **(LA1000)**
	2000Hz	[ ] **(LA2000)**
	4000Hz	[ ] **(LA4000)**
	8000Hz	[ ] **(LA8000)**

Right ear average (air): [ ] **(REAA)**

Left ear average (air): [ ] **(LEAA)**

Appendix 7: Socio-economic status questionnaire

Name of child:

Study number: [ ][ ][ ][ ][ ]

Assessor:

Interviewee: mother / father / other ______________________

Date:

1. How many blood siblings does the child have?

2. Did the child's mother go to school? Y/N

   If yes, which level did she reach?
   (standard 1-3 = **1**; standard 4-8 = **2**; secondary = **3**; tertiary = **4**)

3. Can the child's mother speak English? Y/N

4. What is the occupation of the child's father/man who keeps the family?
   (subsistence farmer = **1**; large-scale farmer (eg. owns cattle, grows cash crops) = **2**; casual labourer = **3**; small business (ie. no employees) = **4**; large business (ie. has employees)/professional = **5**)

5. How many meals do your children eat per day?

6. What do you normally do to get flour?
   (grind at the mill = **1**; buy = **2**)

   Why?

7. Do you own the land you live on? Y/N

   Do you own any land? Y/N

8. Do you listen to the radio?
   (daily = **1**; weekly = **2**; irregularly = **3**; never = **4**)

Appendix 8: Instruction Manuals for Speech and Language Assessments

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A8.1 Receptive grammar assessment: Directions for administration
adapted from TROG manual (Bishop, 1983)

1. Introducing the task:

Present the example picture to the child and give him/her a few seconds to scan the pictures. Then read the following:

Look at each of these pictures (if necessary, point to each one in turn). *If I asked you to point to the one that goes with this sentence: 'The girl is wearing shoes', you would point to this picture* (point to the correct picture). *Do you want to try it?*

Repeat the target sentence. If the child responds correctly, proceed to the practice picture. Say:

Look at each of these pictures (if necessary, point to each picture in turn). *I want you to point to the picture that goes with what I say. Listen carefully.*

Say the practice word. If the child points to the wrong picture, repeat the word. Once the child has pointed to the correct picture, read the following:

Good. Now I am going to show you some more pictures. Each time I say something, you point to the picture that goes with what I say. Remember to look at each picture carefully before you answer.

Once the child has pointed to the correct picture, continue with the test pictures. Before saying the target word/sentence, give the child a few seconds to scan the pictures on each page.

2. Presentation of test items

The full sentence as written on the record form should be spoken clearly and naturally. Critical words or morphemes should be given moderate stress but not to the point of artificiality.

If the child does not respond, wait for about 8 seconds then repeat the test sentence. Repeat the whole sentence. If the subject does not respond after a further 8 seconds, write 'NR' (no response) on the record form and proceed to the next item.

If the child points to more than one picture, say '*Only one picture is right. Listen carefully.*' and repeat the test sentence. If the child persists in pointing to more than one picture, record the picture numbers. Such responses are counted as errors.

If the child points before you have finished speaking, say '*Wait until I have finished speaking. Listen carefully.*' then repeat the test sentence. Do this regardless of whether the premature response was correct. This may be an indication that the child feels under time pressure: make sure you give him/her ample time to scan the pictures before you present the test sentence.

If the subject changes his response, record the final response.

If the child persistently points to one corner of the picture, say '*Remember to look at all four pictures*' and point to each picture in turn. Be careful to give the child ample time to scan the pictures before you present the test sentence.

If the child names the pictures but does not point, repeat the instruction '*I want you to point to the picture that goes with what I say. You don't have to say anything.*' If the child persists in naming the pictures, the assessor should use the vocabulary cards to give further demonstration of what is required.

3. Administering the Vocabulary Check

The vocabulary cards are used to check understanding of the vocabulary used in the receptive grammar assessment (apart from those items already presented in the noun/verb/adjective sections of the test itself). These cards allow you to discover whether errors on the assessment may reflect vocabulary failure rather than grammatical problems. Administer the vocabulary check in the same way as the assessment itself by asking the child to point to the word you say.

4. Marking the Receptive Vocabulary Assessment

During the assessment, record the number of the picture the child points to. After the assessment, calculate the child's score by matching the number recorded to the number in the score box. Each question has a maximum score of '1' so the maximum for each section is '2'.

A8.2 Syntax Assessment: Directions for administration

The aim of this assessment is to test the child's ability to use a set of predefined syntactic and morphological structures. The test consists of two sections. In the first section, real objects are used. The second section has eleven test pictures and five test questions.

1. Section One

Sit facing the child with a table between you. Present the objects (two cups and a banana). Ask the child if he/she knows the objects, if not tell him/her what they are. Then say the following:

I will place this banana in different positions in relation to the cup. I want you to tell me where the banana is.

Place the banana infront of the cup as per example one:

The banana is infront of the cup. Where is it?

If the child responds correctly, proceed to the second example. If not, repeat example one then continue with the second example:

Now, the banana is behind the cup. Where is it?

Continue with the test questions, placing the banana in different positions and asking the child, '*Where is the banana now*?'

2. Section Two

Take the Syntax picture book and open it to the example picture. Give the child the following instructions:

We are going to do something a bit different now. I will show you some pictures. Sometimes I will ask a question about the picture and other times I will start a sentence that I want you to complete. For example, with this picture, I might ask you the question: 'Why is the baby happy?' and you could say: 'Because his mother is giving him a banana'. Or I might start a sentence like this: 'The baby is happy because...'. Then I would want you to finish it by saying something like: 'he can see the banana' or 'his mother has a banana'. Shall we try it together?

Continue by asking the child the example question as above: '*Why is the baby happy?*' then giving the example statement: '*The baby is happy...*' When you are starting a sentence for the child to complete, make sure you use appropriate intonation (i.e. not falling intonation). If the child is able to give answers that demonstrate he understands the format of he test (they don't have to be the same answers as given in the example), say the following:

Well done. Now I will show you some more pictures like that. When you give me your answer, try to use a proper sentence like you would do at school/ for your teacher/ like a grown-up would.

Proceed with the first test picture. The question or statement for each picture should be read exactly as printed on the back of the picture. Some pictures have more than one question/statement. One repetition of the test sentence is allowed if the child is not responding. If the child gives an abbreviated answer, which misses the target construction of the question (e.g. Q. 'What will the boy do with the banana?' A. 'Eat it'. The target construction is the future tense i.e. 'He <u>will</u> eat it), encourage the child to say a 'proper sentence'. If the second response is also abbreviated, proceed with the next question.

Do not give the child any indication whether his/her answer was correct or incorrect. However, encourage the child throughout the test with comments such as 'good' or 'well done'.

3. Recording and Marking

Target answers are written on the record form. If the child's answer is exactly the same as the target answer, simply tick the box adjacent to the target. If the child's response is different, write the response verbatim in the box. Mark the test after administering it using the Syntax Scoring Guidelines (Appendix 17).

A8.3 Higher Level Language Assessment: Directions for Administration

The aim of this test is to assess the child's understanding and use of certain higher level aspects of language. The test comprises five tasks:

- Categorisation task
- Definitions of words
- Homonyms
- Similarities and differences
- Sentence formulation

Before starting the test, position yourself opposite the child and tell him/her that you would like to play some word games. Specific task instructions are presented below:

1. Categorisation task

This section tests the child's ability to name items in a set category while under time pressure.
Say the following instructions to the child when you begin the task:

I am going to give you a category and I want you to tell me as many words as you can think of in that category until I say stop.

Present the first category and time the child for one minute using a watch. Record the words the child gives on the record from so you can check for repetition and appropriateness. After one minute, tell the child to stop and continue with the next category.

2. Definition of words

This section requires the child to give definitions of words of different classes (noun, verb, adjective, abstract). Use the Higher Level Language picture booklet and present the first picture to the child. Say the following:

We are going to do something different now. I will say a word and I want you to tell me what it means. I will give you an example...

Proceed to give the first example on the record form (kikombe):

A cup is something you drink out of.

Then ask the first question. Before asking each question, give the example on the record form. Each class of word has an example:

Verb: Food is something you chew and swallow
Adjective: Cleanliness means to glow
Abstract: Theft means to take something that isn't yours

3. Homonyms

This task requires the description of words, which sound the same but have two meanings (homonyms). Describe a homonym to the child before presenting the task:

There are some words that have more than one meaning. For example, 'kaha' can mean the container you fetch water in or the cloth you put on your head to carry things on.

Use the example pictures in the Higher Level Language picture booklet to describe the example words if this aids the child's understanding. Ask the child if s/he understands the two meanings of 'kaha'. If s/he does, give the second example. If not, repeat the meanings of 'kaha' using the pictures or describing situations with which the child will be familiar.

Another example is 'kufula'. 'Kufula nguo' means to wash clothes whereas 'kufula nazi' means to shred a coconut.

Once you are confident that the child understands the concept of a homonym, proceed with the test questions. If the child gives only one meaning of the test word, prompt him/her that the word also has another meaning.

4. Similarities and differences

This task tests the child's ability to identify and describe similarities and differences between familiar objects. Introduce the task with the following:

I am going to show you a picture and tell you something that is the same and something that is different about the two objects on the picture.

Present the first example picture:

This is a picture of a 'kuku' and a 'batha'. The difference between these two birds is that a 'kuku' can't swim whereas a 'batha' can. Something that is similar between them is that they both have two legs and lay eggs.

Confirm that the child has understood the first example then proceed with the second example.

This picture shows a 'nyundo' and an 'upanga'. The difference between them is that a 'nyundo' is for hitting and an 'upanga' is for cutting. They are similar because they are both made of metal.

Once you are confident that the child understands the concept of similarities and differences, proceed with the test questions. For each question, show the child the relevant picture if this helps him/her to answer.

5. Sentence formulation

This task requires the child to produce a sentence from a single word provided by the assessor. Present the first example picture and say the following:

I will give you a word and I want you to make a sentence with it. For example, if I said the word 'paka', you could say the sentence 'The paka is playing with the ball'.

Continue with the second example picture:

Or I could give you another word like 'kurira'. This time, you could say the sentence 'Muhoho yuyu anaririra mameye'.

Once you are confident that the child understands the task requirements, proceed with the test questions. If the child doesn't respond to the word, encourage him/her to tell you anything he knows about the word.

6. Recording and Scoring

During the assessment, write down exactly what the child says for each question. If the child gives no response, record 'NR'. When scoring, use the Higher Level Language Scoring Guidelines (Appendix 20).

A8.4 Word Finding Assessment: Directions for Administration

The word finding assessment is designed to assess the child's speed and accuracy when naming picture referents of noun target words. It consists of two example pictures, two practice pictures and 40 test pictures.

1. Introducing the task

Sit facing the child and read the following directions:

I will show you some pictures and I want you to tell me the name of each one. Sometimes I will ask you to name the whole picture and sometimes just the part I point to. There is only one word for each answer so remember to give me only one word in your answer. Now, look at this picture.

Show the child the first example picture.

The answer for this picture is 'tsoka'. What does this picture show?

If the child says 'tsoka', continue with example 2. If not, name the picture a second time, then continue with example 2.

The answer or this picture is 'kitswa' because I am only pointing to that part of the picture. What does this picture show?

If the child says 'kitswa', present the practice items. If not, name the picture a second time, then present the practice items.

As the practice items are not test items, answers are not recorded on the response sheet. Before presenting the practice items, remind the child of the instructions for the test:

Remember, I want you to tell me the name of each picture I show you when I say 'ino'. Sometimes I will ask you to name the whole picture and sometimes just the part I point to. Remember to give me only one word in your answer.

2. Presentation of test items

Present the two practice items then continue with the Word Finding Assessment items using the following procedure:

- Present the picture
- Say '*ino*' and silently start counting a 4-second interval
- Write the child's response or tick the subject response column if the response is exactly the same as the target word
- Record the first response given by the child regardless of how many different responses they give

- Record the estimated time response by ticking the relevant column (less than 4 seconds or more than 4 seconds)

- If the child doesn't respond or says 'I don't know', allow 15 seconds before moving to the next item
- Accuracy scores will be completed after the administration of the test

3. Marking

Accuracy: Mark a '1' for all correct responses given by the child and '0' for all incorrect responses

Appendix 9: Consent Form

NB: This is a back-translation from the Kigiryama version.

I am from KEMRI – Community Research Unit. We are assessors of child development and growth. We want to see if there is any relationship between malaria, epilepsy, and problems with growth and development. By comparing children who have been very ill with malaria with those who have not, we will know if there are children who develop epilepsy following malaria.

This will involve children from three (3) groups
1. Those who have been admitted to hospital with cerebral malaria
2. Those who have been admitted to hospital with malaria and seizures
3. Those who have never had severe malaria

We would like to find out about your child's communication, learning and memory and whether s/he can make use of different body parts properly. We would also like to find out about his/her behavioural patterns, for example eating habits, independence, relationships with other children and discipline. We will be testing his/her vision and hearing and examining him/her to see whether s/he has epilepsy. For this (epilepsy), we will refer the child to a doctor but this requires no drugs or injections. The activities we will be doing with the child are designed to measure growth and development through playing and questions, using pictures and so on.

We would like to see the child at home for about 2-3 hours and on another day at the unit for a whole day. The Community Research Unit is situated near Kilifi District Hospital. We also need to talk to the child's guardian about the child's behaviour and communication at home.

We will refer any child we find with problems for further assessment to appropriate doctors. There are no direct benefits from this study to your child. The benefits of the study are to help doctors know how to manage illnesses such as epilepsy. Participation in this study is voluntary. Should you wish to withdraw your child, you are free to do so at any time without affecting your right to future treatment

Do you have any questions?
Do you consent for your child to be part of this study?

Name.. Signature...

Appendix 10: Pilot Study Receptive Language Assessment

Name of child:

Section 1: Receptive vocabulary test

Target	Correct	Incorrect	Comments
Ball			
Spoon			
Chicken			
Bell			
Baby			
Fruit			
Sleeping			
Shoes			
Knot			
Needle			
Axe			
Matches			
Cooking			
Washing clothes			
Climbing			
Hanging			
Fighting			
Thirst			
Sharp (object)			
Hot (object)			
To fear			
Many			
Danger			

Total correct ☐

Total incorrect ☐

Section 2: Commands

1. Show me your head

eyes

ears

nose

mouth

leg

arm — Total: /7

2. Two stage commands

Touch your nose and your leg

Touch your ear then close your eyes

Shake your head then open your mouth — Total: /3

3. Three stage commands

Touch your arm, leg and nose

Touch your eye, ear and mouth

Close your eyes, open your mouth then shake your head — Total: /3

Assessment total: ☐

(maximum=36)

Appendix 11: Pilot Study Syntax Assessment

Name of child:

Target	Actual
Prepositions On the cup In the cup	
Plurals (N-class) These are three houses	
Comparative This cup is like this cup	
Conjunction A pen and a book	
'WH' question Where is my sister?	
Locative She is going to the shop	
Prepositions Under the cup Beside the cup	
Comparative Very tall	
Plurals (Ki-Vi class) These are three cups	
Negative I don't want to go	
Adverb Slowly	
Adjective The hot porridge	
Plurals (M/A class) These are two girls	
Prepositions Behind the cup Infront of the cup	
Imperative Come here	
Plurals (M/Mi class) These are two trees	
'WH' question Who has broken my cup?	
Past tense The boy cut his leg	
Future tense The baby is going to fall	

<u>Prepositions</u> Between the cups	
<u>Plurals (Ji/Ma class)</u> These are two boats	
<u>Passive</u> This boy was given a banana	
<u>Relative clause</u> Likes the one that is green	
	Total (maximum=34)

Appendix 12: Pilot Study Higher Level Language Assessment

Name of child:

1. **Categorisation tasks**
   (1 = less than 3; 2 = 3 or more)
   Tell me as many things as you can that you can eat.

   Tell me as many colours as you can.

   /4

2. **Definitions of words**
   A 'kikombe' is something you can drink out of.
   Can you tell me what a 'kihi' is?

   Can you tell me what 'kutsemberera' means?

   /2

3. **Antonyms**
   The opposite of 'hot' is 'cold'
   What is the opposite of 'tall'?

   What is the opposite of 'happy'?

   /2

4. **Homonyms**
   Can you tell me what 'kaha' can mean?

   Can you tell me what 'panda' can mean? /2

5. **Similarities and differences**
   Can you tell me something that is the same and something that is different between a car and a motorbike.

   Can you tell me something that is the same and something that is different between a cow and a donkey.

   /4

6. **Figurative language**
   What does it mean when we say someone has a 'long hand'?

   /1

7. **Convergent semantic task**
   Can you finish this sentence: 'I sweep with a ____________' /1

8. **Divergent semantic task**
   If you can't use a 'panga' for cutting grass, what else could you use?

   If you can't use a 'jembe' for planting, what else could you use?

/4

9. **Sentence formulation**
   Can you make a sentence using the word 'dog'?

   Can you make a sentence using the word 'take'? (hala also-marry)

/2

10. **Synonyms**
    Can you tell me a word that means the same as 'kikahana'? ('kidziha')

/1

(Use picture of older girl lifting younger girl to pick a mango from a tree for the following questions)

11. **Inferential Reasoning**
    What is the little girl's problem?

/1

12. **Explaining an Inference**
    How do you know this girl can not reach the mango by herself?

/1

13. **Problem solving**
    The little girl can't reach the mangoes by herself. What is the big girl doing about that?

    How else could the girl reach the mangoes?

/2

14. **Determining Causality**
    Some of the mangoes look good but some look bad. What could make a mango look bad?

/1

15. **Generalising: Creating a Sequential Story**
    What does the little girl do with the mango?

    What do you think the little girl has already said to her sister?

/2

16. **Applying General Knowledge**
How do you know these girls are outdoors and not indoors?

