

Behavioural and Psychological Outcomes in Children
Treated for Brain Tumours

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Overview

The thesis will begin with a literature review that examines outcomes in children who have been treated for brain tumours using a surgery-only method. Cognitive, behavioural and psychological outcomes will be considered as well as the factors that relate to these outcomes. The second part of the thesis is the empirical paper, which focuses on describing the cognitive, behavioural and psychological outcomes of children who have been treated for brain tumours in infancy. These children have not received radiotherapy as part of their treatment and are all five years or more post-treatment. The empirical paper also examines factors that relate to behavioural and psychological outcomes and discusses possible interpretations of the findings as well as implications for future work. The final section of the thesis is the critical appraisal. This section was used to reflect on the process of developing the idea and method for the research presented in the empirical paper. It also includes an extended discussion of the limitations of the research presented in the empirical paper and the implications for future studies in this area.

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Part 1: Literature Review

Cognitive, behavioural and psychological outcomes in children treated
for brain tumours using surgery-only

Abstract

There is a sparsity of literature examining the outcomes of those treated for childhood brain tumours using surgery-only. Although several areas of significant long-term problems have been identified, such as deficits in executive functions and raised levels of behavioural and psychological problems, research so far has failed to consistently identify factors that predict outcomes. This makes it very difficult to make recommendations about how to lessen the impact of these cognitive, behavioural and emotional difficulties for this group of children. Nineteen studies that examine cognitive, behavioural and psychological functioning in this population were identified and are reviewed here.

Introduction

Childhood brain tumours occur in around 30 children per million in the UK each year. Over the past 40 years, survival rates have rapidly increased, with the five year survival rate currently reported to be as high as 65% in children diagnosed under the age of 16 (www.cancerhelp.org.uk). The fact that such a high number of children are surviving makes the long-term outcomes, in terms of physical and psychological functioning, all the more important.

Psychological research on long-term outcomes has tended to focus on cognitive functions, such as memory and attention, (Mulhern & Butler, 2004) and, to a lesser extent, behavioural and psychological functioning (Fuemmeler, Elkin & Mullins, 2002). These studies tend to report significant deficits in cognitive and behavioural functioning amongst long-term survivors, particularly those who received radiotherapy as part of their treatment (Fuemmeler et al., 2002; Mulhern & Butler, 2004). Much attention has been given to the deleterious effects of radiotherapy on long-term outcomes with studies showing that those who are younger at the time of treatment tend to be more affected and that these effects tend to become more evident as the children age (Hoppe-Hirsch et al., 1990; Mulhern, Hancock, Fairclough & Kun, 1992). Rather than being the result of a decline in skills over time research suggests that children treated using radiotherapy fail to learn at the rate of their peers, which results in decreasing IQ scores (which are age scaled) but stable, or slowly increasing, raw scores as they age (Palmer et al., 1999). Worse cognitive outcomes are associated with lower white matter volumes in the brains of children treated using

radiotherapy (Mulhern et al., 1999). Younger children are thought to be more at risk of cell damage and cell death as a result of radiotherapy, which impacts on the development of white matter (Stargatt, Anderson, Rosenfeld, 2002).

Although this is an important area of research, particularly as a large number of children diagnosed with a brain tumour receive radiotherapy at some point during their treatment, the result has been that outcomes in children treated using surgery and/or chemotherapy without adjunct radiotherapy have been largely neglected. The reality is that a large number of children are actually treated using a combination of two or more treatment methods, which makes it difficult to disentangle the effects of a single method. However, a significant proportion of children are treated using a surgery-only approach. In studies that compare those treated with radiotherapy (and often chemotherapy) with children treated with surgery-only results consistently point to the conclusion that outcomes are worse for the radiotherapy group. However, a large number of these studies fail to report the outcomes for children in the surgery-only group in relation to the normal population. Consequently, we can conclude that surgery-only children have better long-term psychological outcomes than those treated with radiotherapy and/or chemotherapy, but we cannot make firm conclusions about the outcome of surgery-only patients relative to the normal population. It is important to establish what their outcomes are in order to provide medical professionals with the necessary information when they are making treatment and rehabilitation decisions but also so that parents can be informed about realistic expectations in terms of their child's long-term functioning and quality of life.

Furthermore, examining outcomes in surgery-only patients allows us to gain

greater understanding of the links between cognitive and behavioural functioning and brain localisation. This is something that is difficult to do when a child has been treated using radiotherapy as it is known to have deleterious effects on normal cell growth and function in the whole of the brain (if treated with whole brain radiation) or in the area surrounding the tumour (if treated with focal radiation). This is also the case with chemotherapy as some drugs are known to have damaging effects throughout the brain rather than at the site of the tumour alone (Levisohn, Cronin-Golomb, & Schmahmann, 2000). Recently a small number of studies have examined long-term psychological outcomes in children diagnosed with brain tumours and treated with a surgery-only approach. These will be reviewed here.

The review will begin with an introduction to childhood brain tumours, including different types and locations of tumour, methods of treatment and possible complications arising from surgery. I will then review the findings of 19 papers that have included data on surgery-only outcomes.

Paediatric Brain Tumours

There are several types of brain tumour, each occurring in different cell and tissue types within the brain. These tumours differ in the rate at which they grow and in their malignancy, which impacts on treatment methods and prognosis. The location of the tumour also influences the chosen treatment method and prognosis in terms of brain functions affected. For example, when the brain tumour is found to be in the brain stem, radio- or chemotherapy may be used instead of surgery. This is due to the risk to life if the function of the brain stem, which is to control vital processes such as heart beat and breathing, is interrupted. Tumours are often described as

occurring in the cerebral hemispheres (left or right), cerebellum, or brain stem. However, some papers refer to tumours in the posterior fossa, which includes both brain stem and cerebellar tumours. The locations of these areas are shown in Figure 1 below. A brief description of the functions thought to be controlled by each is given in Table 1 below.

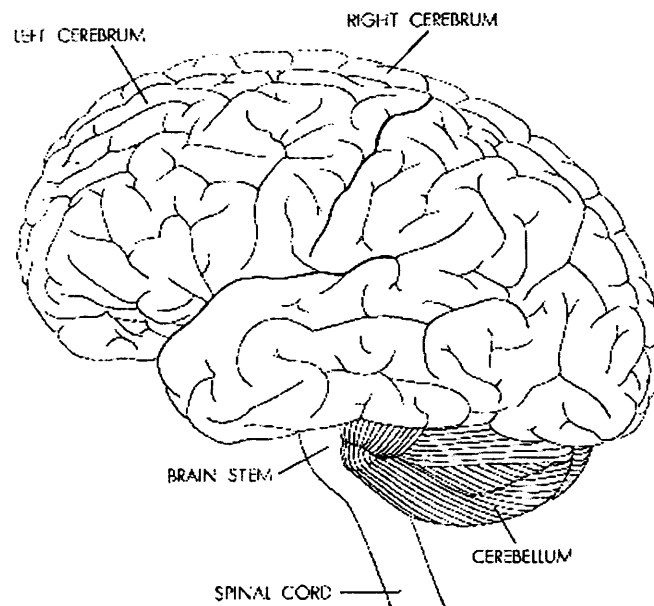


Figure 1 – Image of the brain (www.dyslexiaonline.com)

Table 1

Functions of the Cerebrum, Cerebellum & Brain Stem

Structure	Functions
Cerebrum	Higher cognitive functions such as reasoning, memory, perception, speech and language, attention, executive functioning and emotional experience and expression.
Cerebellum	Balance and coordination. Recent evidence also suggests a role in executive functions such as planning, initiation of action and inhibition.
Brain Stem	Life functions such as breathing, heart beat and swallowing.

In terms of types of tumour, the most common are astrocytomas which account for approximately 15-20% of childhood brain tumours (www.cancerindex.org).

Astrocytomas are so called because they originate in a type of glial cell called an astrocyte. There are several different types of astrocytomas, which are classified as low, intermediate or high-grade depending on their rate of growth. Low-grade astrocytomas are the most common. They are more likely to be treated using surgery-only and tend to have a better prognosis than the other types. One particular type of astrocytoma, is a pilocytic astrocytoma. These most often occur in the cerebellum and have a high survival rate. Craniopharyngioma's are another type of tumour that are often treated with surgery-only, and as a result are mentioned in several of the

studies reviewed here. They tend to occur above and around the pituitary gland, and due to this location, are often referred to as midline tumours. They account for around 6-8% of paediatric brain tumours (Shiminski-Maher & Rosenberg, 1990).

Other types of common childhood brain tumours include medulloblastomas, ependymomas, optic gliomas, choroid plexus papillomas, and meningiomas.