/1

Total score:
(maximum score=31) ☐

Appendix 13: Pilot Study Pragmatics Assessment

Name of child:

Part 1: Analysis of functional errors:

Total number of utterances	
Linguistic nonfluencies	
Revisions	
Delayed responses	
Nonspecific vocabulary	
Inappropriate responses	
Poor topic maintenance	
Need for repetition	

Part 2: Observation

	Examples/Comments	Yes	No
Appropriate physical proximity?			
Appropriate eye contact?			
Appropriate facial expression?			
Appropriate amount of presupposition?			
Not easily distracted?			
Language appropriate to the situation and people present?			
Appropriate amount of language? (verbosity)			

Observations:
(maximum=7)

Part 3: Parental Questionnaire

Use of Language

	Yes	**No**
Can the child ask for help? (If your child was trying to reach something which was too high, what would he say?)		
Can the child label objects?		
Can the child give names to people and animals?		
Can the child offer help? (If a younger child had a problem, what would your child say?)		
Can the child greet people?		
Can the child verbalise a problem? (If your child has a problem, will he tell you? What would he say?)		
Can the child disagree with another? (If your child disagrees with someone, what would he say?)		
Can the child predict outcome? (If someone is cooking with a flame which is too high so the food will burn, will your child predict what will happen? What would he say?)		
Can the child give directions? (If another child wanted to know how to play 'lenga-lenga', would your child explain how to play it? NB: not show but verbally explain)		
Can the child tell others they have made an error?		
Can the child suggest action? (If another child was hurt, would your child be able to say what to do? What would he say?)		
Can the child make choices?		
Can the child speculate? (If an older child had just completed standard 8, would your child be able to talk about what he might do next? What would he say?)		
Can the child tell jokes / play with language?		
Can the child tell stories?		
Can the child express needs and feelings?		
Can the child console? (If a younger child was upset, what would your child say?)		
Can the child deceive? (Has your child ever lied to you? If so, what did he say?)		
Can the child pretend? (Does your child engage in pretend play? If so, give an example.)		

Use of Language: ☐
(maximum score=19)

Appendix 14: Pilot Study Phonological Transcription

Transcription of the first 100 different words produced in the child's spontaneous language sample.

Name of child:

Gloss	Transcription	Gloss	Transcription
1		51	
2		52	
3		53	
4		54	
5		55	
6		56	
7		57	
8		58	
9		59	
10		60	
11		61	
12		62	
13		63	
14		64	
15		65	
16		66	
17		67	
18		68	
19		69	
20		70	
21		71	
22		72	
23		73	
24		74	
25		75	
26		76	
27		77	
28		78	
29		79	
30		80	
31		81	
32		82	
33		83	
34		84	
35		85	
36		86	
37		87	
38		88	
39		89	
40		90	
41		91	
42		92	

43		93	
44		94	
45		95	
46		96	
47		97	
48		98	
49		99	
50		100	

% correct

Appendix 15: Receptive Language Assessment

Name of child: [ ] [ ] [ ]
Study number: [ ] [ ] [ ] [ ] [ ]
Date of assessment: [ ][ ] [ ][ ] [ ][ ][ ][ ]
Assessor: [ ] [ ]

Example picture

The girl has no shoes	

Practice picture

Banana	

Nouns

A 0 Flower	
1 Chicken	

☐ (N)

Verbs

B 2 Sleeping	
3 Digging	

☐ (V)

Adjectives

C 4 White	
5 Long	

☐ (A)

Two element combination

D 6 The girl is running	
7 A big cup	

☐ (TEC)

Negative

E 8 The cow is not standing	
F 9 The girl is not drinking	

☐ (NEG)

Three element combination

G 10 The man is eating a banana	
11 The girl is sitting on the table	

☐ (HEC)

Reversible active

H 12 The girl is chasing the dog	
12 The girl is pushing the cow	

(RA)

Comparative

I 14 The girl is fatter than the man	
15 The knife is longer than the pencil	

(COM)

Plural: N class

J 16 The girl is picking bananas	
17 The girl is dropping plates	

(PN)

Plural: KI/VI class

K 18 The girl is standing on the chairs	
19 The man is wearing shoes	

(PKV)

Plural: M/MI class

L 20 The dog is looking at the trees	
21 The girl is carrying loaves of bread	

Plural: M/A class

M 22 The cow is chasing the people.	
22 The girl is pushing the animals	

(PMA)

Reversible Passive

N 24 The girl is being chased by the dog	
23 The cow is being pushed by the man.	

(RP)

Prepositions: In and On

O 26 The cup is in the box	
27 The pencil is on top of the cup	

(PIO)

Prepositions: Infront and Behind

P 28	The table is infront of the tree	
29	The bottle is behind the box	

(PIB)

Postmodified subject

Q 30	The pencil on top of the table is red.	
31	The cow chasing the dog is black.	

(PS)

Relative clause

R 32	The girl is chasing the dog that is white.	
32	The man is kicking the cow that is big.	

(RC)

Total / 34: (GRG)

Vocabulary check:

Dog		Spoon	
Girl		Dress	
Cow		Cup	
Knife		Box	

Banana		Shoes	
Monkey		Tree	
Plate		Bread	
Chair		Man	

Chasing		Eating	
Sitting		Dropping	
Pushing		Plucking	

Carrying		Standing	
Lying down		Kicking	
Running		Drinking	

Thin		Black	
Fat		Big	
Short		Small	
Red			

Vocabulary check passed? Y/N ☐ **(VC)**

Appendix 16: Syntax Assessment

Name of child: [ ] [ ] [ ]
Study number: [ ] [ ] [ ] [ ] [ ]
Date of assessment: [ ][ ]/ [ ][ ]/ [ ][ ][ ][ ]
Assessor: [ ] [ ]

Equipment: Syntax picture book; two cups; toy banana

Target	Actual	Score	
Mbere ya kikombe **Infront of the cup**			
Nyuma ya kikombe **Behind the cup**			
Dzulu ya kikombe On the cup			(PO)
Ndani ya kikombe In the cup			(PI)
Kanda kanda ya kikombe Beside the cup			(PBS)
Tsini ya kikombe Under the cup			(PU)
Kahikahi ya vikombe Between the cups			(PBT)
Kwa sababu mameye anamupa izu **Because his mother is giving him a banana** **Mameye ana izu** **His mother has a banana**			
Ni nyumba mbiri. They are two houses			(NC)
Mupira na kihi A ball and a chair			(CON)
Mubomu zaidi/mwenye Very tall			(COM1)
Ni vikombe viri They are two cups			(KVC)
Porepore Slowly			(ADV)
Ni kikombe kithithe kithune A small, red cup			(ADJ)
Ni asichana airi They are two girls			(MAC)
Ma……… (past tense)			(PAT)

Ni mihi miri They are two trees			(MMC)
Anenda dukani She is going to the shop			(LOC)
Senzi kwenda I don't want to go			(NEG1)
Rini....... When.......			(WHE)
Akigerwa/ wagerwa izu This boy was given a banana			(PAS)
Anda....... (future tense)			(FUT)
Ni hani........ Who.........			(WHO)

Total /40:
(SA)

Appendix 17: Syntax Scoring Guidelines

Picture	Examples	Score
Preposition: on	Dzulu dzulu ya kikombe/mukopo (on top of the cup/mug) Dzulu ya kikombe/mukopo (on the cup/mug) Raikwa kikombeni dzulu dzulu (it is kept on the cup, on top)	2
	Ho dzulu dzulu (on top) Ho dzulu (on)	1
Preposition: in	Ndani ya kikombe (in the cup) Ndani ya mukopo (in the mug) Mo ndani ya mukopo (inside the mug)	2
	Mo kikombeni (inside the cup) Mukoponi (inside the mug) Mumu ndani (inside here) Ndani (inside)	1
Preposition: under	Tsini ya kikombe/mukopo (under the cup/mug) Ho tsini ya kikombe/mukopo (under the cup/mug)	2
	Kuku tsini / Mahako ga kikombe/ Mahakoni (at the bottom of the cup/at the bottom) Ku tsini (under here)	1
Preposition: beside	Kanda kanda ya kikombe/mukopo (beside the cup/mug) Kanda ya kikombe/mukopo (beside the cup/mug)	2
	Haha hehi na kikombe/mukopo (near the cup/mug) Kuku kanda/lwavuni (beside/at the side of) Haha kanda/lwavuni (here at the side)	1
Preposition: between	Kahikahi ya vikombe (between the cups)	2
	Haha kahikahi (in the middle) Kahikahi (between) Kahikahi ya kikombe (between the cup)	1
Plurals: N-class	Nyumba mbiri (two houses)	2
	Ni mbiri (they are two)	1
Conjunction: 'and'	Mupira na kihi (a ball and a chair)	2
	Mupira, kihi (ball, chair)	1
Comparative: 'bigger'	Mubomu zaidi/sana/zhomu/kamare (very/much/more big) Mure zaidi/sana/zhomu/kamare (more/much/very tall) Ni mure/mubomu kushinda/amukira yuyu (he is tall/ bigger than/he is taller than this one)	2
	Mubomu/mure mwenye (very big/tall)	1

Plurals: Ki/Vi-class	Vikombe viri (two cups) Ni viri (there are two)	2 1
Adverbs	Porepore (slowly) Pore (slow) Anenda pore (it is slow)	2 1
Adjectives	Ni kikombe kithithe kithune (it is a small red cup) Ni kikombe kithithe (it is a small cup) Ni kikombe kithune (it is a red cup) Ni kikombe thithe thune (it is a small red cup: without noun class marker)	2 1
Plurals: M/A-class	Asichana airi (two girls) Ni airi (they are two)	2 1
Past tense	'Ma......' (they......)	2
Plurals: M/Mi-class	Mihi miri (two trees) Ni miri (they are two)	2 1
Locative	Anenda dukani (he/she is going to the shop) Anenda Mombasa (he/she is going to Mombasa)	2 1
Negative	Senzi kwenda (I don't want to go) Sindakwenda (I will not go) Senzi/tsenzi (I don't want)	2 1
WH-question: 'when'	Rini...? (when...?) Saa nyingahi...? (at what time...?)	2
Passive	Muvulana yuyu wagerwa/pewa izu (this boy was given a banana) Yuno akipewa/gerwa izu (this one was given a banana) Akigerwa/pewa naye (was also given)	2 1
Future tense	'...nda...' ('...will....')	2
WH-question: 'who'	Ni hani...? (who...?)	2

NB: Any variants not in the table are assigned a score of '0'

Appendix 18: Lexical Semantics Scoring Guidelines

NB: The scoring guidelines follow the same format as the assessment and thus show its content and layout. Some words have no adequate English translation and are therefore listed in Kigiryama.

Minor Lexemes/ Function words

Social	**Spontaneous** Hi, hello, bye, see you soon	**Response** No, yes, thanks, sorry, I beg your pardon
	Stereotype 'chondoni', 'dekeha'	**Proper Noun**
	Other	
Relational	**Pronominal** 1. I, we, us, mine, ours, me 2. you (sing), you (pl), your, your's 3. he, she, his, her's, him, her, them, they, their's	
	Demonstratives Variants for noun classes: N class; Ki/Vi class; M/A class; M/Mi class; Ji/Ma class, U class, Ku class, Place (defined, not defined, inside). See table below for details.	
	Articles Variants for noun classes: N class; Ki/Vi class; M/A class; M/Mi class; Ji/Ma class, U class, Ku class, Place (defined, not defined, inside). See table below for details.	
	Prepositional Loc -ni [any prepositions] Temp until Other here ya/ wa/ cha/ ra/ wa (for-singular) za/ a/ zha/ ga/ ya/ za (for-prural) (see table below for details)	
	Verbal is	
	Interrogative who when what how many who where	**Tags**
	Connective And, because, then, so	
	Empty	**Other**
Avoidance		

DEMONSTRATIVES

Noun Class		This/these	That/those (near)	That/those (far)
N	*singular*	ii	iyo	iryahu
	plural	zizi	zizo	ziryahu
M/WA	*singular*	yuyu	iye	yuyahu
	plural	aa	ao	aryahu
KI/VI	*singular*	kiki	kicho	kiryahu
	plural	vivi	vizho	viryahu
JI/MA	*singular*	riri	riro	riryahu
	plural	gaga	gago	garyahu
M/MI	*singular*	uu	uo	uryahu
	plural	ii	iyo	iryahu
U	*singular*	uu	uo	uryahu
	plural	zizi	zizo	ziryahu
KU		kuku	kuko	kuryahu
Place	*defined*	haha	haho	haryahu
	not defined	kuku	kuko	kuryahu
	inside	mumu	mumo	muryahu

ARTICLES

Noun Class	Singular	Plural
N	yo	zo
M/WA	ye	o
KI/VI	cho	zho
JI/MA	ro	go
M/MI	wo	yo
U	wo	
KU	ko	
Place	ho/ ko	

PREPOSITIONAL 'OF'

Noun Class	Singular	Plural
N	ya	za
M/WA	wa	a
KI/VI	cha	zha
JI/MA	ra	ga
M/MI	wa	ya
U	wa	za
KU	kwa	
Place	ha/ kwa	

Major Lexemes/ Content words

Domain	Category	Words
Man	**Family**	Father, mother, grandmother, aunt, sibling, Maternal uncle, paternal uncle (young brother to my father), elder sister to mother, step mother/ wife to paternal uncle (young brother to my father), young sister to mum, wife to maternal uncle, grandfather, 'mwenehu', namesake, two men who are married to sisters, brother/sister in law, mother/father/son in law
	Type	Female, male, child, baby, girl, boy, youth, bachelor, 'gungu', elderly/aged
	Jobs	Farmer, plumber, carpenter, house/ 'shamba' man, maid/babysitter, cook
	General	Person, human being
	Group	Locality, clan, 'lukolo', group, a portion of a whole number of people, 'kifudza', troop.
	Contacts	Friend, neighbour, visitor, enemy
	Location	Chinese, Kenyan
	Other	
	Character +	Faithful, clever, happy
	Character –	Stupid, lazy, afraid, dull, liar, enemy, evil-minded, tricky, obstinate, cruel
	Neutral	
Body	**Main parts**	Head , neck, shoulder, back, chest, waist, abdomen, chest, buttocks
	Limbs	Hand, leg, elbow, knee, arm, finger, heel, foot, wrist
	Face	Nose, teeth, chin, ear, eye, face, jaws, gums, eye lashes, forehead, cheeks
	Outside	Hair, moustache, beard, nails, eyebrows, eyelashes
	Health	Health
	Inside	Skull, bone, blood, intestines, placenta, ribs, spleen, liver, pancreas, tongue, veins.
	Character +	Beautiful, cute, strong, thin
	Character -	Untidy, ugly, fat, huge, sliming, wearing out, weak/sick-looking, clear/straightforward
	Neutral	Hot, cold
	Other	Razor blade, shave, give birth, pass urine, comb
Health	**Disease**	Cold, cough, mumps, transmission, polio, ache, dumb, deaf
	Protection	Medicine, tablets, ward, medicine, hospital, operation, practice, chemist/pharmacy
	People	medicine man, nurse, patient, doctor.
	Implements	Toothbrush, needle, splint, bandage, plaster.
	Other	

Clothing	**General**	Clothes, uniform, fashion, change, keep, measure, baby-shawl, taking off, wearing.
	Material	Cotton, nylon, silk, wool
	Outer	Headscarf, cap, jacket, gloves, coat.
	Footwear	Shoes, slippers, boots, socks, sandals
	Man	Shirt, costume, shorts, trousers, kikoi
	Woman	Skirt, blouse, petticoat, pants, kanga
	Neutral	Sweater
	Child	Waterproof pants, nappies
	Parts	Sleeve, button, hem, zip, collar, pocket.
	Other	
	Caring	Wash, iron, needle, thread, sew, tailor, shoe maker, patching
Food (Grown)	**Fruit**	Mango, orange, lime, lemon, paw-paw, groundnuts, coconut, cashewnuts, fruit, 'tamutsungu'
	Part	Peel, stalk, stone, 'kilembo', shell, husks, seed.
	Location	Forest, tree, garden, bush, 'kihundu'
	Vegetables	Pigweed, cassava leaves, 'mutsunga', cow pea leaves, potatoes, tomatoes, onions, 'vongonya', sweet potato leaves, 'muzungwi', 'katsungutsungu', 'tsalakushe', pumpkin leaves, nightshade
	Grain	Maize, rice, 'fwifwi', beans, cow peas, green peas, pigeon peas
	Part	Leaf, stem, roots, husks, peels, maize combs, 'kisi'
	Character	Sweet, watery, ripe, raw, rotten, sour, bitter
	Other	
(Processed)	**Type**	Corn cake, biscuits, flour, bread, 'kinolo', 'poridge', 'dindia', 'kimanga'
	Dairy	Eggs, milk, cholesterol
	Seafood	Fish (salt water), fish (fresh water) 'ukejo', 'kumbu', prawns, shark, octopus, 'simu', 'mborode', 'mutonzi'
	Drinks	Tea, coffee, soda, milk
	Flavouring	Salt, sugar, pepper, 'mbirimbi'
Food (Grown and Processed)	**Action**	Cook, eat, roast, boil, fry, bite, swallow, suck, heat, mix, drink, sip
	Location	Kitchen, cooking stone, 'chango', 'kijaja', shop, tea kiosk, kiosk, 'kibanda'
	Meals	Breakfast, lunch, supper
	Utensils	Tray (for winnowing grain), cooking pan, plate, mug, bowel, knife, glass, 'tuguu', 'kipawa', 'lufudzo', 'kaha', 'bunguu', cooking stick, 'mwiko', 'muvure'
	People	cook, butcher, baker.
	Other	

Moving	**Come/Go** Come, go, come in, move, reach, come/go back, follow, go around, visible	**Static** To sit, stand, rest, wait, stay, lean
	Sleep Doze, snore, dream, wake up, sleep	**Animate** Run away, get out, walk around, jump
	Things Push, drag, bring, catch, fetch, touch, throw, send, put, open, shoot	**Other** Hide, lose, fall
Making/ Doing	**General** Try, start, finish, help, use, able, do, repair	**Specific** Build, close, arrange, repair, join, break, tie, sweep
	Type Work/job, easy, casual job, boring, difficult, quick, well, quickly	**Other** Pound, slaughter, fight, winnow
Happening	Happen, start, finish, remain, lucky, situation, disturb, accident, act, reason, outcome, end, continue, stand/stop	**Other**
Living	Leave, grow, breath, say goodbye, continue, alive, life, stay	**Other** Funeral, bury, grave
Having	**Process +** Get, keep, take, pile, investigate, accept, pray, owner, give	**Process -** Lose, need, miss, loss, theft, stealing
Thinking	**Process** Know, try, accept, remember, decide, understand, forget, think, trust, choose	**General**
	Type Clever, carefully, stupid, silly, sure	**Other**
Feelings	**+** Happy, hope, love, peace, like, laugh, smile	**-** Afraid, angry, bored, hate, sad, annoy, worried, cry, jealousy
	Neutral Boast	**Other**

Sound	**General** Noise, voice, quiet, hear, listening	**Quality** Staying	
	Specific Laugh, cry, mourn	**Implements**	**Other**
Sight	**Act** See, look, snoop, realise	**Implements** Spectacles	**Other**
Smell	**Act** Smell, breath.	**Character** Perfume, smell.	**Other**
Taste	**Act** Taste	**Character** Salt, sweet, sour, bitter	**Other**
Touch	**Act** Listen, catch, beat, rub, brush, squeeze, scratch	**Character** Soft, wind, cold	**Other**
Language	**Speak/Listen** Talk, shout, say, voice.	**Read/Write** Read, write, send, spelling, stamp, letter	
	Act Argue, explain, tell, promise, instruct, welcome, blame, sermon, discussion, joke, pray	**Product** Book, poem, mark, magazine, card	
	People 'mwandishi', 'mutu wa posita', 'muchapishaji'	**Character**	
	Implements Pen, paper, telephone, typing machine, postal box	**Part** Name, page, picture, word	**Other**
Imagination	**Type** Story, pretend.	**People** Witchcraft, 'jini', 'zimu', huge person.	**Other**

Recreation	**Action** Swim, hide, kick, jump, catch, play	**Location** Beach, field
	Games Cards, ball, 'lenga lenga', 'kigogo', 'bablikani'	**Sports** Run
	People Player, goal keeper, team, referee	**Equipment** Ball, goal
	Things Marble, swing, goal, shells, 'makumbi', 'makarara', 'makanza'	**Other**
Occasions	**General** Gift, wedding, Easter, party	
Music	**Instruments** Flute, guitar, trumpet, 'kipopoi', shaker, drum, 'kayamba', 'marimba'	**Type** Song, 'mwanzele', 'gonda', 'chechemeko', 'ndimba', 'namba', 'kifudu'
	Action Play, sing, listen, watch	**People** 'mwimaji', 'mupizi', player
	Parts	**Other**
Road	**Vehicle** Bicycle, Vespa, motor bike, car, tractor	**Parts** Tyre, pedal, steering, spokes, chain
	Action Ride/drive, drag/haul	**Location** Way, road, footpath, junction, mountain
	People Driver, loader, 'manamba', conductor, passengers	**Other**
Water	**Vehicle** Boat, ship	**Action** Sink, float

Animals	**General** Animal	**Pet** Cat, dog	
	Farm Donkey, cow, goat, sheep, guinea pig, pig	**Wild (Small)** Squirrel, rabbit, rat, mouse, bat	
	Water Hippo, octopus, frog	**Wild (Large)** Elephant, baboon, monkey, buffalo, lion	
	Reptile Snake, lizard, monitor lizard, crocodile	**Extinct/Imaginary**	
	Noise Crying	**Location** 'Chaga'	
	Action (Us→Them) Hunt, send, graze	**(Them→Us)** Graze, bite	
	Type Harsh	**Parts** Ribs, head, legs, horns, fur, tail	**Other**
Birds	**Type** Small animal, bird, hawk, 'luhanga', pigeon, guinea fowl	**Parts** Tail, wing, feathers	
	Water Duck	**Farm** Hen, duck	
	Action Fly, shift, roost, lay	**Noise** Cry	
Fish	**Type** Fish, shark, octopus, 'kumbu', 'kumba'	**Parts** Tail, 'kitsidhe', 'miya', scales	
	Action Swim, fish	**Control** Hook, fishing net, fishing line	**Other**
Insects	**Type** Fly, wasp, bees, butterfly, grasshopper, spider, 'mwangalota', cockroach, 'tsungu', safari ant	**Parts** Wings, legs	
	Action Bite, fly, crawl, sting	**Location** Sleep, bee hive	**Other**

Flowers (etc.)	**Type** Flower, grass, bush	**Parts** Seed, thorn, root.	
	Action Pluck, germinate, cut, plant, sword	**Other** Soil	
Trees	**Type** Mango tree, orange tree, paw-paw tree, tree, cashewnut tree	**Parts** Leaves, root, branch, stem	
	Action Cut, climb, drop, 'tsanga'	**Other**	
Light	**Type** Darkness, light, shade, dawn, shiny	**Control** Lamp, candle	**Other**
Colour	**Type** Red, black, white, green	**General**	
	Action Paint	**Implement** Brush	**Other**
Fire	**Type** Fire, smoke, ash, light, sparks	**Fuel** 'kuni', 'makala', 'mafuha'	
	Control Match box	**Other**	
Water	**Type** Water	**Action** Boil, pour	
	Control	**Other**	

Building	**Type** House, tent, home	**Parts** Roof, window, wall, door, room
	Outside Veranda, gate	**Materials** Poles, cement, soil, iron sheets, thatches
	Action Rub, wash, sweep, build, renovate	**People** Builder, mason
	Rooms Kitchen, bedroom	**Other**
Furniture	**General** Chair, table, mirror, cupboard	**Bathroom** Bathroom, toilet, tap
	Bedroom Bed, mattress, mat, 'uriri'	**Living room**
	Kitchen/Dining Cooker, cooking stone	**Other**
Tools	**General** Candle, nail	**Farm/Garden** Hoe, 'jembe', sword, axe
	People Farmer	**Other**
Containers	**Type** Basket, bag, pocket, bottle, suitcase, box, bowl, bucket	**Parts** Top, handle.
	Action Open, cover, fill	**Other**

<table>
<tr><td rowspan="2">Quantity</td><td colspan="3">General
Many, all, alone, enough, already, something, any, other</td><td colspan="3">Specific
One, five, two, half, twins</td></tr>
<tr><td colspan="3">Act
Add, count, divide, plus, add</td><td colspan="3">Other</td></tr>
<tr><td>Size</td><td colspan="3">+
Big, long, fat, wide</td><td colspan="3">-
Thin, small, light, short, less</td></tr>
<tr><td>Shape</td><td colspan="6">‘Kombo’, ‘muviringo’, ‘tsumbi’, ‘musithari’</td></tr>
<tr><td rowspan="3">Time</td><td colspan="3">Day
Day, night, morning, afternoon, shining, evening, midnight</td><td colspan="3">Period
Age, time, there and then, teenage, childish, old age, already</td></tr>
<tr><td colspan="2">Past
Yesterday, soon, before, was, past</td><td colspan="2">Present
Now, today.</td><td colspan="2">Future
Tomorrow, other</td></tr>
<tr><td colspan="3">Frequency
Again, once, normal, completely, always, daily, sometimes</td><td colspan="3">Other</td></tr>
<tr><td rowspan="2">Location</td><td colspan="3">General
Somewhere, far, here, everywhere</td><td colspan="3">Specific
Long rains, short rains, right, left, upstairs, ahead, in, out, address</td></tr>
<tr><td colspan="3">Part</td><td colspan="3">Other</td></tr>
<tr><td rowspan="3">State</td><td colspan="3">Quality
Good, bad</td><td colspan="3">Intensity
Much, completely, for sure, completely</td></tr>
<tr><td colspan="3">Like +
Resemble, same, similar, also, group, comparing, finishing</td><td colspan="3">Like –
Different, opposite, other, comparing</td></tr>
<tr><td colspan="6">Other</td></tr>
</table>

Education	**Type,** School, university, college, nursery	**Part** Class, field, desk, black board	
	Action Learning, teaching	**People** Teacher, student, headmaster, secretary	
	Topic History, English, Maths	**Other**	
Religion	**General** Church, temple, mosque		
Manufacture	**Location** Factory, 'posho', mill, laboratory, processing place	**Equipment** Sawing machine	
	Action Make, start, sell	**People** Worker, supervisor, mechanic	**Other**
Space	**Entities/Events** Sun, moon, eclipse		
World	**Land** Upcountry, mountain, valley, forest, beach, seaside	**Water** Sea, lake, river.	
	Surface Ice, earth, mud, soil	**Depth** Cave, well, trench	
	Location Map	**Climate** Hot, clouds, rain, mist, sunlight, thunder	**Other** Home.
Weapons	**Type** Gun, bow, stone, bomb	**People** Hunter, trapper, army, neighbour	**Other**
Money	**Units** Cent, Shilling, cheque	**Location** Bank, purse	
	Action Have, use, buy, sell, misuse	**Type** Salary, rent, price, cheap, expensive, savings	**Other**
Other			

Appendix 19: Higher Level Language Assessment

Name of child: [ ] [ ] [ ]

Study number: [ ] [ ] [ ] [ ] [ ]

Date of assessment: [ ][ ]/ [ ][ ]/ [ ][ ][ ][ ]

Assessor: [ ] [ ]

1. **Categorisation task**

(a). Tell me as many different things as you can that you can eat. You have one minute to tell me as many as you can.

(CT1) [ ]

(b). Tell me as many different animals as you can. You have one minute to tell me as many as you can.

(CT2) [ ]

(c). Tell me many different girls' names as you can. You have one minute to tell me as many as you can.

(CT3) [ ]

---

2. **Definitions of words**

(a). 'A cup' is something to take a drink like water or tea from.
Can you tell me what **'a chair'** is?

(b). 'Drinking' is swallowing something like water or tea.
Can you tell me what **'eating'** is?

(c). 'Prettiness' is to look good or have beauty.
Can you tell me what **'cleanliness'** is?

(d). 'Theft' is secretly taking something that is not yours.
Can you tell me what '**witchcraft**' is?

(DW)
/8

---

3. **Homonyms**
   There are words that have more than one meaning.

- For example, the word '**kaha**' means a scoop used for fetching water and also means a round pad for carrying a load on your head.
- For example, the word '**kufula**' means to wash clothes and also means to husk a coconut.

(a). Can you tell me what an '**mbuzi**' is? (a goat/an instrument for grating coconut)

Another meaning?

(b). Can you tell me what '**kuhala**' means? (to take/to marry)

Another meaning?

(c). Can you tell me what '**kuloha**' means? (to point/to dream)

Another meaning?

(d). Can you tell me what '**choyo**' is? (selfishness/facial tics)

Another meaning?

(HOM)
/8

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4. **Similarities and differences**
   I will show you one picture and I will tell you something that is similar and something that is different about the two things in that picture.

- For example, one difference between a '**hen**' and a '**duck**' is that a hen cannot swim while a duck can. Similarities between a hen and a duck are that they both have two legs and they lay eggs.

- For example a difference between a '**hammer**' and a '**panga**' is that a hammer is for knocking while a panga is for cutting. A similarity is that both are made of iron.

(a). Can you tell me a difference between '**a car**' and '**a motorbike**'?

A similarity?

(b). Can you tell me a difference between **'a cow'** and **'a dog'**?

A similarity?

(c). Can you tell me a difference between '**a chair**' and '**a table**'?

A similarity?

(d). Can you tell me a difference between '**an axe**' and '**a hoe**'?

A similarity?

(SD)
/8

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5. **Sentence formulation**
I want you to make some sentences using words I will give you.

- For example the word '**cat**'
I will make a sentence with this word: 'the cat is playing with a ball'
- For example the word '**crying**'
I will make a sentence with this word: 'this child is crying for his mother'

(a). Make a sentence with the word '**duck**'

(b). Make a sentence with the word '**laughing**'

(c). Make a sentence with the word **'red'**

(d). Make a sentence with the word **'because'**

(e). Make a sentence with the word **'when'**

(SF)
/15

Total /39:
(HLL)

Appendix 20: Higher Level Language Assessment Scoring Guidelines

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1. Categorisation task

Once the category has been presented and you are timing the child, do not prompt except by saying 'tell me more'.

Each category is scored separately by counting the number of words appropriate to the subject of the category. Do not count repetitions: the first mention of a response earns a score of '1' but all repetitions earn scores of '0'. Indefinite references, even if related to the category (eg. 'food' in the 'things to eat' section), are scored as '0'. The raw score is scaled as follows:

Raw Score	Scaled Score
0	0
1 - 4	1
5 - 8	2
9 - 12	3
13 - 16	4
17 - 20	5

2. Definitions of words

One prompt only is allowed.

Scoring:

0= Repetition of the target word or example only (eg. 'I have a chair at home')

1= Some information on word meaning given but not a full definition (eg. 'A chair is furniture')

2= Correct definition including the use, purpose or action of the target word (eg. 'A chair is something you sit on')

3. Homonyms

One prompt only, for example 'what do you mean?' or 'can you tell me more about that?'

Scoring:

One point for every response indicating knowledge of the target meaning (as in the definition of words task). Each aspect of the homonym is scored separately, thus it is possible for a child to attain a score even if only one of the homonym's definitions is given.

4. Similarities and differences

Use the stimulus pictures if the child requests help or appears to be struggling with the task. Refer back to examples, if necessary, to help the child understand the concept. One prompt only for each question.

Scoring:

0= The response given is in the wrong category (gives a similarity instead of a difference or vice versa) or the response is not a genuine point of comparison between the two items (eg. 'I own a dog but not a cow').

1= The child gives a plausible similarity or difference about any aspect of the objects (eg. use, appearance)

5. Sentence formulation

One prompt only for each question. The stimulus word must be used in the response to receive credit and must be used as presented (without alterations in tense and plurality).

Scoring :

0= Repetition of single word only.

Changed stimulus word, for example, 'tall' to 'taller'

1= Use of the stimulus word but incomplete sentence (reducing the meaning of the sentence)

2= Use of the stimulus word but minor syntactical errors or correct syntax but semantic errors or semantically meaningless

3= Syntactically and semantically sentence containing the stimulus word

Appendix 21: Pragmatics Questionnaire

Name of child: [ ] [ ] [ ]
Study number: [ ] [ ] [ ] [ ] [ ]
Date of assessment: [ ][ ]/ [ ][ ]/ [ ][ ][ ][ ]
Assessor: [ ] [ ]
Respondent: **M**other/**F**ather/**O**ther [ ]

A: COMMUNICATIVE FUNCTIONS

Introduction

The first section concerns how x gains your attention.

1. Attention Directing

a) To self

If you are busy doing something, what does x (name of child) normaly do so that you look at him/her?

Examples: Makes eye contact Taps you Uses signs or brings you something Calls you by name

b) To events, objects, other people

If x (name) wants to show something to you, how does he do it?

Examples: Turns and looks at it, then turns and looks at you Taps you Points Says, '' look at that'' and starts talking about it Shouts

2. Requesting

a) Request for assistance

If x (name) wants assistance in something he/she is doing, how does he/she normally tell you?

Examples: Seeks assistance and explains what is required Points Pulls you towards what he/she wants

b) Request for information

If x (name) has seen or heard something that he/she doesn't know, how does he/she ask about it?

Examples: Looks at you, surprised Asks "what's that?" Keeps pointing and shouting Asks many questions about the thing Doesn't ask

3. Giving Information

When x (name) is telling you something that has happened that day, how does he/she tell you?

Examples: Shows you something, for example a school book or bruise Explains things well. Gives enough explanation to make you understand Keeps explaining the same thing for a long time

4. Giving instructions.

If x (name) is trying to tell you how to play a game or how to do something, how does he/she tell you?

Examples: Explains things well Demonstrates Explains in a disorganised manner

5. Humour

If x (child) makes jokes, what type of jokes does he/she make?

Examples: Does something funny, for example hiding him/herself and coming out suddenly Keeps repeating the same joke Sophisticated jokes

6. Expression of emotion

a) Pleasure

If x (name) is very happy about something, how does he/she show it?

Examples: Claps Shouts and jumps up and down Smiles or laughs Says what he/she feels

a) Upset
If x (name) is upset about something, how does he inform you?

Examples: Cries Explains what he/she feels and why Looks sad until you ask what has happened to him/her Beats others

B: RESPONSE TO COMMUNICATION

Introduction

This second section concerns what you do to gain x (name)'s attention.

7. Gaining Attention.
If you want to get x (name)'s attention, what do you do?

Examples: Tap him/her Mention his/her name Shout

8. Sarcasm.
What does x (name) do when a person makes a sarcastic remark?

Examples: Looks confused Replies with a literal interpretation Understands the real meaning

9. Metalinguistic Awareness

Does x (name) talk about how others speak or use certain words or sayings? What things does x (name) comment on?

Examples: Someone speaking another language Pronunciation Words that are not clear Why something is called what it is

10. Responding with amusement

What makes x (name) laugh?

Examples: Silly plays and childish songs Rude words Laughs aimlessly

11. Negotiation

If another child doesn't do as x (name) wants, how does he/she react?

Examples: Hits him/her Argues for a long time Asks an adult to intervene Agrees

12. Request for clarification

If you told x (name) to do something and he/she did not understand, what would he/she do?

Examples: Tries to do it then gives up Tries to get assistance from another child. Asks for another explanation then tries again

C: INTERACTION AND CONVERSATION.

Introduction

The final section is about what it is like conversing with x (name).

13. Interest in interaction

How does x (name) converse with others when they are together?

Examples: Talks with one other child Joins a group immediately and talks to many children Tends to be left on the sidelines

14. Maintaining an interaction or conversation

When you are conversing with x (name), how does the conversation go?

Examples: Says little Converses well Dominates the conversation Changes from topic to topic

15. Presupposition and Shared Knowledge
When x (name) talks about something or someone you don't know, how does he/she express him/herself so that you understand?

Examples: Gives enough explanation to help you understand Tells you more than what you need to know Explains adequately

16. Conversational Repair
If you and x (name) are discussing something and there is something that you don't understand, what does x (name) normally do?