Paediatric brain tumours are treated using surgery, radiotherapy and chemotherapy. Some children are treated using one of the above, others require a combination of two or three treatment methods. Surgical treatment tends to involve a craniotomy in which the surgeon removes a piece of the skull and attempts to resect as much of the tumour as possible. Depending on the type and location of the tumour it can be impossible to resect all of it with the result that further surgery, or additional radio- or chemo-therapy, may be needed.

In terms of surgery-only patients it is worth noting that there are several factors that could feasibly impact on a child's outcome. Firstly, there are often variations in the approach taken, for example some children are treated using a frontal-surgical approach; others a fronto-temporal approach. Secondly, a large number of children presenting with a brain tumour show symptoms of hydrocephalus. This occurs as the result of cerebro spinal fluid accumulating in the ventricles, which causes them to enlarge and compress brain tissue. This leads to symptoms such as headache, vomiting, balance and coordination difficulties, cognitive impairment, irritability and slowing of development. The most common way of resolving hydrocephalus is to insert a shunt into the ventricles to drain excess fluid. Shunts may be required for several months, or even years, after surgery and can lead to infections which may

affect a child's brain functioning.

Review

The following criteria were applied when searching for articles:

Participants treated for brain tumours under the age of 18

Children treated using surgery-only with no subsequent radio or chemotherapy.

Papers focusing on long-term outcomes, rather than short-term (i.e. majority of the sample assessed at least 4 months after treatment).

(Note: papers that have included children treated with radio and/or chemotherapy as well as surgery-only will also be included, but only the surgery-only data will be reviewed.)

Databases searched were Medline (1950-2008), Embase (1980-2007) and PsychInfo (1970-2008). A search for articles that met the above criteria and included the terms "brain tumour/tumor" and "surgery", "cognitive", "behaviour/behavior" or "psychological" in the abstract or title produced a total of 19 relevant studies.

Table 2

Studies Reviewed

Author(s)	Sample size & age at testing	Age at treatment & time since treatment	Tumour type(s) and location(s)	Methodology	Cognitive outcomes	Behavioural outcomes	Factors relating to outcome
Aarsen et al. (2004)	23 participants aged 6 years 7 months -22 years 11 months.	Under 16 yrs old at treatment. Assessed 1.0-8.10 years after surgery.	All had cerebellar pilocytic astrocytoma. 9 had a vermal incision, 7 incision lateral of the vermis in the right hemisphere and 7 in the left.	Neuropsychological assessments using: Ravens, RAVLT & Rey Complex Figure Test, line bisection test, TMT, Verbal Fluency, WCST, WISC-R Mazes, Stroop Test, Cancellation Test. Observations and parental interviews using DSM criteria.	Significant deficits (as compared to norms) in: sustained attention, executive functioning, visual-spatial functions, visual-spatial memory.	65% (15) children showed some form of behavioural disturbance.	Maximum tumour diameter, hydrocephalus and time since surgery all relayed to outcome. No significant differences in outcome between children with tumours in the vermis, left and right cerebellar hemisphere.
Beebe et al. (2005)	103 children, aged 3 to 18 years at testing	Mean 108 days after surgery, range 30 days - 1 year.	Low-grade cerebellar astrocytomas. Split into 3 groups: cerebellar vermis (51), right cerebellar hemisphere (25), left cerebellar hemisphere (27).	Neuropsychological assessment using: WISC or WAIS, BTVMI & WRAT-R Parent interviews/questionnaires: CBCL.	Mean scores sig. below test means in terms of FIQ, PIQ, Spelling ($p<0.005$), arithmetic ($p<0.01$) & VIQ ($p<0.05$).	CBCL internalising significant impairment (55, mean of 50 $p=0.02$). No significant effect for externalising.	No relationship between test scores and gender, age, surgical approach, tumour location or time since surgery.

Berger et al. (2005)	Clinical group = 7 children, aged 9-17 years. Control group = 7 children matched for sex, age, education and IQ	1-11 years at surgery and at least 2.5 years after surgery.	All benign posterior fossa tumors. Either, astrocytoma grade I or II, pilocytic astrocytoma, or non-malignant cyst. None had transient post-operative mutism.	Computerised task switching paradigm.	Normal learning of task but clinical group exhibited “behavioural rigidity” when rapid behavioural changes were required.	6 out of 7 of clinical group had damage to vermis and right hemisphere. Authors suggest link between vermis involvement and task switching task difficulties.
Berger et al. (2005)	Clinical group = 8 children, aged 9-17 years at testing. Control group = 8 children matched for sex, age, IQ, SES & education.	1-11 at surgery and at least 2.5 years after surgery	All benign posterior fossa tumors. Either, astrocytoma grade I or II, pilocytic astrocytoma, or non-malignant cyst.	Motor and non-motor sequence learning using computerised serial reaction time tasks .	Clinical group did not differ significantly from control group in ability to learn sequences. However, they did find it more difficult to be flexible when task demands changed.	Authors link this to cerebellar functioning.

Cavazzuti et al. (1983)	8 single surgery only patients, 9 one or more surgeries plus radiation & 18 radiation plus conservative surgery. Mean age at testing was 17 years (range 14-25 years).	Average age at treatment 7.4 years for surgery only group. Mean follow-up period at time of testing as 10 years (range 1-19 years).	Craniopharyngioma's	Neuropsychological assessment using: WISC, WPPSI or WAIS, WMS or CMS, Corsi test, Rey-Osterrieth or Taylor complex figure tests, WCST, & TWF. Children under age of 4 were given BSID.	Group mean memory quotient, pair-associate learning, & immediate recall of passages were all significantly below norms, High level of perseverative responses on WCST. Immediate & delayed recall of figures did not differ significantly from norms.	4 out of 8 reported to have psychiatric disorders (rage attacks, hysteria, obsessive-compulsive neurosis, anxiety neurosis)	Link executive function problems to fact all treated with sub-frontal operations, plus hypothesise about role of damage to hypothalamus.
Hetherington et al. (2000)	20 surgery-only participants (11 males, 9 females) aged 10.8-31.3 years (Compared to 20 radiotherapy and chemotherapy treated medulloblastoma participants and 40 controls)	1.2-15.9 years at diagnosis and 5.0-21 years since diagnosis.	Posterior Fossa Astrocytoma's	Neuropsychological assessment using age appropriate Weschler IQ test, WMS or WRAML, Computer based tests of perception and estimation of time.	Mean IQ scores within average range. Only significant difference from controls was on test of general memory (p<0.01). Found deficits in short-duration perception, but not in estimation of long durations.	No correlations between IQ, memory, medical variables or experimental tasks.	

Karatekin et al (2000)	10 participants aged 8-21 years	Age at diagnosis not given. Average time between diagnosis and testing 1 year (temporal group), and 3 years (cerebellar group)	4 cerebella astrocytomas and 6 temporal tumours (4 arachnoid cysts, 1 astrocytoma and 1 craniopharyngioma)	Neuropsychological assessment using WAIS-R or WISC-III & WCST. Interviews with parents and review of medical records.	FSIQ's were in the normal (average-high average) range. Found deficits in executive function in children with cerebellar tumors.	Parents reported "increased distractibility, demoralization, heightened sensitivity about performance and lower frustration tolerance".	No significant difference in IQ's between cerebellar and temporal groups. ¾'s of cerebellar patients performed poorly on executive function tasks as compared to their IQ's (i.e 1-2 sd's lower). Only one patient in the temporal group showed a trend in this direction.
Konczak et al. (2005)	14 surgery only participants , aged 10-28 years and 14 healthy controls aged 11-28 years. (also compared to 8 children treated with chemotherapy and/or radiotherapy.)	1-17 years at surgery. Minimum 3 years post-surgery.	11 grade I astrocytomas, 1 grade II, 1 cavernoma, 1 plexuspapilloma.	Neuropsychological assessment using: Corsi's block tapping task & Wechsler's digit span.	No significant differences between surgery only patients and controls on tests of verbal and visuo-spatial memory.		

Maryniak & Roskowski (2005)	66 children aged 4 - 17 years.	Average age at surgery 6 years.	All had cerebellar pilocytic astrocytomas.	66 parents completed behavioural questionnaires	77% reported disturbances in initiation and realization of activities. 65% were noted to have problems in emotional regulation (including disinhibition, impulsivity and irritability).	No significant difference in outcomes between children with vermis versus cerebellar hemisphere tumours.
Meyer & Kieran (2002)	34 participant's aged 5-21 years.	2 weeks-5 years since treatment.	Heterogeneous tumour types and locations.	Semi-structured clinical interview with the patients and their parents.	56% reported some psychological adjustment problems. 35% symptoms of major depression/dysthymia, 9% symptoms of an anxiety disorder, 35% symptoms of disruptive behaviour disorder.	69% of those in the short term (2 weeks-1 year after treatment) group reported significant psychological problems as compared to 47% of long-term (1-5yrs after treatment) group.