Examples: Tries to show you in another way, for example using signs or gestures Explains satisfactorily Looks bored and ends the conversation Blames you

17. Terminating a Conversation
How does a conversation with x (name) generally end?

Examples: The child loses interest and walks off Terminates abruptly Ends normally Seems not to know how to end a conversation

Appendix 22: Pragmatics Profile Scoring Guidelines

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1. <u>Attention Directing</u>

a) To self

How does x (child's name) usually get your attention?

Examples	Scores
Cries	0
Deliberately does something wrong eg. hits someone	1
Gesturing	4
Calls name	5
Touch / taps you	5

b) To events, objects, other people

If -----(child's name) wants to point something out to you, how does s/he do it?

Examples	Scores
Cries	0
Shouts	1
Points	2
Turns and looks towards the object then turns back to you	3
Pulls at you and vocalises	4
Pulls you to the object	4
Says 'look at that' and starts to talk about it	5

2. <u>Requesting</u>

a) Request for assistance

If ----(child's name) needs help with something s/he is doing, how does s/he usually let you know?

Examples	Scores
Cries	0
Requests for help but does not explain the problem	1
Waves or points to what is required	2
Requests for help and explains the problem	5

b) Request for information

If ----(child's name) sees or hears something strange, how does s/he ask about it?

Examples	Scores
Doesn't ask	0
Points at it	1
Looks at you with a puzzled expression	2
Insistently points and vocalises	3
Says, "what's that?"	4
Asks a lot of questions about it	5

3. Giving Information

If ----(child's name) tells you something about what he has done during the day, how does s/he go about it?

Examples	Scores
Doesn't give enough information for you to be able to understand	1
Goes on and on about it for a long time	2
Answers direct questions with very short replies	3
Shows you something, eg. a school book, a cut or bruise	4
Gives a clear account	5

4. Giving instructions.

If ----(child's name) is trying to tell you how to play a game or how to make something, how does s/he usually do it?

Examples	Scores
Explains in a very disorganised manner	1
By demonstrating	4
Gives clear instructions	5

5. Humour.

If ----(child's name) ever makes jokes, what kind of jokes are they?

Examples	Scores
Never makes jokes	0
Same joke repeatedly	2
Does funny things like hiding and suddenly appearing	3
Practical jokes.	4
Sophisticated jokes	5

6. **Expression of emotion**

a) **Pleasure**

If ---(child's name) is really pleased about something, how does s/he let people know?

Examples	Scores
Keeps it to him/ herself	0
Becomes over-excited	1
Smiles or laughs	5
Claps and hugs	5
Says how s/he feels	5

b). **Upset**

If ---(child's name) is hurt or upset about something, how does s/he let you know?

Examples	Scores
Hits out	1
Stays alone	2
Cries and appears moody or sulky so you have to ask what is wrong	4
Explains how s/he feels and why	5

7. **Gaining Attention**.
If you want ------(child's name)'s attention how do you do it?

Examples	Scores
No response to attempt to gain attention	0
Have to do something extreme	1
Walk in front of the child so s/he can see you and raise your voice	2
Gestures	3
Touch/ tap him	4
Say his/ her name.	5

8. **Sarcasm.**

How does -----(child's name) react if someone is being sarcastic?

Examples	Scores
Seems confused	0
Ignores it	1
Takes it literally/ contradicts them	2
Understands the intended meaning	5

9. **Metalinguistic Awareness.**

Does -----(child's name) ever comment on the way people talk or why they use particular words or expressions? What kinds of things does s/he comment on?

Examples	Scores
Never comments	0
Someone speaking a different language	2
Accent	3
Unknown words	4
Why something is called what it is	5

10. **Responding with amusement**

What kinds of things make ----(child's name) laugh?

Examples	Scores
Never laughs	0
Laughs for no apparent reason	1
Tickling	2
Running and chasing one another	3
Slapstick and visual jokes. eg. making faces	4
Funny games and singing	5
Rude words	5

11. **Negotiation**

If another child is not going along with what ----(child's name) wants him/ her to do, how does (child's name) react?

Example	Scores
Mainly non-verbally: pushing and hitting	0
Gives up	1
Gets involved in lengthy argument	2
Asks an adult to sort out	4
Negotiates a compromise	5

12. Request for clarification

If you have asked ----(child's name) to carry out an activity and s/he hasn't understood exactly what is wanted, what is s/he likely to do?

Examples	Scores
Makes no attempt to do it	0
Tries to do the task but soon give up	1
Tries to get help from another child	4
Asks for clarification and has another try	5

13. Interest in interaction

How does----(child's name) interact with other children in a group?

Example	Scores
Takes no notice of the other children	0
Tends to be left on the sidelines	1
Talks to one other child	4
Listens and responds to several children	5

14. Maintaining an interaction or conversation.

When you are chatting with ----(child name), how does the conversation flow?

Examples	Scores
Child doesn't talk at all	0
Plays a minimal part	1
Jumps from topic to topic	2
Child monopolises	3
Conversations are short-lived	4
Talks/ takes an equal share	5

15. Presupposition and shared knowledge.

When ----(child's name) is talking about something you don't know about, how clearly does s/he put you in the picture?

Examples	Scores
Doesn't say anything	0
Doesn't give enough information to help you understand	1
Assumes that you know more than you do, eg. mentions people out of blue	2
Fills in details you know already	3
Tells you more than you need to know	4
Explains everything clearly	5

16. Conversational Repair.

If you and ------ (child's name) are talking together and you can't understand something s/he says, how does (child's name) usually react?

Examples	Scores
Seems upset and gives up	0
Makes out that it is your fault	1
Keeps repeating it	2
Tries to show you in a different way eg. gestures or demonstration	4
Clarifies adequately	5

17. Terminating a Conversation

How does a conversation with ----- (child's name) generally end?

Examples	Scores
Doesn't seem to know how to end it	0
Gets distracted and loses interest	1
It stops abruptly	3
It draws to a close naturally	5

Appendix 23: Phonological Assessment

Name of Child: [ ] [ ] [ ]
Study number: [ ] [ ] [ ] [ ] [ ]
Date of assessment: [ ][ ]/ [ ][ ]/ [ ][ ][ ][ ]
Assessor: [ ] [ ]

Target	Transcription	Errors
Kuku (Chicken)		
Nyumba (House)		
Maembe (Mangoes)		
Mbuzi (Goat)		
Mutu (Person)		
Samaki (Fish)		
Magulu (Legs)		
Muryango (Door)		
Dirisha (Window)		
Maizu (Bananas)		
Ng'ombe (Cow)		
Paka (Cat)		
Kalamu (Pencil)		
Saa (Watch)		
Gari (Car)		
Mukono (Hand)		
Muhi (Tree)		
Kithabu (Book)		
Jembe (Hoe)		
Muswaki (Toothbrush)		
Chala (Finger)		
Kikombe (Cup)		
Meza (Table)		
Makuti (Thatching)		
Virahu (Shoes)		
Kijiko (Spoon)		

Nanasi (Pineapple)		
Thupa (Bottle)		
Kitanda (Bed)		
Basikili (Bicycle)		
Nyoka (Snake)		
Shati (Shirt)		
Kihi (Chair)		
Kikahana (Basket)		
Mupira (Ball)		
Rinda (Dress)		
Lushero (Broom)		
Taa (Lamp)		
Mufereji (Tap)		
Kipawa (Wooden spoon)		

Phonological Assessment Scoresheet

Initial Phoneme	Words	✓/✗	1/0
p	**p**aka (cat)		
b	**b**asikili (bicycle)		
t	**t**aa (lamp)		
d	**d**irisha (window)		
k	**k**uku (chicken)		
	kalamu (pencil)		
	kithabu (book)		
	kikombe (cup)		
	kijiko (spoon)		
	kitanda (bed)		
	kihi (chair)		
	kikahana (basket)		
	kipawa (wooden spoon)		
g	**g**ari (car)		
m	**m**aembe (mangoes)		
	mutu (person)		
	magulu (legs)		
	muryango (door)		
	maizu (bananas)		
	muhi (tree)		
	muswaki (toothbrush)		
	meza (table)		
	makuti (thatching)		
	mupira (ball)		
	mufereji (tap)		
n	**n**anasi (pineapple)		
ɲ	**ny**umba (house)		
	nyoka (snake)		

η	**ng'**ombe (cow)		
v	**v**irahu (shoes)		
θ	**th**upa (bottle)		
s	**s**amaki (fish)		
	saa (watch)		
ʃ	**sh**ati (shirt)		
r	**r**inda (dress)		
l	**l**ushero (broom)		
tʃ	**ch**ala (finger)		
dʒ	**j**embe (hoe)		

Medial Phoneme	Word		1/0
p	mu**p**ira (ball)		
	ki**p**awa (wooden spoon)		
b	nyum**b**a (house)		
	maem**b**e (mangoes)		
	ng'om**b**e (cow)		
	kitha**b**u (book)		
	jem**b**e (hoe)		
	kikom**b**e (cup)		
t	mu**t**u (person)		
	maku**t**i (thatching)		
	ki**t**anda (bed)		

	shati (shirt)		
d	kitanda (bed)		
	rinda (dress)		
k	kuku (chicken)		
	samaki (fish)		
	paka (cat)		
	muswaki (toothbrush)		
	kikombe (cup)		
	makuti (thatching)		
	kijiko (spoon)		
	nyoka (snake)		
	kikahana (basket)		
	basikili (bicycle)		
g	magulu (legs)		
	muryango (door)		
m	ng'ombe (cow)		
	nyumba (house)		
	maembe (mangoes)		
	jembe (hoe)		
	samaki (fish)		
	kalamu (pencil)		
	kikombe (cup)		
n	muryango (door)		
	mkono (hand)		
	nanasi (pineapple)		
	kitanda (bed)		
	rinda (dress)		
f	mufereji (tap)		
θ	kithabu (book)		
s	nanasi (pineapple)		
	basikili (bicycle)		

z	mbu**z**i (goat)		
	diri**sh**a (window)		
	lu**sh**ero (broom)		
h	mu**h**i (tree)		
	vira**h**u (shoes)		
	kika**h**ana (basket)		
w	kipa**w**a (wooden spoon)		
r	di**r**isha (window)		
	ga**r**i (car)		
	mupi**r**a (ball)		
	lushe**r**o (broom)		
	mufe**r**eji (tap)		
l	magu**l**u (legs)		
	ka**l**amu (pencil)		
	cha**l**a (finger)		
	basiki**l**i (bicycle)		
ʤ	mufere**j**i (tap)		
TOTAL (PHO)			

NB: mbuzi and mkono have not been included under initial /m/ as they are syllabic phonemes or for medial /b/ and /k/ respectively as they are not true medial phonemes

Appendix 24: Word Finding Assessment

Name of child: [ ] [ ] [ ]
Study number: [ ] [ ] [ ] [ ] [ ]
Date of assessment: [ ][ ]/ [ ][ ]/ [ ][ ][ ][ ]
Assessor: [ ] [ ]

Target	1/0	Subject Response	Est time response	
		1st response	< 4 sec	> 4 sec
Example				
Tsoka (Axe)				
Kitswa (Head)				
Practice				
Shindano (Needle)				
Mukira (Tail)				
Kuku (Chicken)				
Nyumba (House)				
Maembe (Mangoes)				
Mbuzi (Goat)				
Mutu (Person)				
Samaki (Fish)				
Magulu (Legs)				
Muryango (Door)				
Dirisha (Window)				
Maizu (Bananas)				
Ng'ombe (Cow)				
Paka (Cat)				
Kalamu (Pencil)				
Saa (Watch)				
Gari (Car)				
Mukono (Hand)				
Muhi (Tree)				
Kithabu (Book)				
Jembe (Hoe)				
Muswaki (Toothbrush)				
Chala (Finger)				
Kikombe (Cup)				
Meza (Table)				
Makuti (Thatching)				
Virahu (Shoes)				
Kijiko (Spoon)				
Nanasi (Pineapple)				
Thupa (Bottle)				
Kitanda (Bed)				
Basikili (Bicycle)				
Nyoka (Snake)				

Shati (Shirt)				
Kihi (Chair)				
Kikahana (Basket)				
Mupira (Ball)				
Rinda (Dress)				
Lushero (Broom)				
Taa (Lamp)				
Mufereji (Tap)				
Kipawa (Wooden spoon)				

Accuracy score /40 (WFA) ☐

Delayed items /40 (WFD) ☐

Appendix 25: Neurological Examination Data

The table below presents a detailed description of the findings of the neurological examination.

ID	Grp	Abnormalities	Category
021	CM	Decreased plantar reflexes Abnormal heel/toe test	Ataxia
023	CM	Increased left and right knee reflexes (Refused gait and co-ordination tasks)	Spasticity
034	CM	Ataxia	Ataxia
036	CM	Increased arm tone Right and left arm rigidity Abnormal power in arm Increased left and right biceps/knee reflexes Abnormal finger-nose test Abnormal gait Abnormal Fogg test Abnormal heel-toe test	Spasticity
053	CM	Decreased knee/ankle/plantar reflexes (left and right) Abnormal finger-nose test Abnormal heel-knee-shin test Abnormal heel-toe test (Refused imitating gestures)	Ataxia
138	CM	Increased leg tone Spasticity (left and right lower limbs) Decreased right and left biceps/knee/ankle/plantar reflexes	Spasticity
145	CM	Left eye squint Increased left and right biceps/knee reflexes Decreased ankle reflexes Abnormal piano-playing test Abnormal heel-toe test	Ataxia
151	CM	Increased knee/ankle reflexes Hyperreflexia, particularly in left lower limb	Spasticity
173	CM	Leg wasting Increased left and right biceps/knee/ankle reflexes (Refused plantar reflexes)	Spasticity
184	CM	Left arm spasticity Left leg spasticity Increased left biceps/left and right knee/left and right ankle reflexes Decreased left and right plantar reflexes (Unable to complete gait or co-ordination tests)	Spasticity
314	CM	Abnormal piano playing test Cannot imitate gestures Abnormal heel-toe test	Ataxia

408	CM	Abnormal Fogg test Abnormal heel-toe test	Ataxia
415	CM	Decreased left and right plantar reflexes Abnormal heel-knee-shin test Abnormal piano-playing Dysdiadochokinesia (DDK) Abnormal heel-toe test Cannot imitate gestures	Ataxia
451	CM	Decreased plantar reflexes - left and right Abnormal finger-nose test Abnormal heel-knee-shin test Abnormal piano-playing test Abnormal gait Abnormal Fogg test Abnormal heel-toe test	Ataxia
471	CM	Decreased left and right plantar reflexes Cannot imitate gestures	Fine motor
487	CM	Decreased right knee/ankle/ plantar, left plantar reflexes Abnormal piano-playing test Abnormal heel-toe test	Ataxia
028	M/S	Decreased left and right knee/ankle/plantar reflexes Abnormal finger-nose test Abnormal heel-knee-shin test DDK Abnormal heel-toe test	Ataxia
057	M/S	Abnormal Fogg test (Refused imitating gestures task)	Ataxia
059	M/S	Decreased left and right plantar reflexes Abnormal Fogg test	Ataxia
062	M/S	Decreased left and right knee/ankle/plantar reflexes Abnormal heel-knee-shin test Abnormal piano playing test DDK Abnormal heel-toe test	Ataxia
098	M/S	Decreased left and right knee reflexes /plantar reflexes Abnormal piano-playing test DDK Abnormal gait Abnormal Fogg test Abnormal heel-toe test	Ataxia
174	M/S	Decreased left and right biceps/plantar reflexes Increased left and right knee/ankle reflexes Abnormal piano-playing test	Spasticity
253	M/S	Abnormal Fogg test Abnormal piano-playing test Abnormal heel-toe test Abnormal finger-nose test	Fine motor
271	M/S	Decreased left and right ankle reflexes Abnormal heel-knee-shin test Abnormal heel-toe test	Ataxia

351	M/S	Abnormal heel-knee-shin test Abnormal Fogg test	Ataxia
402	M/S	Decreased left and right plantar reflexes Abnormal heel-toe test	Ataxia
421	M/S	Increased right and left biceps/knee/ankle/plantar reflexes Abnormal piano-playing test Abnormal Fogg test Abnormal heel-toe test	Spasticity
428	M/S	Right arm spasticity Increased right biceps/knee reflexes Decreased left knee, left and right ankle reflexes Abnormal finger-nose test Abnormal piano-playing test DDK Abnormal Fogg test Abnormal heel/toe test	Spasticity
446	M/S	Arm wasted and increased tone Right arm rigidity and spasticity Increased right knee/ankle reflexes Decreased right and left plantar reflexes Abnormal finger-nose test Abnormal piano-playing test DDK Abnormal gait Abnormal Fogg test Abnormal heel-toe test	Spasticity
047	Un*	Increased left and right knee/ankle reflexes Abnormal heel-knee-shin test Abnormal heel-toe test	Spasticity
050	Un	Decreased left and right ankle/plantar reflexes Abnormal heel-knee-shin test Abnormal piano-playing test Abnormal heel/toe	Ataxia
228	Un	Decreased right and left reflexes/plantar reflexes Abnormal Fogg test Abnormal heel-toe test	Ataxia
233	Un	Abnormal piano-playing test Cannot imitate gestures Abnormal Fogg test Abnormal heel-toe test	Fine motor
385	Un	Abnormal finger-nose test Abnormal piano-playing test Cannot imitate gestures Abnormal Fogg test Abnormal heel-toe test	Ataxia

Table A25. 1: Neurological abnormalities

Key: * Un= unexposed group

Appendix 26: Speech and Language Assessment Results

Raw data and detailed analyses of elements of the speech and language assessment battery (receptive grammar assessment, syntax assessment and higher level language assessment) are presented in this appendix.