Mulhern et al. (1999)	18 participants (surgery only) compared to a group of children with Medulloblastomas (treated with radio and chemo).	All aged under 21 at time of diagnosis and tested at least 1 year after completion of treatment.	All posterior fossa low grade astrocytomas	Neuropsychological assessment using age-appropriate Wechsler IQ test.	Mean IQ scores did not differ significantly from test norms.	
Richter et al. (2005)	12 children in the clinical group aged 9-19 years. 27 children in the control group aged 8-19 years.	Treatment between 1-13.4 years before testing	All cerebellar astrocytomas. 11 grade I, 1 grade II. 6 right hemisphere, 4 left hemisphere and 1 both.	Neuropsychological assessment using: letter-cancellation test, line bisection, AAT, HSET, computerised visual extinction task, verb generation task & syllable-repetition task.	Children in the clinical group did not have higher levels of aphasia or deficits in visuo-spatial functioning.	Left sided cerebellar lesions were related to increased errors on the letter-cancellation task.

Richter et al. (2005)	12 children in the clinical group aged 9-19 years. 27 children in the control group	Treatment between 1-13.4 years before testing	All cerebellar astrocytomas. 11 grade I, 1 grade II. 6 right hemisphere, 4 left hemisphere and 1 both. 9 out of 12 children had lesions that included the vermis.	2 raters ranked children on various dimensions thought to be representative of the cerebellar affective syndrome. Interviews with children and parents. The ADS-K was used to assess for depression.		Disagreement between raters. 9 children were not observed to have any problems in the dimensions covered. 7 children/parents reported either no changes or positive changes since treatment. 5 children reported to display psychological and behavioural problems.	No significant differences between those who reported negative changes and those who reported no changes/positive changes in terms of verbal involvement, mean lesion volume or hydrocephalus.
Riva et al. (1989)	7 children aged 6.8-14.7 years in the clinical group. 6 siblings or first cousins aged 6.1-14.6yrs old in the control group. (also compared with a group of 8 children treated for meduloblastoma's using chemo and radiotherapy)	4.8-8.3years at surgery and 0.4-7.1 years since surgery.	Posterior fossa astrocytomas.	Neuropsychological assessment using: WISC, TMT & CPT.	PIQ and FSIQ significantly lower than those of the controls. Significantly slower than controls on trails A (p=0.04) and B (p=0.04). No significant difference between clinical group and controls in prolonged computerized attention tests.		Authors hypothesise about the link between trails performance/attention and closeness of lesions to the ascending activating system in the brain stem.

Riva et al. (1998)	12 participants aged 6 years – 15 years 6 months	2-14 years at diagnosis, time since treatment, 7months - 9 years 3 months	Craniopharyngiomas	Neuropsychological assessment using WISC-R, Raven's test, Digit Span, BVRT, Cancellation Test & TMT Form A. Parents completed the PISC, frontal symptoms assessed using a guided questionnaire.	All but 1 patient had normal or above average IQ's and verbal and spatial memory. 3 children had difficulties (2s.d's or more below norm) on tests of attention and perceptual/motor ability.	10 patients were found to have an "inability to withstand frustration", 5 found to have "unmotivated fits of anger", 3 "moderate to severe emotional lability" Depression was commonly reported.	The following factors were assessed but none were significantly related to neuropsychological or behavioural outcome: no. of surgical interventions (1 vs>1), frontal vs fronto-temporal approach, mild vs severe visual deficit.
Shiminski-Maher & Rosenberg (1990)	15 patients and families Ages not given .	Age at diagnosis and time since treatment not given.	Craniopharyngioma's	Chart review and telephone interviews with children or parents covering neuropsychological dysfunction and psychosocial effects.	10 patients reported to have memory problems. 8 patients reported to have moderate – severe decline in academic performance.	5 patients displayed frontal symptoms. 4 patients and families had had counselling (1 for OCD, 3 for depression). Several parents mentioned emotional and behavioural changes.	Those with most academic problems had undergone more than one surgical procedure.

Steinlin et al. (2003)	24 participants aged 7.6-26.7 years	3.6-15.5 years at diagnosis, 2.1-18.25 years at follow-up	All located in the cerebellum. 19 pilocytic astrocytomas, 2 choroid plexus papilloma's, 1 astrocytoma (grade II), 1 gangliocytoma, 1 hemangioblastoma.	Neuropsychological assessment using HAWIK-R or HAWIE-R, TAP, VLMT, RVDLT, Stroop Test & ROCFT.	Mean group scores significantly below norms on tests of immediate memory, vocabulary, visual recall and recognition, selective and divided attention, processing speed, visuo-constructive skills, verbal fluency and interference.	No formal testing but 8/24 had diagnosis including three with severe attention deficitis, and others had selective mutism, phobia, anorexia, gambling addiction and uncontrolled temper tantrums.	FSIQ, vocabulary, digit span and figures scores all significantly lower in children with left compared to right sided cerebellar lesions. Seven of the eight children with behavioural/psychiatric problems had vermal lesions.
Yule et al. (2001)	16 children, ages not given.	Age at presentation was between 1-13yrs. Testing took place one year after end of treatment.	Astrocytomas. More than half were cerebellar, some were central midline supratentorial and the rest were either in the cerebral hemispheres or the cervical spinal cord.	Neuropsychological assessment using the WISC-III	Children treated with surgery alone had a median FSIQ of 81 (range 69-123).		Best predictor of IQ was having experienced a longer duration of symptoms of increased intracranial pressure before diagnosis and surgery.

AAT = Aachener Aphasietest, BSID = Bayley Scales of Infant Development, BTVMI = Beery Test of Visual-Motor Integration, BVRT = Benton Visual Retention Test, CPT = Continuous Performance Test, HSET = Hiedelberger Sprachentwicklungstest, PISC = Personality Inventory Scale for Children, TMT = Trial Making Test, TWF = Thurstone Word Fluency, RAVLT = Ray Auditory & Verbal Learning Test, ROCFT= Rey-Osterrieth Complex Figure Test RVDLT = Rey Visual Design Learning Test, VLMT = Verbal Learning Memory Test, WCST = Wisconsin Card Sorting Test

The reader should be aware that there was a degree of variability in the sample sizes of the studies reviewed, with over half of them having a sample size of 20 surgery-only patients or less. Small sample sizes are common in this area of research and are reflective of the low incidence rate of childhood brain tumours, which is even more restrictive if a researcher wishes to focus on a specific population such as children with posterior fossa astrocytomas. As a result, several of the studies reviewed were not able to perform statistical analysis on their data, which impacts on the validity of their results as well as our ability to make conclusions on the basis of their data. However, they are included in this review due to the small number of studies that have actually examined outcomes in this area and the fact that they can provide us with some information in terms of trends and areas that require further investigation.

The studies under review varied greatly in terms of the age at which treatment was given, time since treatment and age at time of study. Some papers did not report these details in full, for example, Aarsen, Van Dongen, Paquier, Van Mourik, and Catsman-Berrevoets (2004) report that the children in their sample were all less than 16 years of age at time of treatment but do not give the mean or range of ages. Of those that do report this information Meyer & Kieran (2002) included children with the least amount of time since treatment (2 weeks) and Steinlin et al. (2003) included participants with the most (18.25 years). Berger et al. (2005a), Berger et al. (2005b), Yule, Hide, Cranney, Simpson, and Barrett (2001) and Konczak, Schoch, Dimitrova, Gizewski, and Timmann (2005) all reported inclusion of children as young as one year old at the time of treatment. Konczak et al. (2005) also included participants aged 17 years at the time of surgery, which was the oldest reported in any of the

studies reviewed. The participants in Hetherington, Dennis and Spiegler's (2000) research were the oldest in terms of age at testing, with one being 31.1 years of age. In comparison Beebe et al. (2005) assessed children as young as 3.

Most researchers chose to focus on a specific group of patients, in terms of tumour type and location, whereas some included a heterogeneous group. Overall, seven studies focused exclusively on astrocytomas located in the cerebellum, three studies included children who had had astrocytomas but in a variety of different locations, three focused on different types of cerebellar tumours, three reported data on children who had been treated for different tumour types occurring in a variety of locations, and three focused exclusively on children who had had craniopharyngiomas.

Cross-sectional designs were employed across all studies reviewed. In terms of the methods used for data collection, a large percentage of the studies reviewed included some neuropsychological assessment, such as the Weschler scales for IQ and memory. A large number also included interviews, with both parents and children, whereas others utilised questionnaires such as the Child Behaviour Checklist (CBCL). Methods adopted varied depending on the aims of the study. Seventeen of the studies aimed to collect data on cognitive outcomes and ten reported information about the behavioural and psychological outcomes for these children.

Cognitive Outcomes

Of the seventeen studies that included information about cognitive outcomes fifteen utilised one or more standardised neuropsychological tests. The remaining two studies chose to rely on semi-structured interviews with parents and patients, (Meyer & Kieran, 2002) and a review of medical notes plus telephone interviews with parents and patients (Shiminski-Maher & Rosenberg, 1990), to assess neuropsychological status. A summary of the number of studies that included data on different cognitive abilities is shown in Table 3 below.

Table 3

Number of Studies Reporting Data on Specific Cognitive Functions

Cognitive Function Assessed	Number of Studies
Intellectual Quotient	11
Memory and Learning	9
Attention	5
Executive Functioning	5
Visuo-spatial/visuo-constructive abilities	4
Motor function/speed	4
Perception & estimation of time	1
Verbal Fluency	1

Intellectual Quotient Out of the eleven studies that report data on intellectual

quotient, nine found that the mean full scale IQ score of the participants was in the average range (90-110) or above. The remaining study (Yule et al. 2001) reported the median, rather than the mean and gave this as 81 with a range of 69-123. Three of the studies compared their participants' IQ scores to the test norms, two compared them to a control group of healthy children and five did not compare them to norms or compared them to a group of children treated using radiotherapy. Out of the three studies which compared the children's performance to test norms, two reported no significant difference in overall IQ scores (Mulhern et al, 1999; Steinlin et al, 2003), although one reported a significantly lower score in digit span and vocabulary sub-test scores as compared to norms (Steinlin et al., 2003). The other study (Beebe et al., 2005) reported that performance and full scale IQ scores were significantly lower than norms, whereas verbal IQ scores were not. There are two possible reasons for this difference. Firstly, the number of participants in Beebe et al's (2005) study was much higher (91 participants as compared to 24 and 18) than in the other two. It seems possible that the finding of significant differences in Beebe et al.'s (2005) study may be the result of a larger sample size, which results in more power.

Mulhern et al. (1999) and Steinlin et al's (2003) studies are not as reliable as their sample sizes were much smaller, which may have led to type 2 errors. Secondly, the participants in Beebe et al's (2005) study were assessed within the first year post-treatment. In comparison the children in the other studies were all more than one year post-treatment. Research suggests that most of the recovery from brain injury occurs in the first year (Yeates et al., 2002) and so the results reported here may be due to the fact that the children in Beebe et al's (2005) sample had not yet fully recovered in terms of cognitive functioning, whereas the children in Steinlin et al.(2003) and Mulhern et al's (1999) studies had. A similar pattern was noted in the two studies

that compared the participants scores to healthy controls with one reporting that they were significantly lower (Riva et al., 1989) and one reporting that there was no significant difference (Hetherington et al). This may be explained by the fact that Riva, Pantaleoni, Milani and Belani (1989) included children who were only 0.4 years post-treatment whereas the participants in Hetherington et al.'s (2000) study were all five years or more post-treatment.

Collectively these studies suggest that, as a group, the mean IQ scores for these children are within the average range. However, it seems that there may be some impairment in functioning within the first year or so following treatment, which then appears to resolve as time since treatment increases.

Memory Of the nine studies that considered memory functioning, five reported some form of memory problems and four reported no problems. Of the five studies that reported problems, only Hetherington et al. (2000) found that the general memory index scores (which include both visual and verbal memory items) of children who had been treated for cerebellar astrocytomas was significantly below the scores of healthy controls. Two studies reported that participants' verbal memory scores did not differ significantly from test norms but their ability to recall a figure was significantly below the expected level (Aarsen et al., 2004; Steinlin et al., 2003). Cavazzuti, Fischer, Welch, Belli and Winston (1983) reported contrasting results, with their participants showing significant difficulties on verbal memory tests, such as recall of names and paired-associates learning, but immediate and delayed figure recall that did not differ from test norms. This contrast may be the result of differences in tumour location, as Cavazzuti et al.(1983) focused exclusively on

children who had craniopharyngioma's, which occur in the pineal region, whereas Steinlin et al.(2003) and Aarsen et al. (2004) focused on children who had been treated for cerebellar tumours. Shiminski-Maher & Rosenberg (1990) did not formally assess memory functioning but found that 10 out of 15 children and/or parents reported having memory problems that were having a significant impact on functioning in terms of school and activities of daily living.

The four studies that reported no problems with memory functioning were less methodologically sound. Only one assessed both visual and verbal memory and compared them to test norms (Ronning, Sundet, Due-Tonnessen, Lundar, & Helseth, 2005) but their small sample size makes their findings questionable as it may have been too small to detect a difference. Riva et al.(1998) reported data from a similarly small sample and did not compare the scores to norms or a control group. They found average or above average performance in all but one participant on tests of verbal and spatial memory.

Berger et al.(2005a) and Konczak et al.(2005) investigated learning of sequences, a very specific area of memory, and both reported no significant impairments in the performance of brain tumour survivors as compared to healthy controls.

Overall, methodologically stronger studies tended to find significant memory difficulties in participants who had been treated for childhood brain tumours. Interestingly, tumours in the cerebellum appear to be linked to visual, but not verbal, memory deficits. This links with the findings of Schmahmann & Sherman (1997)

who describe a cerebellar cognitive affective syndrome that is characterised by, amongst other things, deficits in visual memory. The opposite pattern was found in one study (Cavazzuti et al., 1983) that examined outcomes in those treated for craniopharyngioma's, which do not occur in the cerebellum. Two studies examined learning of sequences and both reported no significant problems in the brain tumour versus control group.

Attention Four of the five studies that assessed attention found significant difficulties in brain tumour survivors as compared to norms (Steinlin et al., 2003; Aarsen et al., 2004; Ronning et al., 2005) or healthy controls (Riva et al., 1989). The fifth study was conducted by Riva et al. (1998), who did not perform statistical analyses on their data but reported that 25% of their sample performed two standard deviations or more below the mean on tests of attention.

There was some variation in the types of attention assessed, for example Steinlin et al. (2003) chose to focus on selective and divided attention whereas Aarsen et al. (2004) assessed sustained attention. There was also some variation in the methodology used, with some researchers choosing to employ well validated tests such as the PASAT (Ronning et al., 2005) whereas others developed computerised tests of attention themselves (Riva et al. 1989).

Overall, attention was consistently found to be a problem in all of the studies that assessed it, irrespective of the type of attention assessed or the methods used. This suggests that those who have been treated for childhood brain tumours, using a surgery-only method, have significant difficulties with attention.

Visuo-Spatial Abilities Three studies included assessment of visual-spatial abilities, using tasks such as the Rey-Osterrieth complex figure test (Steinlin et al., 2003), line bisection (Aarsen et al., 2004 & Richter et al., 2005b) and the cancellation test (Richter et al., 2005b). Steinlin et al.(2003) and Aarsen et al.(2004) reported significant visuo-spatial problems for brain tumour survivors as compared to test norms. Richter et al. (2005b) found no significant differences in visuo-spatial abilities between the brain tumour group and controls but did note that the clinical group had difficulties in neglect tasks and that their results almost reached the level for significance for difference from controls. Although there have not been many studies that have investigated visuo-spatial abilities, results so far appear to suggest that long-term survivors have difficulties in this area.

Executive Functioning Executive functioning is a broad term that includes abilities such as initiation of activities, planning, organisation and impulse control. Executive functioning deficits are consistently reported in the literature on this group of brain tumour survivors. Seven out of seven studies that assessed executive functioning reported problems. Aarsen et al.(2004), Ronning et al.(2005) and Steinlin et al.(2003) found significant executive function deficits in brain tumour survivors as compared to published norms. Riva et al.(1998), Cavazutti et al. (1983) and Karatekin, Lazareff and Asarnow (2000) did not perform statistical analysis on their data but noted a high level of perseverative responses in their samples. Five of the studies employed neuropsychological tests as a measure of executive functioning whereas the other (Maryniak & Roszkowski, 2005) relied on the questionnaire responses of parents and psychological examination of the children. They found that

77% were experiencing problems with initiation and realisation of activities and 65% were having difficulties in emotional regulation such as disinhibition, impulsivity and irritability. The evidence supporting the presence of long-term executive functioning deficits is consistent across all six studies in this area.

Other cognitive functions Studies in this area have also noted significant deficits in brain tumour survivors' performances on tests of processing speed (Ronning et al., 2005 & Steinlin et al., 2003) and verbal fluency (Steinlin et al., 2003) as compared to test norms. Hetherington et al. (2000) also noted significant deficits in their samples' short-duration perception, but not long-duration, as compared to a control group.