A26.1 Receptive grammar assessment

An error analysis suggested no obvious patterns in the question types resulting in poorer levels of performance in the groups (figure A26.1). Assessment items were ordered by hypothesised level of difficulty (easy to difficult from the bottom to the top of the figure). Overall performance was comparatively poor on the relative clause, postmodified subject and preposition items, although poor performance was also concentrated on the comparatives question, originally hypothesised to be one of the easier items. Performance on the singular/plural noun class items was erratic. Grammatical errors were more common than lexical errors on all items with the exception of the comparative and relative clause questions, despite the high failure rate on the vocabulary check. Table A26.1 indicates that the proportion and pattern of errors was similar across the individual exposure groups.

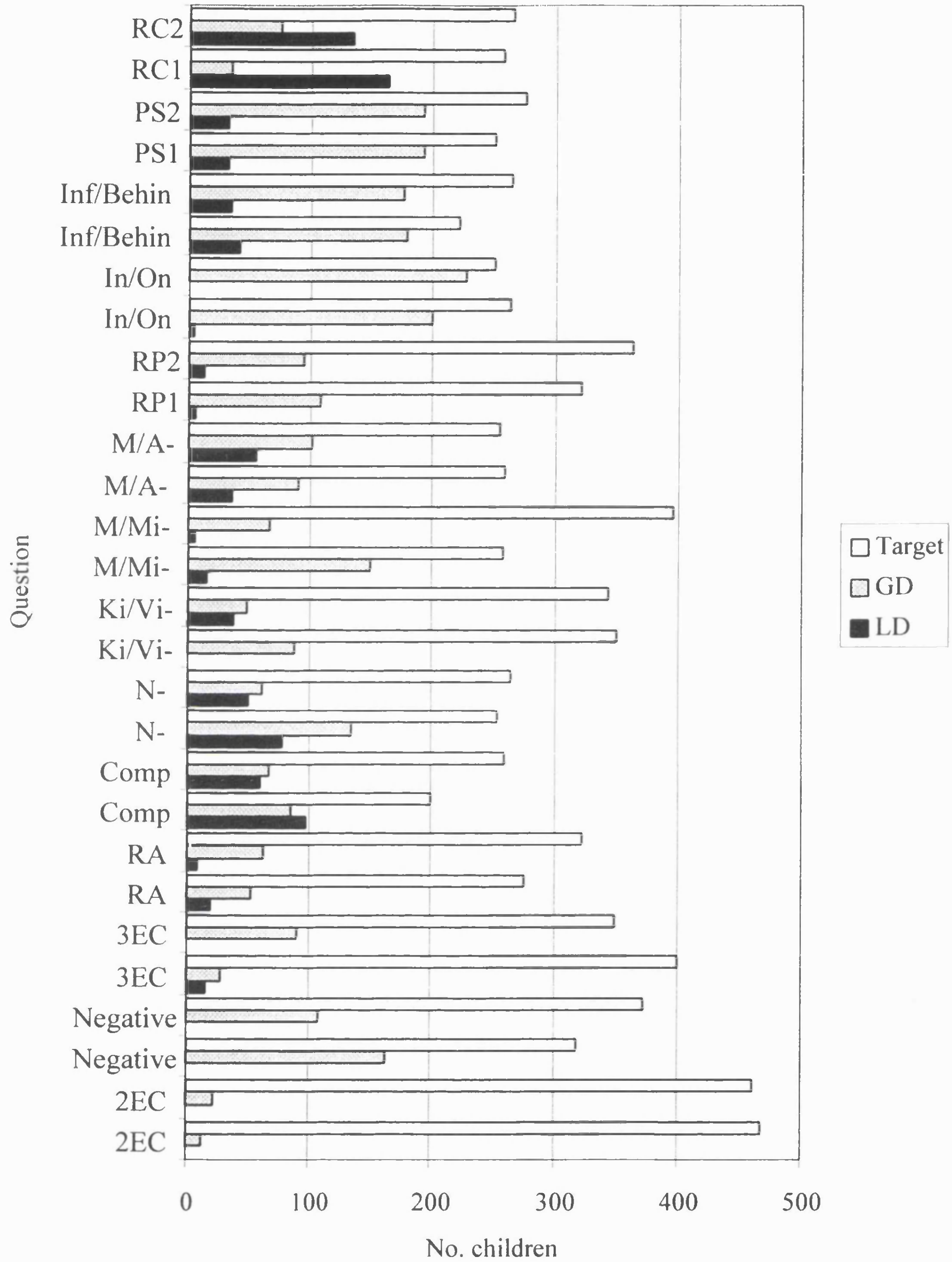

Figure A26. 1: Error patterns on the receptive grammar assessment for the whole cohort

Key:

RC relative clause
PS postmodified subject
RP reversible passive
Comp comparative
RA reversible active
3EC three element combination
2EC two element combination

Legend:
GD grammatical distractor
LD lexical distractor

	Target			Grammatic. distractor			Lexical distractor		
Qu.	**CM**	**M/S**	**Unex**	**CM**	**M/S**	**Unex**	**CM**	**M/S**	**Unex**
					%				
2EC1	94	96	99	5	3	1	0	0	0
2EC2	95	95	95	4	5	5	0	0	0
Neg1	71	61	65	28	39	35	0	0	1
Neg2	78	74	78	20	25	22	0	1	0
3EC1	78	83	87	7	7	3	6	1	2
3EC2	70	70	75	18	19	18	1	0	0
RA1	53	59	59	12	12	9	6	3	3
RA2	65	67	67	13	14	12	2	2	1
Com1	38	42	44	19	15	18	24	18	18
Com2	52	54	54	15	11	15	12	12	13
NC1	51	52	53	29	28	26	11	19	17
NC2	49	59	55	14	10	14	9	12	11
KV1	72	66	78	16	21	17	0	1	0
KV2	70	71	72	11	11	8	9	6	8
MM1	48	60	51	36	24	33	4	5	1
MM2	77	83	85	18	12	11	1	1	2
MA1	49	55	56	28	35	27	10	6	7
MA2	43	55	58	25	21	17	11	13	11
RP1	62	64	72	24	26	17	2	1	0
RP2	74	73	77	20	20	18	2	3	3
I/O1	57	50	56	37	46	40	1	1	1
I/O2	47	55	53	49	44	47	1	0	0
I/B1	47	45	46	32	37	41	9	10	7
I/B2	55	55	54	36	37	36	6	7	8
PS1	45	55	54	42	37	40	9	7	4
PS2	58	54	59	11	14	16	21	26	19
RC1	50	55	54	8	6	8	32	35	35
RC2	50	58	56	20	10	16	27	31	26

Table A26. 1: Raw data showing error patterns on the receptive grammar assessment for the whole cohort

Key same as figure **

A26.2 Syntax assessment

Individual item performance, as measured by the proportion of the maximum score attained by each group on each question, was similar across the three exposure groups (figure A26.2). The performance of the CM group was consistently poorer than that of the unexposed and M/S groups, although the differences were small. Overall, poor performance was concentrated on the following items: the preposition 'between', comparative, when, who, past tense and negative.

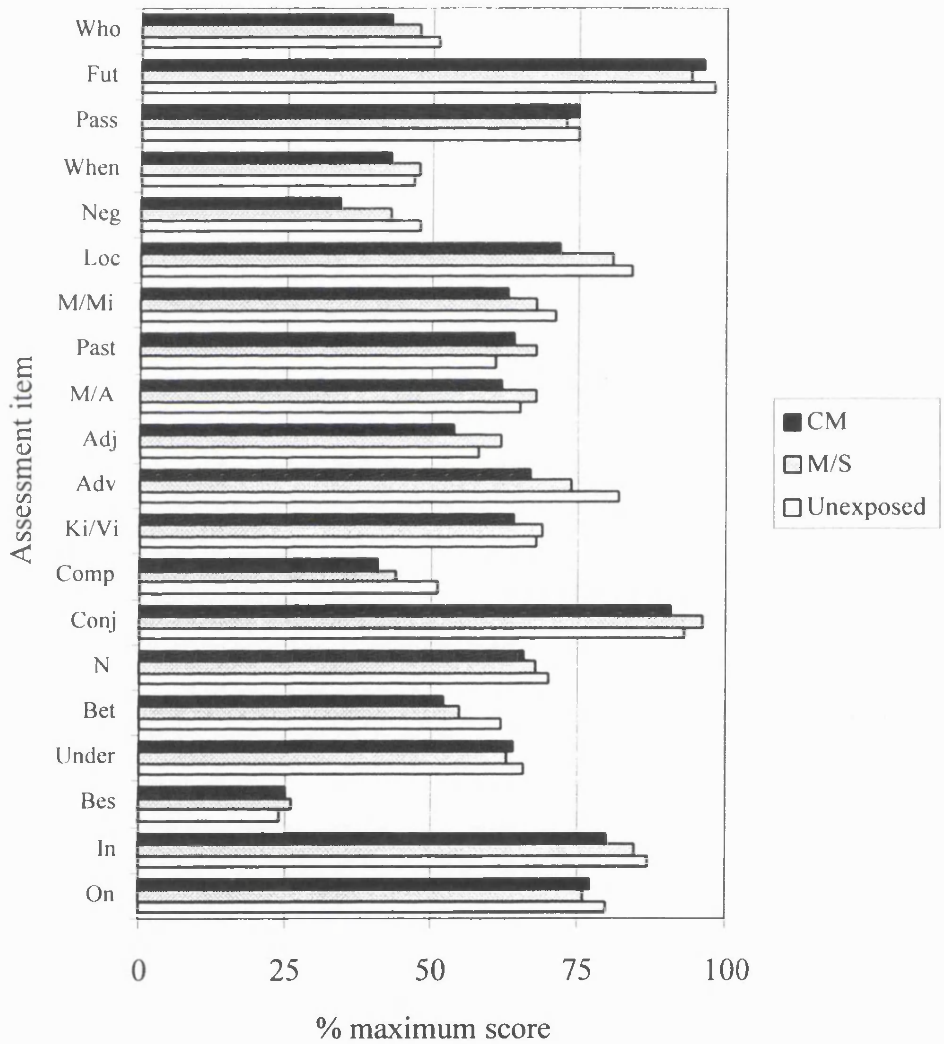

Figure A26. 2: Individual item analysis on the syntax assessment expressed as the proportion of the maximum score attained by each exposure group

Key:

Bes beside	Ki/Vi Ki/Vi-class	Loc locative
Bet between	Adv adverb	Neg negative
N N-class	Adj adjective	Pass passive
Conj conjunction	M/A M/A-class	Fut future tense
Comp comparative	M/Mi M/Mi-class	

A26.3 Higher level language assessment

This section presents a detailed analysis of the higher level language subtests.

Categorisation task

The raw scores for the three categorisation tasks (foods, animals, girls' names) were scaled from zero to five because the use of the raw scores would have disproportionately weighted the final score to this task (figures A26.3 to A26.5). The distribution of scores was similar in each task, therefore the mean was calculated for the three scores to make a total possible score of five.

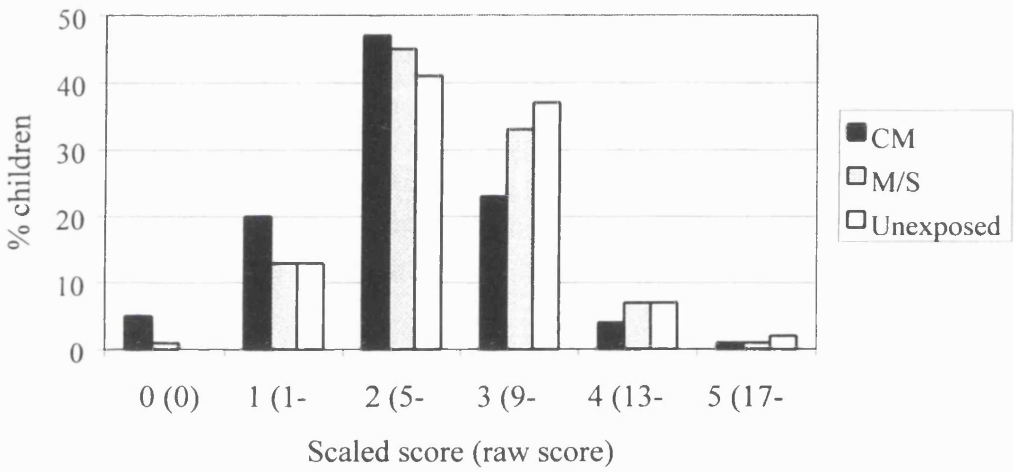

Figure A26. 3: Distribution of food categorisation task scores by exposure group

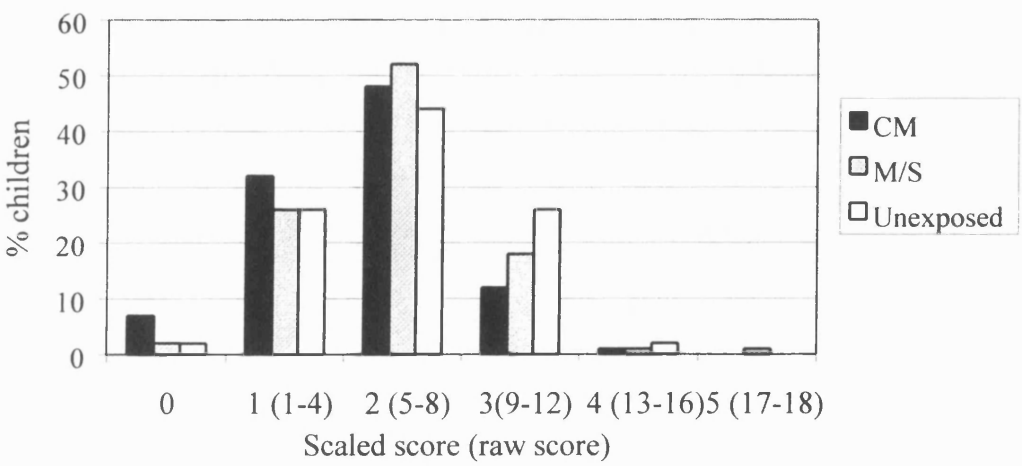

Figure A26. 4: Distribution of animals categorisation task scores by exposure group

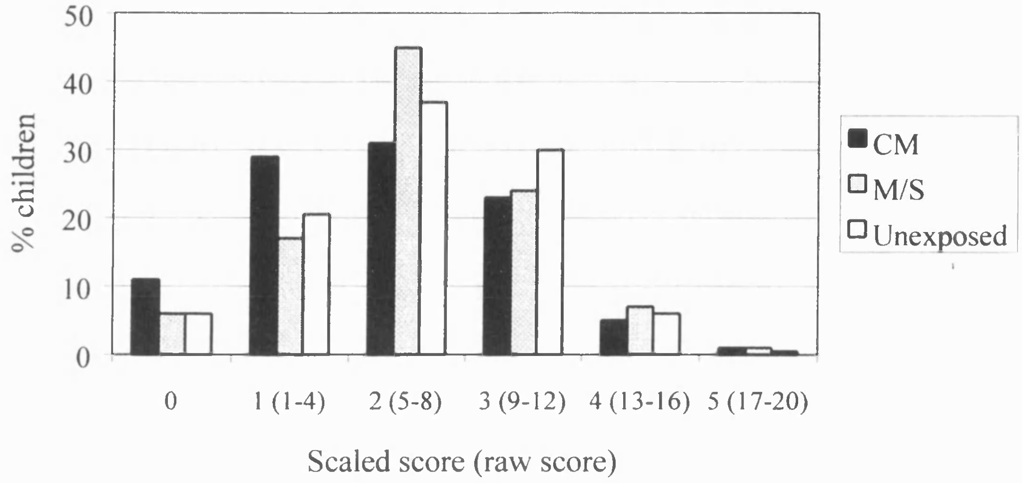

Figure A26. 5: Distribution of girls' names categorisation task scores by exposure group

The distribution of total categorisation task scores was similar to those of the individual tasks: the CM group had larger proportions of low scores in comparison to the M/S and unexposed groups (figure A26.6). The trend for the group as a whole was towards mid-range scores with very few high scores in any group.

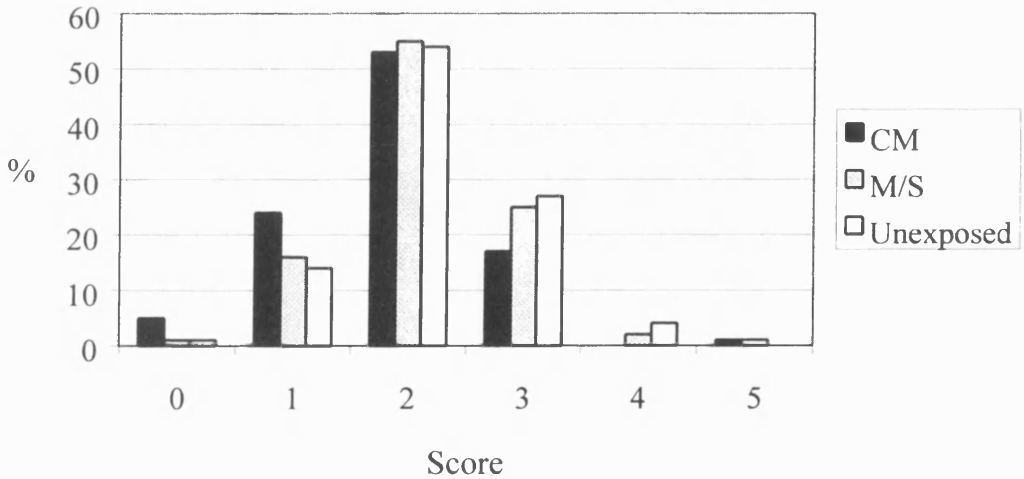

Figure A26. 6: Distribution of total categorisation task scores by exposure group

Definitions of Words

Four questions (each with a possible total of 2) comprised this task testing definitions of nouns, verbs, adjectives and adverbs, which were added together to produce a total score of eight. The total score was normally distributed: there were larger proportions of low scores in the CM group but the proportion of high scores was similar across the three groups (figure A26.7). There was a trend towards lower scores on each task in the CM and M/S groups relative to the unexposed group, with the exception of the adjectives task on which the distribution of scores was similar across the groups.