Correlates/Predictors of Cognitive Outcomes

Fifteen of the seventeen studies that examined cognitive outcomes also investigated correlates and/or predictors of these outcomes. Three of these studies (Hetherington et al., 2000; Konczac et al., 2005; Yule et al., 2001) reported on correlates of outcome, but in the whole of their sample (i.e. children also treated with chemotherapy and radiotherapy) rather than surgery alone. For this reason their findings will not be reported in this section of the review.

In the twelve remaining studies there was some variability in the factors considered in relation to cognitive outcomes in children who had undergone surgical treatment for a brain tumour. A summary of the factors considered and the number of studies examining each factor is given in Table 4 below.

Table 4

Number of Studies that Investigated Each Factor

Factors investigated	Number of studies
Tumour location	6 studies
Age	5 studies
Time since tumour	4 studies
Number of surgical interventions	2 studies
Hydrocephalus/pre, peri & post surgical scores	3 studies
Surgical approach	2 studies
Visual deficits	1 study
Presence of a shunt	1 study
Tumour size	1 study

Tumour location Of the six studies that reported on the relationship between tumour location and cognitive outcome, five focused on the effects of tumours within different areas of the cerebellum and one examined the differences in outcome between children who had tumours in the temporal lobes and those who had tumours in the cerebellum. At this point it is worth noting that clinicians and researchers often refer to tumours located within the cerebellum as being in the left cerebellar hemisphere, right cerebellar hemisphere or vermis. These locations are shown in Figure 2 below.

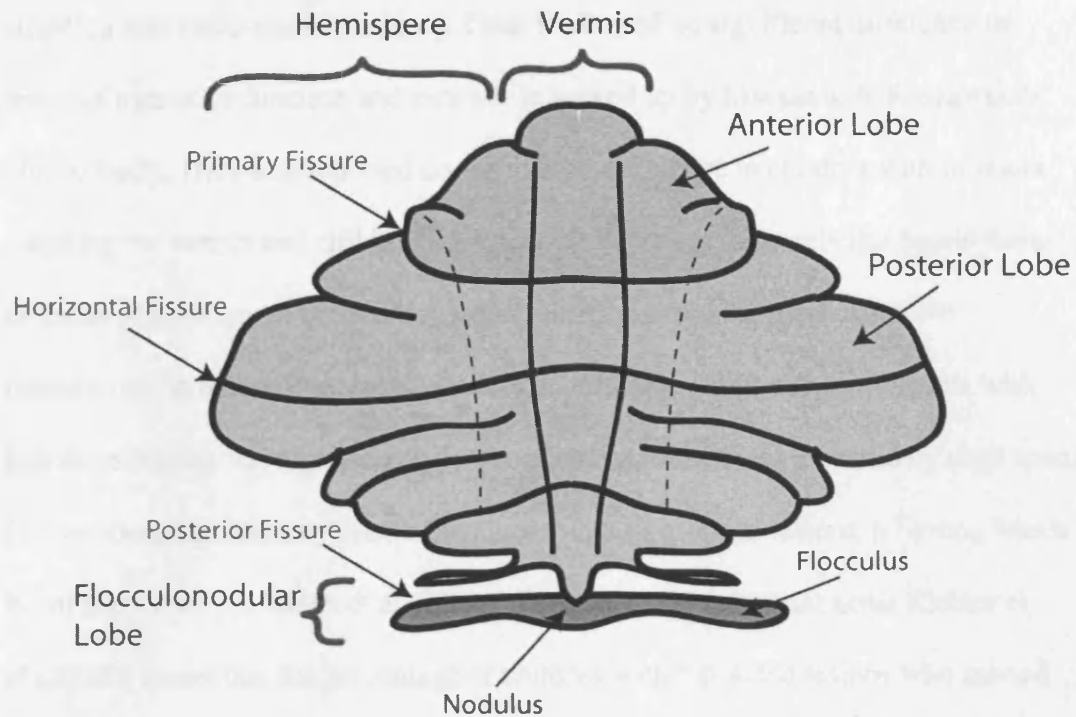


Figure 2 – Illustration of the cerebellar hemisphere and vermis (en.wikipedia.org)

In terms of the relationship between IQ and tumour location within the different areas of the cerebellum, Steinlin et al reported that those participants with left-sided cerebellar lesions had significantly lower scores on tests of full scale IQ and vocabulary than those with right-sided cerebellar lesions. They also noted that IQ scores were lower in those patients who had suffered vermal atrophy or had undergone a vermal resection, although these differences were not statistically significant. In contrast, Beebe et al. (2005) found no significant difference in verbal, performance or full scale IQ, or academic achievement when they compared children with lesions in the vermis, right cerebellar, and left cerebellar hemispheres. Aarsen et al. (2004) also reported finding no significant differences in terms of outcome and location in the vermis, right and left sided cerebellar hemispheres. However, they did not assess IQ, choosing to focus on executive function, visual-spatial skills, sustained

attention and visuo-spatial memory. Their finding of no significant difference in terms of executive function and location is backed up by Maryniak & Roszawski's (2005) study. They also reported no significant difference in children with tumours effecting the vermis and children with tumours effecting the cerebellar hemispheres in terms of their scores on questionnaires aimed at assessing their executive functioning. In terms of memory, Steinlin et al.(2003) report that participants with left-sided lesions had significantly lower working memory (as assessed by digit span) and visuo-spatial memory scores than those with right-sided lesions, a finding which is not supported by Aarsen et al.(2004). In terms of visuo-spatial skills Richter et al.(2005b) found that the percentage of children with left-sided lesions who missed letter-cancellation targets was higher than those with right (50% vs. 33.3%) but that deviations in line-bisection tasks were more obvious in those with right-sided lesions. Karatekin et al.(2000) compared children who had had cerebellar tumours to those whose tumours had been in the temporal lobe. Although they found no significant differences in IQ scores between the two groups they did find that those in the cerebellar group performed more poorly on a test of executive functioning than those in the temporal group.

The majority of studies that investigated the role of tumour location appear to suggest that there is no statistically significant link to cognitive outcomes. Evidence in terms of executive function is consistent between two studies. However, contrasting results were found in terms of the relationship between tumour location and IQ, visuo-spatial skills and memory, making it difficult to make any firm conclusions. This may be due to participant factors such as differences in length of time since treatment between participants included in each study. More research on

the link between tumour location and cognitive outcome are needed to allow for more definite conclusions to be made.

Age Five studies examined the relationship between age and cognitive outcome. Of these, two reported no relationship and three reported a significant relationship or a trend to significance between age and functioning. In terms of the studies that reported a significant relationship, findings seem to suggest that those children who were younger at the time of treatment tend to have better cognitive outcomes. Shiminski-Maher & Rosenberg (1990) noted that those participants who reported functioning at or above the expected level for their age, in terms of academic achievement, were aged 12 or younger at the time of surgery. They concluded that younger age at the time of surgery seemed to be linked to better outcomes, although they did not perform any statistical tests to confirm this hypothesis. Ronning et al. (2005) reported similar findings, with those children who were younger at time of treatment showing a trend to have higher IQs, although it should be noted that this did not reach statistical significance. This may be a result of the small sample size of 12 surgery-only participants in this study, which is unlikely to have provided the power required to obtain a statistically significant result. In comparison, Steinlin et al. (2003) compared children aged 3.5-6.5 years with those aged 7-9.5 years and those aged 10-15.5 years at treatment. They found that children in the middle age group tended to have more difficulties across IQ sub-tests, but particularly in verbal areas. They also had slightly more problems with memory and learning. However, it should be noted that the only difference that was statistically significant was on the information sub-test, with children in the older age group performing significantly better than those in the middle age group.

Overall current findings in this area appear to suggest that children who are younger at the time of treatment have better outcomes in terms of cognitive functioning. This is in line with current understanding of brain plasticity, which suggests that the degree of plasticity, and therefore the potential for recovery, is highest in early childhood (Stiles, 2000).

Time since treatment Four studies examined the relationship between time since treatment and cognitive outcome with mixed findings. Aarsen et al. (2004) reported a significant relationship between performance on tasks of sustained attention and time since surgery. Meyer & Kieran (2002) noted that 40% of children who were two weeks to one year after surgery reported academic problems as compared to 29% of those who were one year to five years after surgery. In contrast to these results Beebe et al.(2005) and Hetherington et al.(2000) found no significant relationship between cognitive outcome and time since treatment. Of note is the fact that Beebe et al.(2005) assessed all of their participants within the first year after treatment. The consequences of this being that, relative to participants in other studies, all of the children were a similar length of time post-surgery, making any differences between them difficult to detect. The participants in Hetherington et al's (2000) study were assessed 5-21 years post-treatment. Evidence from studies that have examined recovery in children following traumatic brain injury suggests that this may be too long after treatment for recovery to be still underway. For example, Yeates et al.(2002) found that significant recovery, in terms of neuropsychological functioning, occurred in the first year following brain injury, but then reached a plateau.