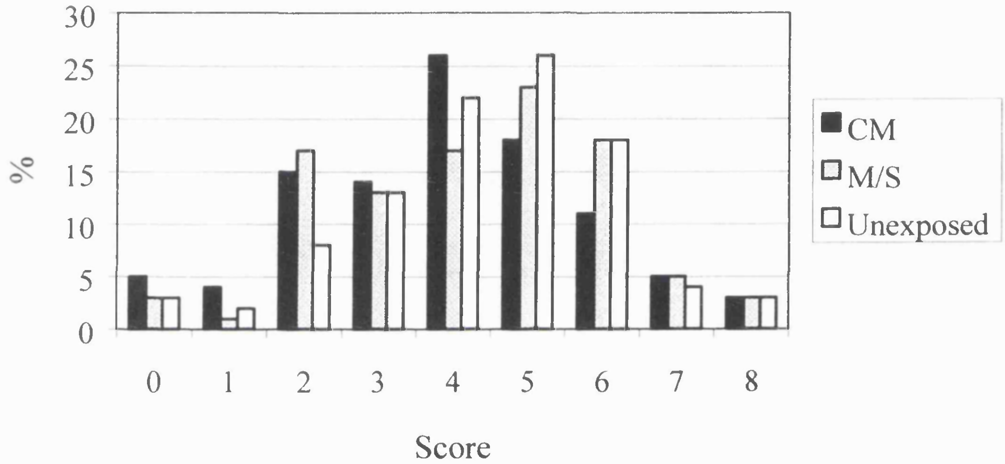

Figure A26. 7: Distribution of definitions of words task scores by exposure group

Homonyms

The homonyms task consisted of four questions: two points were awarded per questions, one for each of the two possible definitions, making a total score of eight. The results were normally distributed (figure A26.8). There was a larger proportion of low scores in the CM group compared to the M/S (χ^2=5.38 p=0.02) and unexposed groups (χ^2=7.43 p=0.01).

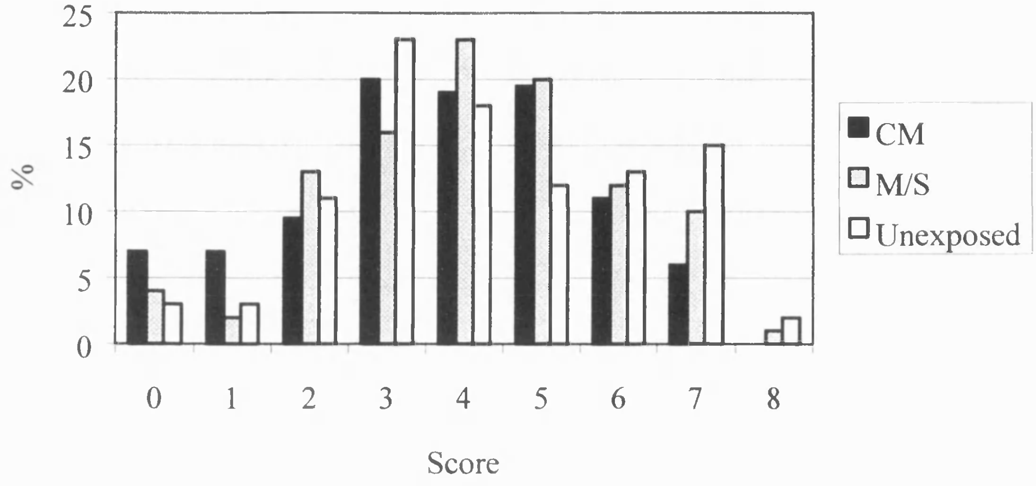

Figure A26. 8: Distribution of homonyms task scores by exposure group

Similarities and Differences

The similarities and differences task comprised four questions, each of which had a maximum score of two (one for the similarity, one for the difference), making a total score of eight. The distribution of scores suggests that children from all groups found this to be a difficult task (figure A26.9). The distribution of scores in the CM group was particularly skewed towards the low scores.

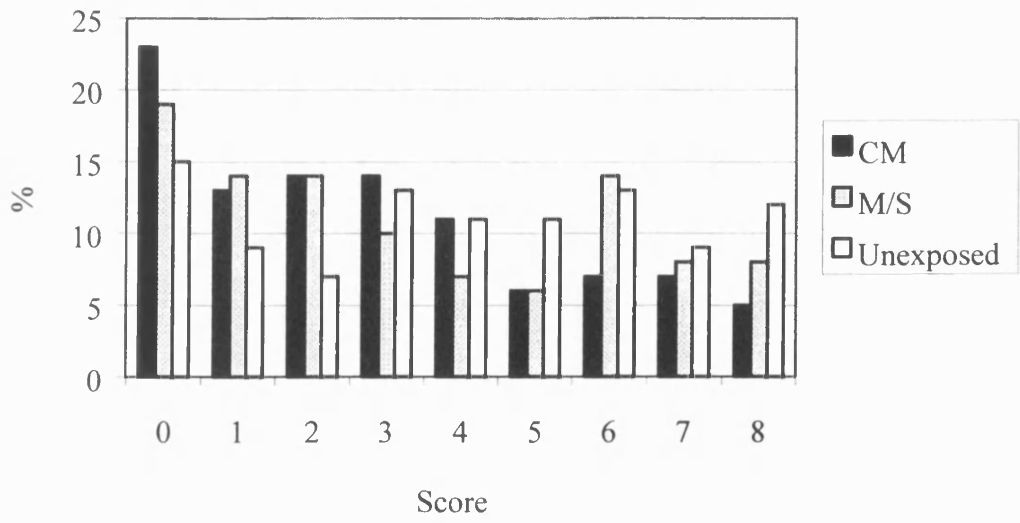

Figure A26. 9: Distribution of similarities and differences task scores by exposure group

Sentence Formulation

This task comprised five questions, requiring the child to construct a sentence using a noun, verb, adjective and two function words: each question was scored from zero to three. The proportion of children achieving the maximum score for each question reduced appreciably as the hypothesised difficulty of the questions increased (noun to function words: easy to difficult). The proportion of children attaining the maximum score was consistently lower in both exposed groups compared to the unexposed group (with the exception of the noun question, for which the M/S group had the largest proportion of maximum scores).

The scoring guidelines for this task were based on those used in the CELF-R (Semel, et al., 1987). However, scores of one or two were rarely awarded, suggesting that the guidelines were unclear for scores other than the minimum or maximum. Therefore, scores of one or two were combined to make a range of scores from zero to two for each question, resulting in a total task score of ten. The small proportion of mid-range scores awarded is reflected in the uneven distribution of the total score (figure A26.10). In a qualitative analysis of task performance, the speech and language assessors commented that children found this task more difficult than the others in the assessment. This is highlighted by the large proportion of zeros and the small proportion of high scores across the groups, particularly in the CM group in which 20% of children attained no score.

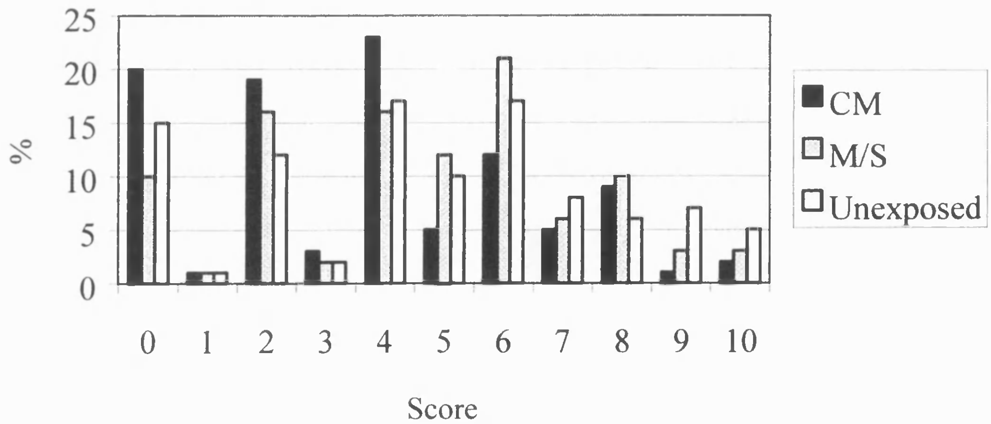

Figure A26. 10: Distribution of sentence formulation task scores by exposure group

Appendix 27: Kilifi Creek Behavioural Memory Test Results

A27.1 Conversion of KCBMT raw scores to scaled scores

There was a trend towards poorer performance in the unexposed group relative to the performance of UK children on the RBMTC. To illustrate the discrepancy in scores, the proportion of a sample of 223 children of the same age from mainstream UK schools attaining each score on the RBMTC (Wilson, et al., 1991) will be presented in brackets adjacent to the scores of the Kilifi cohort on the KCBMT or will be discussed in the text.

Remembering a Name (RN)

The RBMTC does not score for 6 and 7 year olds on this subtest because the task shows a developmental pattern, with low scores in younger age groups and scores increasing with advancing age (Wilson, et al., 1993). Table A27.1 shows that the raw scores are skewed to the lower end of the range in these age groups, therefore the KCBMT has maintained this convention.

	RN raw scores % children in each age group (% UK children)					
Age (yrs)	**0**	**1**	**2**	**3**	**4**	**Total n**
6	27 (30)	27 (15)	19 (22)	10 (4)	17 (26)	41
7	11 (19)	32 (15)	19 (17)	14 (12)	24 (35)	37
8	8 (14)	15 (2)	25 (20)	17 (10)	35 (54)	48
9	6 (1)	21 (3)	21 (22)	6 (11)	46 (60)	52
	Scaled score	2	**Raw score**	2-4	**% unexp group**	75
		1		1		18
		0		0		7

Table A27. 1: Generation of scaled scores for the remembering a name task

Remembering a Hidden Object (RHO)

The 'remembering a hidden object' and 'remembering an appointment' subtests were omitted from the KCBMT because the pattern of scores could not be matched to the RBMTC. As tables A27.2 and A27.3 show, a maximum of 60% of children from the unexposed group attained a scaled score of '2'. This suggests that these tasks are not appropriate for this population and that their inclusion would skew the final score.

	RHO raw scores % children in each age group (% UK children)					
Age (yrs)	**0**	**1**	**2**	**3**	**4**	**Total n**
6	0 (1)	54 (1)	34 (20)	10 (22)	2 (53)	41
7	0 (0)	46 (0)	32 (17)	19 (15)	3 (66)	37
8	2 (0)	23 (2)	40 (2)	27 (16)	8 (80)	48
9	0 (0)	38 (0)	35 (0)	25 (16)	2 (83)	52
	Scaled score	2	**Raw score**	2-4	**% unexp group**	60
		1		1		39
		0		0		1

Table A27. 2: Generation of scaled scores for the remembering a hidden object task

Remembering an Appointment (RA)

	RA raw scores % children in each age group (% UK children)			
Age (yrs)	**0**	**1**	**2**	**Total n**
6	56 (19)	32 (14)	12 (66)	41
7	46 (5)	43 (12)	11 (82)	37
8	42 (0)	35 (16)	23 (84)	48
9	33 (3)	42 (5)	25 (90)	52

	Scaled score	2	**Raw score**	2	**% unexp group**	19
		1		1		38
		0		0		43

Table A27. 3: Generation of scaled scores for the remembering an appointment task

Picture Recognition (PR)

Following the reasoning in the RBMTC for the RN subtest, 6 and 7 year olds were omitted from the scoring of this subtest (table A27.4). Picture-based items are difficult for children in this culture, particularly for younger children who are less likely to be schooling. One hundred percent of six, eight and nine year olds and 97% of seven year olds attained a raw score of 9 or 10 on the RBMTC version of this subtest (Wilson, et al., 1991).

	PR raw scores % children in each age group							
Age	**<4**	**5**	**6**	**7**	**8**	**9**	**10**	**Nos**
6	26	2	5	0	5	17	45	42
7	22	0	0	0	14	8	56	36
8	8	2	0	0	13	10	67	48
9	4	0	0	2	0	21	73	52
			Scaled	2	**Raw**	6-10	**%**	93
			score	1	**score**	5	**unexp**	1
				0		<4	**group**	6

Table A27. 4: Generation of scaled scores for the picture recognition task

Story Recall

Immediate Story Recall (ISR)

The RBMTC story recall scores were scaled by age, giving each age group a different cut-off for attaining a scaled score of '2'. The KCBMT followed this convention (table A27.5). The RBMTC cut-off scores were 10, 13, 14 and 14 for six, seven, eight and nine year olds respectively. At least 85% of each age group obtained the RBMTC cut-off score or greater.

	ISR Raw Scores % children in each age group								
Age	**<2.5**	**3-3.5**	**4-4.5**	**5-5.5**	**6-6.5**	**7-7.5**	**8-15.5**	**16-31**	**No.**
6	12	2	7	2	10	10	43	14	42
7	3	3	3	0	10	3	43	35	37
8	0	0	2	4	2	7	27	58	48
9/10	0	0	4	4	2	6	30	54	52
				Scaled score					
Age				2	1	0		**% unexposed group**	
6				>4	3-3.5	<2			
7				>6.5	5.5-6	<5		2	89
8				>7	6-6.5	<5.5		1	3
9				>7	6-6.5	<5.5		0	8

Table A27. 5: Generation of scaled scores for the immediate story recall task

Delayed Story Recall (DSR)

The RBMTC cut-off scores for the delayed story recall task were 10, 12, 14 and 14 for six, seven, eight and nine year olds respectively. At least 88% of each age group obtained the RBMTC cut-off score or greater. As in the immediate story recall task, the cut-offs had to be reduced for the KCBMT group (table A27.6).

	DSR Raw Scores % children in each age group								
Age	**<2.5**	**3-3.5**	**4-4.5**	**5-5.5**	**6-6.5**	**7-7.5**	**8-15.5**	**16-31**	**No.**
6	12	0	6	12	7	7	41	15	41
7	3	5	0	8	8	6	38	32	37
8	4	0	0	7	4	4	35	46	48
9	0	2	0	4	4	4	42	44	52
				Scaled score					
Age				2	1	0		**% unexposed group**	
6				>4	3-3.5	<2			
7				>5	4-4.5	<3.5		2	89
8				>6.5	5.5-6	<5		1	2
9				>7	6-6.5	<5.5		0	9

:Table A27. 6: Generation of scaled scores for delayed story recall task

Face Recognition (FR)

As in the Picture Recognition subtest, a high proportion of children from the younger age groups attained low scores. Therefore, 6 and 7 year olds were omitted from the scaled scoring, producing a pattern of scaled scores similar to that in the RBMTC. The cut-off (resulting in a scaled score of '2') in the RBMTC was 4: at least 96% of all age groups attained the cut-off score or higher (Wilson, et al., 1991).

	FR Raw Scores % children in each age group						
Age	**<0**	**1**	**2**	**3**	**4**	**5**	**Nos.**
6	39	7	13	24	2	15	41
7	31	11	14	19	22	3	36
8	8	0	21	23	33	15	48
9	4	10	17	19	25	25	52
		Scaled	2	**Raw**	>2	**%**	89
		score	1	**score**	1	**unexp**	5
			0		<0	**group**	6

Table A27. 7: Generation of scaled scores for the face recognition task

Route Recall

Immediate Route Recall (IRR)

To attain a scaled score of '2' in the RBMTC, the cut-off score was 3 for six and seven year olds and four for eight and nine year olds. At least 93% of all age groups obtained this score or higher (Wilson, et al., 1991). The KCBMT scores are shown in table A27.8.

	IRR Raw Scores % children in each age group						
Age	**0**	**1**	**2**	**3**	**4**	**5**	**Nos.**
6	2	15	20	16	20	27	41
7	0	11	31	11	11	36	36
8	0	9	9	9	14	59	46
9	0	8	6	4	26	56	52
		Scaled	2	**Raw**	>2	**%**	90
		score	1	**score**	1	**unexp**	10
			0		0	**group**	0

Table A27. 8: Generation of scaled scores for the immediate route recall task

Delayed Route Recall (DRR)

The RBMTC cut-off scores for DRR were the same as for IRR. At least 91% of all age groups attained this score or more (Wilson, et al., 1991). The KCBMT scores are shown in table A27.9.

	DRR Raw Scores % children in each age group						
Age	**0**	**1**	**2**	**3**	**4**	**5**	**Nos.**
6	0	16	20	20	22	22	41
7	0	8	33	17	6	36	36
8	0	9	15	11	15	50	46
9	0	8	12	6	28	46	52
		Scaled	2	**Raw**	>2	**%**	90
		score	1	**score**	1	**unexp**	10
			0		0	**group**	0

Table A27. 9: Generation of scaled scores for the delayed route recall task

Remembering a Message (MR): Immediate (IMR) and Delayed (DMR)

The MR scaled scores were created to be age-specific to better reflect the differences in age shown in the raw scores (tables A27.10 and A27.11).

		IMR/DMR Raw Scores % children in each age group (% UK children)				
Age	**Imm/Del**	**0**	**1**	**2**	**3**	**No.**
6	**I**	5 (0)	12 (12)	59 (43)	24 (44)	41
	D	5 (0)	8 (9)	52 (28)	35 (61)	40
7	**I**	11(0)	12 (5)	44 (38)	33 (56)	36
	D	8 (0)	12 (7)	47 (21)	33 (71)	36
8	**I**	4 (0)	9 (4)	39 (26)	48 (70)	46
	D	2 (0)	3 (2)	43 (12)	52 (86)	46
9	**I**	2 (0)	8 (0)	34 (28)	56 (70)	52
	D	4 (0)	8 (0)	42 (12)	46 (87)	52

Table A27. 10: Raw scores for the remembering a message task

	MR Raw Scores % children in each age group							
Age	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**Nos**
6	3	0	10	5	42	20	20	40
7	8	3	3	12	33	19	22	36
8	2	0	2	11	22	26	37	46
9	0	2	2	12	27	19	38	52
			Scaled score					
Age			2	1	0		**% unexposed group**	
6			>2	1	0			
7			>3	2	<1		2	88
8			>4	2-3	<1		1	8
9			>4	2-3	<1		0	4

Table A27. 11: Generation of scaled scores for the remembering a message task

Orientation Questions (OQTOTAL)

The total score for the orientation questions subtest of the RBMTC is 11. Of the 18 questions included in the KCBMT, seven were removed after analysis, resulting in the same total score (table A27.12). Questions 4a to 4d – schooling-related questions – were omitted because of the large numbers of children who were not attending school. Eighty percent of the unexposed group scored '0' on question 6b, 72% on question 6c and 98% on question 7. These questions tested knowledge of the current month, the current year and the child's year of birth. The high number of incorrect answers highlights the different concept of time in this community.

	Individual Orientation Questions Raw Scores % children in each age group											
Age	**Q1**		**Q2**		**Q3**		**Q5**		**Q6a**		**Q8**	
	0	**1**	**0**	**1**	**0**	**1**	**0**	**1**	**0**	**1**	**0**	**1**
6	0	100	85	15	38	62	20	80	70	30	65	35
7	0	100	86	14	39	61	17	83	72	28	61	39
8	0	100	60	40	21	79	21	79	46	54	40	60
9	0	100	73	27	15	85	8	92	40	60	37	63

	Individual Orientation Questions Raw Scores % children in each age group									
Age	**Q9a**		**Q9b**		**Q10**		**Q11**		**Q12**	
	0	**1**	**0**	**1**	**0**	**1**	**0**	**1**	**0**	**1**
6	0	100	28	72	5	95	0	100	83	17
7	8	92	17	83	3	97	0	100	67	33
8	4	96	10	88	6	94	0	100	46	54
9	2	98	15	85	4	96	4	96	44	56

Table A27. 12: Raw scores for the orientation question tasks

The cut-off scores to attain a scaled score of '2' on the RBMTC were 6, 8, 8 and 9 for six, seven, eight and nine year olds respectively. One hundred percent, 92%, 96% and 99% obtained the cut-off score or more in each of the respective age groups (Wilson, et al., 1991). The KCBMT group scores are shown in table A27.13.

	OQTOTAL Raw Scores % children in each age group									
Age	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**Nos**
6	0	5	10	21	27	20	12	5	0	40
7	3	6	8	14	22	17	19	11	0	36
8	0	0	4	8	16	23	19	17	13	48
9	0	2	0	8	21	13	19	27	10	52
					Scaled score					
					2	1	0		**%unexposed group**	
6					4	3	<2			
7					5	4	<3		2	97
8					6	5	<4		1	2
9					6	5	<4		0	1

Table A27. 13: Generation of scaled scores for the orientation questions task

Total KCBMT score

The total score was calculated by adding all of the scaled scores together, omitting two of the subtests included in the RBMTC (RHO and RA) and omitting 6 and 7 year olds from the RN, PR and FR subtests. The total possible scores for each age group are shown in table A27.14.

Age	Normal	Borderline	Impaired
6	10-12	6-9	0-5
7	10-12	6-9	0-5
8	16-18	12-15	0-11
9	16-18	12-15	0-11

Table A27. 14: Total KCBMT score by age group

The number of children from the unexposed group attaining these levels is shown in table A27.15.

Age	Normal (%)	Borderline (%)	Impaired (%)
6	35 (83)	6 (14)	1 (2)
7	32 (86)	6 (14)	0 (0)
8	36 (75)	7 (17)	4 (8)
9	43 (84)	4 (8)	4 (8)

Table A27. 15: Distribution of KCBMT scores by age group

A27.2 KCBMT individual task data

This section presents a detailed comparison of group performance on individual KCBMT subtests (section 15.2.3).

Remembering a name
(0=2-4; 1=0,1)

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	0.88	0.54 to 1.43	0.6
	M/S	0.73	0.45 to 1.2	0.21
Epilepsy status	Active epilepsy	1.69	0.62 to 4.58	0.3
	Inactive epilepsy	1.21	0.41 to 3.54	0.73
Age	7 years	0.71	0.42 to 1.2	0.01
	8 years	0.39	0.22 to 0.7	
	9 years	0.41	0.22 to 0.77	
Sex	Female	0.53	0.36 to 0.8	0.002
Schooling status	Nursery	0.64	0.4 to 1.01	0.02
	Standard 1	0.34	0.17 to 0.69	
	Standard 2	0.69	0.3 to 1.57	
Nutritional status	Weight/height	0.92	0.45 to 1.89	0.81
	Height/age	1.15	0.6 to 2.18	0.68
	Weight/age	1.2	0.51 to 2.81	0.68
SES status	Mother's education	0.76	0.49 to 1.17	0.21
	Father's occupation	0.91	0.61 to 1.38	0.67

Table A27. 16: Estimated odds of a poorer performance on the remembering a name task

Prospective items

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	-0.53	-1.01 to –0.05	0.03
	M/S	-0.02	-0.49 to 0.46	0.94
Epilepsy status	Active epilepsy	-1.2	-2.27 to –0.12	0.03
	Inactive epilepsy	0.33	-0.71 to 1.37	0.53
Age	7 years	0.39	-0.16 to 0.94	0.003
	8 years	0.95	0.37 to 1.53	
	9 years	1.03	0.41 to 1.64	
Sex	Female	0.01	-0.39 to 0.4	0.97
Schooling status	Nursery	0.37	-0.1 to 0.85	0.003
	Standard 1	1.07	0.45 to 1.68	
	Standard 2	1.15	0.37 to 1.93	
Nutritional status	Weight/height	0.36	-0.34 to 1.07	0.31
	Height/age	0.08	-0.57 to 0.73	0.81
	Weight/age	-0.97	-1.84 to –0.09	0.03
SES status	Mother's education	0.52	0.09 to 0.94	0.02
	Father's occupation	0.08	-0.32 to 0.49	0.68

Table A27. 17: Estimated differences in prospective task scores

Picture recognition

(0=2+; 1=<2)

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	0.73	0.36 to 1.46	0.37
	M/S	0.23	0.1 to 0.56	0.001
Epilepsy status	Active epilepsy	2.17	0.59 to 7.98	0.24
	Inactive epilepsy	1.28	0.23 to 7.11	0.78
Age	7 years	0.67	0.34 to 1.35	0.001
	8 years	0.23	0.09 to 0.59	
	9 years	0.12	0.04 to 0.41	
Sex	Female	0.69	0.38 to 1.25	0.22
Schooling status	Nursery	0.41	0.2 to 0.81	0.01
	Standard 1	0.07	0.01 to 0.56	
	Standard 2	0.22	0.03 to 1.9	
Nutritional status	Weight/height	0.81	0.28 to 2.41	0.71
	Height/age	2.4	1.03 to 5.56	0.04
	Weight/age	0.89	0.29 to 2.73	0.84
SES status	Mother's education	0.82	0.41 to 1.63	0.57
	Father's occupation	1.33	0.72 to 2.46	0.37

Table A27. 18: Estimated odds of a poorer performance on the picture recognition task

Story recall

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	-0.61	-3.14 to 1.93	0.64
	M/S	1.31	-1.19 to 3.81	0.3
Epilepsy status	Active epilepsy	-4.71	-10.41 to 0.99	0.11
	Inactive epilepsy	0.86	-4.65 to 6.37	0.76
Age	7 years	4.2	1.29 to 7.11	<0.001
	8 years	7.22	4.18 to 10.26	
	9 years	7.76	4.53 to 10.99	
Sex	Female	-2.09	-4.16 to –0.02	0.05
Schooling status	Nursery	3.42	0.93 to 5.91	<0.001
	Standard 1	9.01	5.76 to 12.25	
	Standard 2	14.99	10.87 to 19.12	
Nutritional status	Weight/height	1.12	-2.59 to 4.83	0.55
	Height/age	-1.55	-4.95 to 1.84	0.37
	Weight/age	-5.66	-10.21 to –1.1	0.02
SES status	Mother's education	2.1	-0.13 to 4.33	0.07
	Father's occupation	1.45	-0.67 to 3.57	0.18

Table A27. 19: Estimated differences in story recall scores

Face recognition

(0=1+; 1=<1)

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	1.06	0.58 to 1.91	0.86
	M/S	0.31	0.15 to 0.63	0.001
Epilepsy status	Active epilepsy	2.02	0.64 to 6.43	0.23
	Inactive epilepsy	0.57	0.1 to 3.11	0.51
Age	7 years	0.77	0.42 to 1.41	<0.001
	8 years	0.26	0.12 to 0.57	
	9 years	0.13	0.05 to 0.35	
Sex	Female	0.9	0.54 to 1.5	0.68
Schooling status	Nursery	0.51	0.29 to 0.91	0.01
	Standard 1	0.27	0.09 to 0.77	
	Standard 2	*	-	
Nutritional status	Weight/height	0.63	0.24 to 1.68	0.36
	Height/age	2.04	0.96 to 4.34	0.06
	Weight/age	1.28	0.47 to 3.49	0.63
SES status	Mother's education	1.18	0.67 to 2.09	0.56
	Father's occupation	1.1	0.65 to 1.87	0.71

Table A27. 20: Estimated odds of a poorer performance on the face recognition task

* Dropped because variable predicts success perfectly

Route recall

(0=2+; 1=<2)

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	1.19	0.51 to 2.79	0.69
	M/S	0.74	0.3 to 1.83	0.52
Epilepsy status	Active epilepsy	3.03	0.71 to 12.89	0.13
	Inactive epilepsy	1.36	0.26 to 6.97	0.72
Age	7 years	0.52	0.21 to 1.29	0.41
	8 years	0.51	0.18 to 1.41	
	9 years	0.83	0.3 to 2.28	
Sex	Female	0.83	0.42 to 1.67	0.61
Schooling status	Nursery	0.77	0.36 to 1.62	0.12
	Standard 1	0.12	0.01 to 0.95	
	Standard 2	*	-	
Nutritional status	Weight/height	0.16	0.02 to 1.32	0.09
	Height/age	1.08	0.4 to 2.92	0.88
	Weight/age	1.34	0.35 to 5.14	0.67
SES status	Mother's education	0.26	0.1 to 0.67	0.01
	Father's occupation	1.57	0.77 to 3.2	0.21

Table A27. 21: Estimated odds of a poorer performance on the route recall task

* Dropped because variable predicts success perfectly

Orientation questions

(0=6+; 1=<6)

	Variable	Odds Ratio	95% C.I.	p-value
Exposure group	CM	3.36	1.61 to 7.0	0.001
	M/S	0.99	0.43 to 2.26	0.98
Epilepsy status	Active epilepsy	0.16	0.02 to 1.35	0.09
	Inactive epilepsy	0.28	0.03 to 2.61	0.26
Age	7 years	0.94	0.46 to 1.89	0.02
	8 years	0.25	0.09 to 0.67	
	9 years	0.42	0.16 to 1.12	
Sex	Female	0.67	0.37 to 1.21	0.18
Schooling status	Nursery	0.48	0.25 to 0.93	0.01
	Standard 1	0.06	0.01 to 0.49	
	Standard 2	0.16	0.02 to 1.37	
Nutritional status	Weight/height	1.47	0.55 to 3.91	0.44
	Height/age	1.4	0.59 to 3.32	0.44
	Weight/age	2.42	0.83 to 7.09	0.11
SES status	Mother's education	0.37	0.17 to 0.78	0.01
	Father's occupation	1.27	0.69 to 2.35	0.44

Table A27. 22: Estimated odds of a poorer performance on the orientation questions task

Immediate recall

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	-0.5	-1.89 to 0.89	0.48
	M/S	0.95	-0.42 to 2.32	0.17
Epilepsy status	Active epilepsy	-2.93	-6.05 to 0.19	0.07
	Inactive epilepsy	-0.25	-3.27 to 2.76	0.87
Age	7 years	2.38	0.79 to 3.97	<0.001
	8 years	4.44	2.77 to 6.12	
	9 years	4.78	3.0 to 6.56	
Sex	Female	-0.97	-2.1 to 0.17	0.1
Schooling status	Nursery	1.96	0.59 to 3.32	<0.001
	Standard 1	5.31	3.53 to 7.09	
	Standard 2	8.12	5.86 to 10.39	
Nutritional status	Weight/height	1.43	-0.62 to 3.47	0.17
	Height/age	-0.77	-2.66 to 1.12	0.42
	Weight/age	-3.28	-5.82 to –0.74	0.01
SES status	Mother's education	1.46	0.24 to 2.69	0.02
	Father's occupation	0.58	-0.59 to 1.74	0.33

Table A27. 23: Estimated differences in immediate story and route recall scores

Delayed recall

	Variable	Estimated difference	95% C.I.	p-value
Exposure group	CM	-0.03	-1.47 to 1.4	0.96
	M/S	0.75	-0.67 to 2.16	0.3
Epilepsy status	Active epilepsy	-3.31	-6.53 to –0.09	0.04
	Inactive epilepsy	0.99	-2.12 to 4.1	0.53
Age	7 years	2.57	0.93 to 4.22	<0.001
	8 years	4.22	2.49 to 5.95	
	9 years	4.66	2.83 to 6.5	
Sex	Female	-1.25	-2.42 to –0.08	0.04
Schooling status	Nursery	2.08	0.67 to 3.49	<0.001
	Standard 1	4.92	3.08 to 6.76	
	Standard 2	8.43	6.1 to 10.76	
Nutritional status	Weight/height	0.66	-1.44 to 2.77	0.54
	Height/age	-1.22	-3.17 to 0.73	0.22
	Weight/age	-2.97	-5.56 to –0.37	0.03
SES status	Mother's education	1.25	-0.01 to 2.51	0.05
	Father's occupation	0.9	-0.3 to 2.09	0.14

Table A27. 24: Estimated differences in delayed story and route recall scores

Appendix 28: Characterisation of the Impaired Group

This appendix presents individual impairment data for each child classified as 'impaired' on any of the developmental domains assessed in the study. Section A28.1 describes patterns of impairment across the spectrum of development domains and section A28.2 details speech and language impairments.

A28.1 All impairments

ID	S/L	N-V	Behav	Mem	Atten	Neuro	Special senses	Epilepsy
023	✓	✓	✓	✓	✓	✓		
036	✓	✓		✓	✓	✓		Y(active)
184	✓		✓	✓		✓		
034	✓			✓	✓	✓		Y(active)
285	✓		✓	✓				
333		✓		✓	✓			Y (inact)
375	✓				✓		✓	
451	✓			✓		✓		
471	✓			✓		✓		
054	✓			✓				
173	✓					✓		
193	✓			✓				Y(active)
256	✓			✓				
415	✓					✓		
487	✓					✓		Y(active)
021						✓		
031							✓	
037				✓				
053						✓		Y(active)
055				✓				
130	✓							
138						✓		Y (inact)
145						✓		
151						✓		
170							✓	
206				✓				
243				✓				
280			✓					
311	✓							
314						✓		
368		✓						
369	✓							
408						✓		
423				✓				
430	✓							
455							✓	

Table A28. 1: Patterns of impairments in the CM group, ordered by severity

Key (applicable to all tables in this section):

S/L speech/language — Mem memory (KCBMT)

N-V non-verbal functioning — Atten attention

Behav behaviour — Neuro neurological (motor)

ID	S/L	N-V	Behav	Mem	Atten	Neuro	Special senses	Epilepsy
010	✓	✓	✓	✓				
253	✓			✓		✓		Y(active)
271	✓				✓	✓		
428	✓			✓		✓		Y(active)
028				✓		✓		
103	✓		✓					
239	✓			✓				
244	✓				✓			
318	✓	✓						
421					✓	✓		
472	✓			✓				
057						✓		Y (inact)
059						✓		
062						✓		Y(active)
098						✓		
118	✓							
120				✓				
125							✓	
174						✓		
241			✓					Y(active)
259							✓	
261	✓							
274	✓							
281				✓				
319				✓				
337			✓					
350			✓					
351						✓		
371			✓					
402						✓		
403			✓					
416	✓							
417			✓					
429				✓				
432	✓							
446						✓		Y (inact)
480			✓					

Table A28. 2: Patterns of impairments in the M/S group, ordered by severity

ID	S/L	N-V	Behav	Mem	Atten	Neuro	Special senses	Epilepsy
207	✓	✓		✓				
484	✓		✓				✓	
071	✓						✓	
385			✓			✓		
047						✓		
050						✓		
096	✓							
117				✓				
213							✓	
226							✓	
228						✓		Y (inact)
233						✓		
360				✓				
363				✓				
392							✓	
461				✓				
462			✓					
475							✓	

Table A28. 3: Patterns of impairments in the unexposed group, ordered by severity

A28.2 Speech and Language Impairments

ID	GRG	RV	Syntax	Lex	HLL	WF	Phono	Prag
023	✓	✓	✓		✓	✓	✓	✓
471	✓	✓	✓	✓	✓	✓	✓	
034	✓	✓		✓		✓		✓
285	✓	✓			✓	✓		✓
375	✓	✓		✓	✓		✓	
184	✓				✓	✓		✓
415		✓		✓		✓	✓	
451		✓		✓	✓	✓		
036	✓	✓	✓					
286	✓	✓				✓		
054				✓				✓
130						✓	✓	
173							✓	✓
193					✓			✓
256		✓	✓					
311				✓	✓			
369		✓				✓		
487				✓				✓

Table A28. 4: Areas of speech and language impairment in the CM group, ordered by severity

Key (applicable to all tables in this section):

GRG receptive grammar (GROG)

RV receptive vocabulary

Lex lexical semantics

HLL higher level language

WF word finding

Phono phonology

Prag pragmatics

ID	GRG	RV	Syntax	Lex	HLL	WF	Phono	Prag
428	✓	✓			✓	✓		✓
253	✓		✓		✓		✓	
472	✓	✓				✓	✓	
010	✓	✓			✓			
103							✓	✓
118							✓	✓
239					✓			✓
244							✓	✓
261		✓				✓		
271		✓				✓		
274				✓		✓		
318		✓		✓				
416		✓					✓	
432	✓			✓				

Table A28. 5: Areas of speech and language impairment in the M/S group, ordered by severity

ID	GRG	RV	Syntax	Lex	HLL	WF	Phono	Prag
207	✓	✓	✓			✓		
484				✓	✓			✓
071		✓	✓					
096				✓			✓	

Table A28. 6: Areas of speech and language impairment in the unexposed group, ordered by severity

Appendix 29: Word Finding Assessment Response Analysis

This appendix presents qualitative data from the word finding assessment. A response analysis was carried out with the 16 children who had an impairment-level performance on the assessment. Examples of errors indicative of word finding difficulties are presented in table A29.1 to illustrate the error patterns seen in this group of children.