Collectively findings in this area suggest a significant relationship between time since treatment and cognitive outcomes in the first few years after surgery, but not once the child is five years post-surgery. This is in line with research which suggests that brain recovery after injury reaches a plateau at around the one year mark.

Number of surgical interventions Two studies considered the effects of multiple surgical interventions on cognitive and academic functioning. Riva et al.(1998) reported that cognitive test scores did not correlate with the number of surgical interventions. Shiminski-Maher & Rosenberg (1990) found that multiple surgical procedures were common in those children who were experiencing academic difficulties, although they did not perform statistical tests on their results.

Other factors In terms of other factors, two studies investigated the link between pre-surgery hydrocephalus and cognitive functioning, and one investigated the link between pre, peri and post-surgical scores (which included presence of hydrocephalus) and cognitive outcome. Two of these found no correlation (Beebe et al., 2005 & Richter et al., 2005b) and the other (Aarsen et al., 2004) reported a significant relationship between severe hydrocephalus and lower scores on the Rey Complex Figure Test (copy version). Two studies also looked at the relationship between surgical approach and outcomes (Riva et al., 1998 & Beebe et al., 2005). Both reported no statistically significant relationship. Other factors that were found to be related to cognitive outcome included longer symptoms of intracranial pressure before treatment (Yule et al., 2001), presence of a shunt (Ronning et al., 2005), maximum tumour diameter (Aarsen et al., 2004), presence of a severe visual deficit and signs of frontal dysfunction (Riva et al., 1998).

Behavioural & Psychological Outcomes

Ten of the studies reviewed included some data on behavioural and/or psychological outcome. Various methods were used to obtain information about the children's behavioural and psychological functioning, including the use of interviews (4 studies), questionnaires (3 studies), assessments or observation of the child (3 studies), presence of psychiatric diagnoses (3 studies) and psychotherapy/counselling attendance (2 studies).

Of the ten studies reviewed only one (Beebe et al., 2005) performed any statistical analysis on their behavioural data, which makes it difficult to make definite conclusions about behavioural and psychological outcomes in this group of children as compared to the normal population.

Studies that utilised the interview method included that of Meyer and Kieran's (2002). They found that 56% of their sample reported some psychological adjustment problems, 35% had symptoms of major depression/dysthymia, 35% had symptoms of disruptive behaviour disorder and 9% reported symptoms of an anxiety disorder. Meyer & Kieran (2002) note that prevalence of depressive and disruptive disorders are much more frequent in their sample than in the normal population (where levels are estimated to be 6.2% and 10.3% respectively) but that prevalence of anxiety disorders is not. Several children and parents reported emotional and behavioural changes, such as "aggressive compulsive behaviour" and "labile affect" in Shiminski-Maher & Rosenberg's (1990) study. Karatekin et al.(2000) also found that a high number of parents reported behavioural and emotional difficulties

including “increased distractibility, demoralisation, heightened sensitivity about performance and lower frustration tolerance”. At this point it seems worth noting the limitations of the interview method. Firstly, interviews are not standardised because the questions and psychological symptoms covered vary from study to study, as do the terms used to describe them. It is not clear what exactly is meant by Karatekin et al’s (2000) use of the term “demoralization” and to what degree this is similar to, or different from, Meyer & Kieran’s (2002) “major depression”. This makes it difficult for us to make general conclusions based on several studies in this area. Furthermore, a lack of standardisation in interviews means that we cannot reliably say whether the rates of psychological problems reported by parents and children is higher than what we could expect in the normal population. Asking participants about psychological symptoms is likely to lead to them reporting any problems that they have noted, whether of a clinically significant level or not.

Riva et al.(1998), Beebe et al.(2005) and Maryniak and Roszkowski (2005) utilised questionnaires to assess behavioural and psychological functioning in their samples. Maryniak & Roszkowski (2005) also chose to “psychologically examine” their participants. Beebe et al. (2005) utilised the Child Behaviour Checklist in their research. This is a well normed questionnaire with good reliability and validity for assessing symptoms of various psychological and behavioural problems of childhood. Problems are divided into those of an internalising nature, such as anxiety and depression, and those that are externalising in nature, such as aggressive and rule-breaking behaviour. Beebe et al.(2005) found that in a sample of 71 children treated for cerebellar astrocytomas, the average internalising index score on the Child Behaviour Checklist was significantly higher than the mean of the normative sample,

whereas the externalising index score was not.

Riva et al. (1998) asked parents to complete the Personality Inventory Scale for Children and to complete a guided questionnaire to assess frontal symptoms. 10 out of 12 children were found to have an “inability to withstand frustration”, five experienced “unmotivated fits of anger”, three displayed “moderate to severe emotional lability” and three were found to have “behavioural characteristics of a frontal type, including lack of flexibility in mental and learning abilities”. Depression was also a common finding in their sample, although they did not statistically analyse this data or comment on any differences from rates in the normal population. Maryniak & Roszkowski (2005) also report findings of problems in functions that are often linked to the frontal lobe, for example 77% of their sample reported “disturbances in initiation and realization of activities” and 65% were found to have problems regulating their emotions, such as “disinheriting, impulsivity and irritability”.

A further methodological issue that presents itself in all the interview and questionnaire based studies above is the reliance on child and parent reports. It is known that, following a life threatening illness, parents in particular can become overly anxious and alert to potential difficulties in their child. The result of this may be that parents of children who have had brain tumours over-report difficulties. Therefore it is useful to get multiple-perspectives on a child’s behaviour and psychological functioning, for example by asking class teachers to complete questionnaires and/or interviews. Unfortunately multiple-perspectives on the childrens’ behaviour and psychological functioning were not considered in any of the

studies reviewed here.

Three studies (Aarsen et al., 2004; Maryniak & Roszkowski, 2005; Richter et al., 2005a) observed or psychologically assessed the child, which allows the researcher to form some opinions about the child's behavioural and psychological functioning that are not entirely based on parent reports. Richter et al.(2005a) chose to have two raters rank children on various behavioural and psychological dimensions, as well as asking parents and children if they had noticed any emotional changes since tumour treatment. 42% of children and parents reported problems, which included "aggressive and depressive behaviour, reduced self-confidence, insecurity, fear, introversion, somatic symptoms and mental imbalance". The conclusions of the two raters were not consistent, with one rating three out of 12 children as having difficulties and the other none. The results of Aarsen et al.(2004) and Maryniak & Roszkowski's (2005) studies are reported above. Again, there are validity issues with this method. Observing children in a strange environment over a short period of time is unlikely to provide a valid and reliable assessment of their psychological functioning.

Of the studies that reported on the number of children with a psychiatric diagnosis, Steinlin et al.(2003) found that 33% had a diagnosis and that these diagnoses included severe attention deficits, selective mutism, phobias, anorexia, gambling addiction and uncontrolled temper tantrums. Aarsen et al.(2004) also reported on psychiatric diagnoses following clinical interviews and observations. They found that 65% of their sample showed some form of behavioural disturbance and that 30% of these could be classified under DSM-IV criteria as overanxious

disorder, alcohol abuse, Asperger syndrome, ADHD or PTSD. Cavazzuti et al.(1983) found that 50% of their sample had psychiatric disorders, which included rage attacks, hysteria, obsessive-compulsive neurosis and anxiety neurosis.

Two studies (Richter et al., 2005a & Shiminski-Maher & Rosenberg, 1990) reported rates of psychotherapy and counselling as 17% and 24% respectively. No discussion of whether this is an abnormal level in the normal population was included.

Correlates of Behavioural Outcomes

Of the ten studies that included information on behavioural and psychological outcomes, six included some discussion of factors relating to outcome. As with cognitive outcomes, the most common factor considered was tumour location. In terms of the behavioural and psychological outcomes, studies tended to focus exclusively on the role of the vermis, which has been linked to behaviour and psychological disorders in research on both adults (Lee et al., 2007) and children (Riva & Giorgi, 2000).

Vermal involvement Of the five studies that considered the role of vermal involvement, three were able to run statistical analysis on their data (Maryniak & Roszkowski, 2005; Richter et al., 2005a; Beebe et al., 2005). Although Richter et al.(2005a) noted that five out of seven children in whom negative changes were reported had vermal involvement, statistical tests showed that there were no significant differences between those children with and without vermal involvement, in terms of behavioural and psychological problems. In fact, they noted that four

children, who had larger vermal lesions, were not reported to have any emotional or behavioural difficulties. Maryniak & Roszkowski (2005) and Beebe et al.(2005) also found no significant difference between reported and observed psychological problems in children with lesions involving the vermis and those with lesions in the cerebellar hemispheres. Steinlin et al.(2003) did not carry out statistical analyses but reported that seven out of eight children in their sample who had psychiatric diagnoses had vermal involvement. This would suggest that vermal involvement is linked to psychological problems and Steinlin et al.(2003) conclude that their findings support the “postulation of Schmahmann and Sherman (1998) of a cerebellar limbic system within the vermis”. However, this conclusion is misleading as 17 out of 24 of their overall sample had vermal involvement, but ten of these children had no psychiatric diagnoses. Aarsen et al.(2004) found that 15 out of 19 children with a vermal tumour had problems with “affect regulation”, whereas the four children with hemispheric rather than vermal tumours did not. It is difficult to make firm conclusions on the basis of this finding due to the small number of children in the hemispheric group.

Collectively these findings do not support earlier studies, which suggested links between behavioural and psychological functions and vermal lesions in both brain tumour and non-brain tumour populations.

Other factors Although Cavazzuti et al.(1983) did not perform statistical analysis on their results, they hypothesise that the executive function problems found in their sample may have been related to the fact that all of the children were treated using a frontal surgical approach. Riva et al.(1998) found that “frontal signs” and

“unmotivated fits of anger“were not correlated with type of surgical approach. They also report no significant correlation with number of interventions. However, the fact that there were only 12 participants in their study makes it difficult to reject the possibility of a type two error occurring. More studies are needed before we can make any definite conclusions about the relationship between surgical approach and number of interventions, and behavioural and psychological outcomes in children treated for brain tumours using surgery-only.

In terms of time since treatment, Meyer & Kieran (2002) found that 69% of children interviewed two weeks to one year after treatment reported significant psychological problems, compared to 47% of children in the long-term (one to five years post treatment) group. Unfortunately, they did not perform statistical tests to assess whether this difference was significant. Finally, other factors that were found not to significantly relate to outcome include lesion volume, hydrocephalus (Richter et al., 2005a), age, sex and time since treatment (Beebe et al., 2005).

Summary

In terms of cognitive outcomes, almost all of the studies reported mean IQ scores within the average range. However, some of these studies did report differences between sample means and normal controls or test means in terms of index or sub-test scores. It appears that worse outcomes were found in those children who were one year post-treatment or less, which suggests that functioning improves with time. Several studies reported memory functioning impairments, with either verbal or visuo-spatial memory deficits being present depending on the type and location of tumours in the sample studied. Significant deficits in attention and executive

functioning were a common finding. Problems in visuo-spatial abilities, processing speed, verbal fluency, perception and estimation of time were also found in children treated for brain tumours with surgery only, although more studies are needed.

In terms of factors relating to cognitive outcome, several of the studies examined the effect of location of the tumour in the vermis, left or right cerebellar hemisphere. The results of these studies are inconclusive as some show significant differences in cognitive functioning depending on tumour location (e.g. Steinlin et al., 2003), whereas other do not (e.g. Beebe et al., 2005). Age was also found to be a factor by some researchers, with younger time at treatment appearing to lead to better rather than worse outcomes. Time since treatment was also reported to link to outcome with shorter time since treatment being related to worse outcome.

In terms of behavioural and psychological outcomes, the studies reviewed suggest significant difficulties. Studies that reported on rates of psychiatric diagnoses suggest that, in this sample, between 30-50% have a diagnosis. In comparison, current UK estimates suggest that around 10% of children and 20-25% of adults suffer from psychological problems (www.mind.org.uk). Signs of depression were commonly reported across studies, whether results were based on questionnaire responses or semi-structured interviews. Several studies also made reference to difficulties that could be classified under the term “emotional regulation”, for example labile affect (Shiminski & Rosenberg, 1990), inability to withstand frustration (Riva et al., 1998), aggressive behaviour (Richter et al., 2005a) and impulsivity and irritability (Maryniak & Roszkowski, 2005). However, methodological issues, such as the failure of the majority of studies to employ

standardised, well validated measures, means it is difficult to make definite conclusions about behavioural and psychological outcomes in this population, other than to say that a high level of problems are being reported and further investigation is required.

Factors relating to behavioural outcome were similar to those included in the literature on cognitive outcomes. Verbal involvement in behavioural and psychological functioning has been suggested in several recent studies (Lee et al., 2007 & Riva & Giorgi, 2000). However, the studies reviewed here do not support this finding. It appears that, although children with verbal lesions do have behavioural and psychological problems, children without these problems also have verbal involvement. Furthermore, none of the studies reported a statistically significant difference between those with verbal lesions and those without, in terms of behavioural and psychological outcomes. One study also reported higher rates of behavioural and psychological problems in children who had received treatment less than one year ago than in those who were more than a year post-treatment.

Of interest is the work of Schmahmann & Sherman (1998), who have identified what they term the “cerebellar cognitive affective syndrome” in adults. Their findings suggest that damage to the cerebellum leads to impairments including “executive functioning, ... abstract reasoning and working memory.....personality change with blunting of affect or disinhibited and inappropriate behaviour.” This conception of psychological deficits associated with cerebellar damage is consistent with the findings of Richter et al.(2005a) and Maryniak & Roskowski (2005), who report that children treated for cerebellar tumours exhibit aggressive behaviour and

impulsivity and irritability in the long-term. Also, Karatekin et al.(2000) found that those with tumours in the cerebellum made more errors on executive function tasks than those who had been treated for temporal tumours. However, the fact that other studies, which did not include those with cerebellar damage, found similar behavioural and emotional problems suggests that tumour location in the cerebellum is not the only factor in these outcomes. Several of the studies in this review focused exclusively on children treated for craniopharyngiomas, which occur in the region of the pituitary gland. These tumours are noted to lead to compression of surrounding structures such as the pituitary gland and the hypothalamus (Shiminski-Maher & Rosenberg, 1990). Riva et al.(1998) hypothesise that damage to the hypothalamus, which has connections with the limbic system and the frontal lobes, is linked to the emotional and behavioural problems reported by their sample.

Methodological Critique

As noted in this review, many studies in this area have significant methodological limitations, which impacts on our ability to make conclusions about the cognitive, behavioural and psychological outcomes for this group of brain tumour survivors. The impact of these methodological issues is discussed below.

As highlighted earlier, over half of the studies reviewed report data on sample sizes of 20 participants or less. This is an issue as it increases the likelihood of type two errors occurring. It also makes it difficult for the researcher to use statistical tests to analyse the data, which restricts ability to make conclusions on the basis of the study. To overcome these problems some researchers chose to include children with different tumour types in different locations and children of different ages. However,

this can result in further methodological issues as it can also be difficult to make conclusions about outcomes in such heterogeneous samples. Fortunately, over half of the studies reviewed here chose to focus on participants who had had tumours in a specific location, for example the cerebellum, or of a particular type, for example astrocytomas. This makes their samples more homogeneous, making it easier to draw conclusions about outcomes in terms of children treated for tumours of specific types, in specific locations using surgery only. Other studies purposefully included children with tumours in different locations in order to compare outcomes between the different groups. This can be informative when thinking about the differences in function associated with different areas of the brain.

There is a great deal of variation, both within and between the studies reviewed, in terms of age at treatment, time since treatment and age at assessment. For example, Yule et al.(2001) assessed the outcomes of tumour survivors who ranged in age from 1 to 13 years at the time of the treatment. Including children treated at a range of different ages can be useful if the study aims to examine the differences in outcome in terms of age at treatment. However, several studies, such as the one by Yule et al.(2001), include children of a wide range of ages without commenting on differences or similarities between those treated at different ages. Of those studies that did investigate the effects of age at treatment on outcome, three out of five concluded that there was a relationship. If age at treatment affects outcome then it seems important for studies that include children treated at such different ages to take this into account.

In terms of time since treatment, there was also a high level of variability both

within and between studies with one study including children only two weeks after surgery (Meyer & Kieran, 2002) and others assessing some survivors 18 years after treatment (Steinlin et al., 2003). The literature reviewed here appears to suggest that levels of functioning can improve over time, particularly in the first year or so following treatment. For this reason it seems more useful to assess children after several years to allow for changes due to brain plasticity, or at several time points following treatment in order to understand the process of changes in functioning. Although some of the studies reviewed did assess children who were several years post-treatment, none repeated the assessments at different time points. All of the studies reviewed were cross-sectional, with the result that it is difficult to understand how outcomes progress and if there are improvements or declines in functioning over time.

Another issue is that the nature of this sample makes it impossible to get baseline assessments. Even if children were assessed before surgery their presentation would be confounded by the presence of a brain tumour. Parent and child retrospective reports may not be reliable, making it difficult to draw firm conclusions about cognitive and behavioural changes in the child following tumour occurrence and treatment. In an attempt to overcome this, researchers often employ the use of a control group (which can be matched on variables such as age and socio-economic status) or choose to compare participant test results to test norms. In the studies reviewed, seven utilised a control group and five compared participants' performance to test norms.