ID	Group	Error type	Description: target → actual
023	CM	Lexical paraphasia	chicken → cow finger → leg chair → table
		Perseveration	bottle → pencil broom → pencil tap → pencil
034	CM	Lexical paraphasia	chicken → goat hoe → axe
		Perseveration/ Neologism	chair → 'juga' broom → 'juga' tap → 'juga'
130	CM	Perseveration	cup → house table → house door → house
286	CM	Lexical paraphasia	banana → tomato cat → goat
		Perseveration	door → table window → table cup → tomato ball → tomato
415	CM	Lexical paraphasia	banana → mango cow → fish
		Perseveration	car → clock cup → clock
		Neologism	thatching → 'shamu'
		Circumlocution	cat → big animal hoe → thing
451	CM	Perseveration	house → car person → car cup → car
		Neologism	broom → 'luu'

471	CM	Lexical paraphasia	wooden spoon → cup cat → cow
		Perseveration	tree → hand cup → hand
		Neologism	spoon → 'shang' chair → 'cluma'
		Delayed target	tap → lamp (previous target)
261	M/S	Perseveration	door → house book → house table → house
271	M/S	Perseveration	leg → book hoe → book
		Circumlocution	spoon → big thing
274	M/S	Lexical paraphasia	cat → monkey dress → shirt
		Perseveration	toothbrush → comb thatching → comb hand → comb
472	M/S	Lexical paraphasia	chicken → dog bicycle → car
		Perseveration	finger → car bed → car hand → car
207	Unexposed	Perseveration	table → house thatching → house
		Circumlocution	kikombe → little thing

Table A29.1 : Word finding assessment response analysis

Appendix 30: Publications Arising from the Study

Accepted

1. **Carter JA**, Murira GM, Ross AJ, Mung'ala-Odera, V, Newton CRJC. Speech and language sequelae of severe malaria in Kenyan children. Brain Injury, in press.
2. Versteeg AC, **Carter JA**, Dzombo J, Neville BG, Newton CRJC. Seizure disorders among relatives of Kenyan children admitted with severe falciparum malaria. Trop Med Int Health 2002; 7: 1-5.

Submitted

3. **Carter JA**, Ross AJ, Neville BGR, Obiero E, Katana K, Mturi N, Otieno G, Mung'ala-Odera V, Lees JA, White S, Newton CRJC. Epilepsy and developmental impairments following severe falciparum malaria in children. Submitted: N Eng J Med.
4. **Carter JA**, Neville BGR, Newton CRJC. Neuro-cognitive sequelae of acquired central nervous system infections in childhood: a systematic review. Submitted: Brain Res Rev.

In preparation

5. **Carter JA**, Gona J, Murira GM, Rimba K, Lees JA, Ross AJ, Neville, BGR, Newton CRJC. Speech and language impairments following severe falciparum malaria.
6. **Carter JA**, Murira, GM, Gona J, Rimba K, Lees JA, Neville BGR, Newton CRJC. Development of speech and language assessment tools in resource-poor countries.

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Speech and language sequelae of severe malaria in Kenyan children

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Primary objective: To conduct a preliminary investigation into the occurrence of speech and language impairments following severe malaria in Kenyan children.
Research design: Cohort study comparing the prevalence of impairments in children exposed or unexposed to severe malaria.
Methods and procedures: The study recruited 25 children who had previously been admitted to hospital with severe falciparum malaria and 27 unexposed to the disease. Assessments of comprehension, syntax, lexical semantics, higher level language abilities, pragmatics and phonology were administered to each child at 8–9 years of age, at least 2 years after admission to hospital in children exposed to severe malaria.
Main outcomes and results: Exposed children were found to have lower scores on each assessment and significantly lower scores on four aspects of language ability: comprehension ($p = 0.02$); syntax ($p = 0.02$); content word ($p = 0.02$) and function word ($p = 0.004$) components of lexical semantics.
Conclusions: These data suggest that speech and language deficits may be an important and under-recognized sequela of severe falciparum malaria.

Introduction

Malaria affects 40% of the world's population in over 90 countries and is associated with between 0.5–2.5 million deaths each year, primarily in young children living in sub-Saharan Africa. *Plasmodium falciparum*, transmitted by the female Anopheles mosquito, is the most severe of the four strains of human malaria and is responsible for most of these deaths and neurological morbidity [1]. *P. falciparum* infection may also be one of the major causes of acquired neurological impairment in children in the tropics.

Approximately 2% of clinical infections result in severe disease, of which one of the most severe forms is cerebral malaria [2]. Most survivors of severe falciparum malaria are reported to make a full neurological recovery. In African children with cerebral malaria, neurological deficits occur in 10.9% (95% CI 8.3–13.5%) with

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some form of speech and language deficit noted in 2.1% [1], although no detailed studies have been reported. In most of the cases described, the deficits resolved or markedly improved by 18 months post-insult. However, long-term follow-up was not performed and few studies have attempted to describe the nature or severity of persisting speech and language deficits.

A preliminary investigation was conducted into the nature of persisting speech and language impairments following severe malaria in children who had previously been admitted to Kilifi District Hospital (KDH) on the coast of Kenya.

Materials and methods

Children were selected from a database of patients admitted to KDH with severe malaria using the following criteria: children born in 1990–1991 who lived in a clearly defined study area under demographic surveillance. Children who had suffered severe malaria were recruited to the study. Severe malaria can present in several ways, which may include neurological manifestations in the form of cerebral malaria. As previous evidence for speech and language impairments has come solely from the study of children with a history of cerebral malaria, children with previous severe malaria were sub-divided into two groups, based on whether they had fulfilled the criteria for cerebral malaria:

- Cerebral malaria, defined as a deep level of unconsciousness with inability to localize a painful stimulus (Blantyre coma score of <2 for 4 or more hours); a *P. falciparum* asexual parasitaemia and exclusion of other encephalopathies such as bacterial meningitis [1].
- Non-cerebral malaria, defined as prostration, multiple seizures or severe anaemia [3].

Twenty-five children were identified using these criteria: 13 with cerebral malaria and 12 with non-cerebral malaria. None of the children had been exposed to drugs such as Mefloquine, which have been associated with CNS disturbances.

Twenty-seven children who had not been admitted to hospital with severe malaria were recruited from the community as a comparison group. Most children living in this malaria-endemic community will have experienced mild or moderate forms of malarial disease. However, survival from severe malaria is unlikely without hospital treatment; therefore, the admissions database was checked to ensure that the comparison group had not been previously admitted with severe malaria, thus fulfilling the main inclusion criterion for the unexposed group. Children from the unexposed group were the same age (8–9 years) and lived in the same villages as the children exposed to severe malaria. All children were from rural homesteads and spoke the local language of the area, Kigiryama.

Speech and language assessments

There are no pre-existing, standardized assessments of speech and language in Kigiryama. Assessments were developed by JAC and an assessor whose first language is Kigiryama (GMM), who also administered the tests. The battery included tests of comprehension, syntax, lexical semantics, higher level language, pragmatics and phonology.

All assessments were derived from validated instruments in common use in the UK or used assessment methods routinely in use in the UK. Each assessment was adapted according to the culture and experience of children in the area. This was a multi-step process: first, new questions or statements were developed based on the format of the original test questions. Thus, the content of the assessments was changed but the basic format remained the same. The suitability of the content to the age and experience of local children was assessed by GMM and a local schoolteacher. Secondly, culturally-appropriate picture stimuli were drawn then piloted for level of recognition, as many children in this area are not familiar with pictures. An 80% level of recognition was accepted or the picture was redrawn. The process of adaptation and cultural validation will be reported elsewhere. The details of each assessment are below and sample questions are shown in the appendix:

Comprehension

To measure understanding of spoken language. A single-word comprehension test was adapted from one used in a previous study in the same area [4]. Understanding of simple and complex commands was also assessed and included in the final score.

Syntax

To measure use of grammar and sentence structure. This was based on the format of the South Tyneside Assessment of Syntactic Structures (STASS) [5]: each question and picture targets a particular syntactic element. The analysis was simplified as the authors' knowledge of the grammar of the Kigiryama language is not yet sufficient to permit the level of analysis in the original STASS. Kigiryama is an agglutinative language: an English phrase such as 'he/she will hit him' would be represented by one word consisting of four morphemes in Kigiryama ('a/nda/mu/piga').

Lexical semantics

To measure size and breadth of vocabulary—split into 'minor' function words and 'major' content words, based on the Profile in Semantics–Lexicon (PRISM-L) [6], a naturalistic method of assessing vocabulary size from the child's spontaneous speech.

Higher level language

This assessment aimed to identify children who may be functioning well at a basic level of language use but have problems with the more advanced aspects of language. As it was difficult to know the types of questions that would be sensitive and applicable to Kigiryama language and culture, a wide variety of question types identified from a range of (non-standardized) assessments were included. Questions were incorporated testing synonyms, homonyms, sentence formulation, antonyms, categorization, definitions of words, figurative language, classification and similarities and differences.

Pragmatics

To measure functional language usage. An analysis of functional errors was undertaken, a method previously used in this area [4], taken from a study of Spanish/ English bilingual speakers [7].

Phonology

To assess the integrity of the child's sound system. The first 100 different words from the child's spontaneous speech were transcribed and profiled on a chart of all the consonant phonemes used in Kigiryama. Kigiryama has no final consonant phonemes; initial and medial phonemes were assessed separately. A phoneme was assessed as 'correct' if the child produced it correctly in all words in which it featured in either the initial or medial position.

The two assessors were blind to each child's group status. Informed consent was obtained and children were seen at home, as this has been found to be more conducive to spontaneous speech production. The assessor first engaged the child in play then recorded a sample of spontaneous speech comprising conversation, picture description and storytelling (a traditional activity in this area). The other assessments were administered after the child had been given a break.

Statistical analysis

Analysis was carried out using STATA version 6. Multiple regression was used to estimate the difference between the exposed and unexposed group scores, adjusting for age and sex.

Results

On discharge, eight children exposed to severe malaria were reported to have sequelae, four of whom had been admitted with cerebral malaria and four with non-cerebral severe malaria. Two of the cases were mute, four had limited speech and language (single words) including two with visual impairment and two had motor deficits (one of whom had disordered behaviour). Seventeen children were reported to have no neurological deficits on discharge from hospital. Twenty children were assessed 5–6 years after admission to KDH and five, 2–4 years after admission. Children exposed to severe malaria had a median age of 8 years 8 months (range 8 years 3 months to 9 years 9 months). Twelve were female and 13, male. The 27 comparison children had a median age of 8 years 11 months (range 7 years 8 months to 10 years 4 months). There were 11 females and 16 males. None had been admitted to hospital with severe malaria. All children were able to communicate verbally.

Children who survived severe falciparum malaria had significantly lower scores for the comprehension, syntax and both components of the lexical semantics assessments than children unexposed to the disease (see table 1). The exposed group's mean scores were lower in the higher level language and pragmatics assessments but the difference was not statistically significant. Only two children (both from the exposed group) had minor phonological problems so this was not included in the statistical analysis.

Table 1. Results of speech and language assessments for exposed and unexposed groups

Assessment	Exposed mean (SD) ($n = 25$)	Unexposed mean (SD) ($n = 27$)	Estimated difference: exposed vs unexposed*	95% CI	*p*-value
Comprehension	30.88 (4.32)	33.52 (2.56)	−2.35	−4.36– −0.34	0.02
Syntax	18.27 (3.83)	21.35 (3.35)	−2.64	−4.91– −0.37	0.02
Lexical semantics—function words	0.28 (0.09)	0.34 (0.08)	−0.06	−0.11– −0.01	0.02
Lexical semantics—content words	0.54 (0.09)	0.63 (0.09)	−0.08	−0.14– −0.03	0.004
Higher level language	14.46 (4.79)	17.24 (3.89)	−2.35	−4.84–0.15	0.07
Pragmatics**	4.03 (3.24)	3.13 (3.15)	−0.80	−1.05–2.64	0.39

* Estimated differences are adjusted for age and sex.
** A lower score indicates a superior performance.

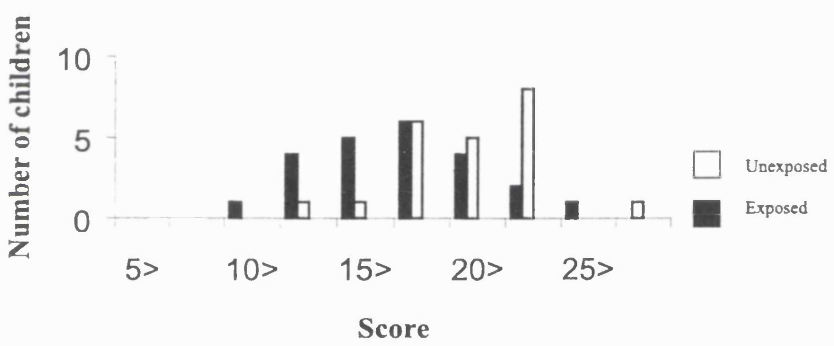

Figure 1. Distribution of syntax assessment scores

The distribution of scores was in general lower in children from the exposed group compared to children from the unexposed group, suggesting an overall effect rather than one or two very impaired children (see figure 1 of syntax scores for example). There was no evidence that the scores of exposed children reported to have no sequelae on discharge were significantly different to the scores of those discharged with sequelae.

Discussion

Children who had previously been admitted to KDH with severe malaria had, in general, significantly lower scores on the language assessments. These data suggest that children who have had severe malaria may have impairments in language functions, which persist 2–6 years after discharge. Speech (i.e. the child's sound system) seems to remain unaffected: the minor phonological deficits seen in two of the exposed children did not impair intelligibility. Unlike previous studies, a detailed follow-up of speech and language functions was carried out several years after the initial insult. The improvement in the six children with speech and language problems on discharge implies that initial deficits may improve beyond the stage of mutism or severe aphasia but do not completely resolve by 6 years post-onset.

The pattern of scores indicates that basic language functions may still be affected years after the malarial episode. If the deficits in these children have any parallels with those of children with acquired aphasia as a result of other aetiologies, this would suggest that many of the cases had not reached the final stage of recovery, usually characterized by high-level deficits [8]. As all of these children had passed the first 2 years post-insult, it may be postulated that they will never fully recover their language functions. Certainly, other infectious disease aetiologies are associated with a poorer prognosis [9, 10], although the mechanisms of infection are different to malaria. Other studies indicate that even small levels of impairment can affect the child's schooling and be a significant handicap for future life [11, 12].

A surprising result was that there was a significant difference between results on tests of basic language functions but not on the test of higher level language function. This may reflect problems with the test itself. Particular difficulties were experienced in selecting culturally-appropriate tasks to assess higher level functions and included a wide variety of tasks from non-standardized UK assessments. In hindsight, it is recognized that several questions were inappropriate: for example, Kigiryama has very few synonyms and figurative language is rarely used amongst children, so very few children scored anything on either of these questions. In addition, more explanation was necessary for some of tasks as the concepts were unfamiliar (e.g. antonyms): lack of understanding of test requirements may have been the reason for failure on these tasks.

The number of children discharged with sequelae was very small and the greater spread of scores found in this study suggests that the assessment may be more sensitive to brain damage following severe malaria than the screening assessment performed on hospital discharge. This also suggests that language deficits may be an important but under-reported sequela of severe malaria.

A striking observation, possibly due to the small numbers, was that there was no evidence of a difference between the scores of children who had suffered cerebral malaria and those who had non-cerebral malaria. The prevalence of acquired neurological impairment following non-cerebral malaria has not previously been investigated, but it is possible that certain manifestations of severe non-cerebral malaria may also result in sequelae. Waruiru *et al.* [13] found that 84% of children with otherwise uncomplicated *falciparum* malaria have prolonged, focal or repetitive seizures, which in the case of febrile seizures have been associated with neurological damage [14].

The present study was intended as a preliminary investigation into the occurrence of persisting speech and language impairments following severe malaria. The cognitive development of young children in resource-poor countries may be influenced by a complex range of factors relating to conditions of poverty such as malnutrition [15], intestinal parasites [16] and socioeconomic status [17]. However, the investigation of these factors was beyond the scope of this study. A larger study is now in progress to look at possible antecedents of language impairment, for instance, malnutrition and the children's more detailed language, neurological and cognitive profile to look for potentially preventable causes of such impairments in a malaria endemic area.

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Appendix

Sample questions are presented for the comprehension, syntax and higher level language assessments. The lexical semantic, pragmatics and phonological assessments were based on a spontaneous speech sample.

Comprehension

Single word comprehension: sample words
Ball, spoon, chicken, axe, to cook, to fight, many, danger.

Commands
Touch your ear then close your eyes.
Touch your arm and leg, then open your mouth.

Syntax

Prepositions
Assessor's prompt: Where is the banana? [in relation to the cup].
Expected response: Under the cup.

Negation
Prompt: This mother [referring to picture] asks the boy to go to the shops but he doesn't want to go. What do you think he will say?
Response: I don't want to go/I won't go.

Adverbs
Prompt: This animal [referring to picture of two animals] is going quickly and this one is going ...
Response: Slowly.

Passives
Prompt: This boy [referring to a picture of two boys] was given a mango and this one ...
Response: Was given a banana.

Higher level language

Categorization task
Tell me as many things as you can that you can eat.

Antonyms
The opposite of 'hot' is 'cold'. What is the opposite of 'tall'?

Similarities and differences
Can you tell me something that is the same and something that is different between a cow and a donkey?

Divergent semantic task
If you couldn't use a hoe for planting maize, what else could you use?