Future Directions for Research

This review has highlighted several future directions for research. These include further investigation of cognitive, behavioural and psychological outcomes for this group of brain tumour survivors, as the research in this area is still sparse and sometimes contradictory. Further research into the factors relating to outcome is also needed, in terms of methodologically stronger studies. In terms of improving the validity and consistency of studies in this area, the following methodological points should be considered:

- Larger sample sizes are needed to increase the power of studies in this area. This may mean that more multi-centre research trials are undertaken.
- Use of well validated, standardised measures, particularly in terms of research into behavioural and psychological outcomes.
- Statistical analysis to compare brain tumour survivors' data with that of test norms or control groups.
- Multiple-perspectives on behaviour and psychological functioning, for example the use of teacher versions of well validated questionnaires.
- Longitudinal follow-up data at different time points.
- Use of more homogeneous samples in terms of age at treatment, time since treatment, tumour type and location, and age at assessment.
- Statistical comparison to check for differences between groups if homogeneous samples are not used.

High levels of cognitive, behavioural and psychological problems are being reported in this population but studies have so far failed to provide any conclusive

evidence as to the factors relating to poorer outcome. It is interesting that none of the studies reviewed investigated the relationship between neuropsychological functioning, such as memory and executive function, and behavioural and psychological outcome. Research in other areas has found links between internalising problems and cognitive flexibility (Motipara-Chavan, 2008) and memory and social problem solving (Goddard, Dritschel & Burton, 1996), making this an important area of investigation.

Conclusions

Nineteen studies that included data on children treated for brain tumours using a surgery-only method were reviewed. Long-term deficits in memory, attention and executive functioning were consistently found. High levels of behavioural and psychological problems were reported by children and their parents. Factors relating to outcome were investigated in some of the studies but the results are inconclusive. Studies in this area suffer from methodological weaknesses such as very small sample sizes. Methodologically strong research into outcomes, and particularly predictors of outcomes, is needed for this group of children.

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Part 2: Empirical Paper

Behavioural & psychological outcomes in children treated for brain
tumours in infancy

Abstract

This study aimed to document behavioural and psychological outcomes in children treated for brain tumours with surgery and / or chemotherapy during infancy and to investigate the relationship between tumour/treatment factors, neuropsychological functioning and behavioural and psychological outcome. Participants were 30 children aged 7 – 14 years who had been diagnosed and treated for brain tumours under the age of three years. Neuropsychological assessment included tests of cognitive functioning (WASI), memory (CMS) and executive functioning (BADS-C). Parents' and teachers completed a measure of behavioural and psychological functioning (CBCL). IQ and memory functioning scores were within the normal range but executive function was significantly below the expected level. Parents and teachers reported high levels of behavioural and psychological difficulties in these children. Lower socio-economic status, male gender, more than one surgical intervention, motor problems and speech and language difficulties were found to be related to clinical range behavioural and psychological problems. Further research in this area is needed to allow for development of appropriate support packages for those who are most at risk.

Introduction

Childhood brain tumours occur in around 30 children per million in the UK each year and are the second most common childhood cancer, accounting for around 24% of cases (www.statistics.gov.uk). Over the past 40 years, survival rates have rapidly increased, with the five year survival rate currently reported to be as high as 65% in children diagnosed under the age of 16 (www.cancerhelp.org.uk). It is well documented that those who have received treatment for childhood cancer are at risk for long-term problems such as physical disabilities, hormonal imbalances, sensory impairments, and cognitive deficits (Mulhern & Butler, 2004). The fact that such a high number of children are surviving makes the long-term outcomes, in terms of physical and psychological functioning, all the more important.

In terms of neuropsychological outcomes, a review of the literature on childhood brain tumour outcomes reveals a wealth of research examining cognitive functioning in survivors. These studies tend to report significant deficits in cognitive functioning amongst long-term survivors, particularly those who received a higher dose of radiotherapy and/or where younger at the time of diagnosis and treatment (Mulhern & Butler, 2004). It is thought that younger children are especially vulnerable to the effects of radiotherapy (Mulhern, Merchant, Gajjar, Reddick, & Kun, 2004). Findings such as these have led to new guidelines on the treatment of brain tumours in young children in order to minimise their exposure to radiotherapy. If possible radiotherapy is not given to children under the age of 3. Other options include delaying until the child is older, usually by using surgical procedures and chemotherapy to control disease progression, or by administering very focal doses of radiotherapy to the tumour area, rather than the whole brain (Mulhern et al., 2004).

Since the development of these guidelines there have been few studies examining outcomes for children treated in infancy without radiotherapy. A review of the literature reveals only one study, by Moore, Ater & Copeland (1992) that report data on the cognitive performance of children treated under the age of 3 without radiotherapy. Their findings are encouraging, with mean IQ and memory scores being within the normal range of functioning. Other studies, that have examined cognitive outcomes in older children treated without radiotherapy, also tend to report normal range IQ functioning (Mulhern et al., 1999; Steinlin et al., 2003). In these samples data on memory outcomes is less uniform with some studies reporting significant deficits in specific areas of memory functioning (Aarsen, Van Dongen, Paquier, Van Mourik, & Catsman-Berrevoets, 2004; Steinlin et al., 2003) and others finding no difference in performance compared to test norms (Ronning, Sundet, Due-Tonnessen, Lundar, & Helseth, 2005; Riva et al., 1998). Research examining executive functioning in older children treated using surgery-only consistently points to significant deficits, which include problems with perseveration, initiation of activities and impulsivity (Aarsen et al., 2004; Ronning et al., 2005; Steinlin et al., 2003).

Historically, cognitive outcomes have received the most attention in the literature on childhood brain tumour survivors. However, the importance of behavioural and psychological outcomes for these children is being recognised to a much greater extent. A number of studies have examined outcomes, and factors relating to outcome. Fuemmeler, Elkin & Mullins (2002) conducted a comprehensive review of studies examining behavioural, emotional and social adjustment in

survivors of childhood brain tumours. They noted that several studies had found significant difficulties for these children in terms of internalising problems, such as anxiety and depression, but that high levels of externalising problems, such as aggressive behaviour and rule-breaking, were rarely reported. Few of these studies tried to determine risk factors for psychosocial and behavioural difficulties. For those studies that did, the factors that emerged as being significantly related to outcome included demographic and family factors such as lower socio-economic status, younger maternal age, single parent families and families that had experienced a greater number of negative life events, as well as illness related factors such as longer time since diagnosis or treatment, being younger at the time of diagnosis and disfigurement. It is worth noting at this point that studies reporting a longer time since diagnosis as significantly related to worse behavioural and psychological outcome tended to include children treated using radiotherapy in their samples, which is known to lead to increasing neurological sequelae over time. Studies examining the relationship between time since treatment and functioning in children treated without radiotherapy have tended to report lower levels of functioning for those within the first year since treatment compared to those more than one year post treatment (e.g. Meyer & Kieran, 2002). The improved outcome for these children over time is likely to be related to brain plasticity and the fact that the brain is known to make the most recovery during the first year following injury before level of functioning reaches a plateau. Some of the studies also found tumour location (supratentorial rather than infratentorial) and tumour type (medulloblastoma rather than astrocytoma) significantly related to behavioural and psychological outcome. However, Fuellmeyer et al.(2002) note that those children with tumours in the supratentorial region and/or with medulloblastoma's were more likely to have

received radiotherapy making it difficult to draw any definite conclusions about the relationship of tumour location and/or type to outcome. Fuemmeler et al.(2002) conclude that studies examining links between tumour location and psychological outcome have not been able to disentangle the effects of treatment (particularly cranial radiotherapy) and therefore their “approach to localisation makes examination of adjustment related to location quite difficult and the findings relatively meaningless”. They call for further research to focus on the links between neurological damage, neuropsychological deficits (such as memory and executive functioning) and psychosocial outcome.

Very few published studies have examined the links between neuropsychological factors and behavioural and psychosocial outcome in children who have received treatment for a brain tumour. Of those that have Mulhern, Carpentieri, Shema, Stone & Fairclough (1993) found that lower IQ was significantly associated with social and behavioural problems. Holmquist & Scott (2002) examined behavioural and social outcomes in children who were 3 years post-treatment. They reported that certain types of chemotherapy, IQ, verbal fluency, verbal memory and verbal learning abilities all accounted for a significant amount of variance in behavioural functioning. Nassau & Drotar (1997) hypothesise that the link between cognitive impairments and psychosocial and behavioural functioning could be related to a diminished ability to attend to, encode and interpret social cues as well as difficulties ‘accessing alternative behavioural responses’ in social situations.

As documented above, children who receive treatment for a brain tumour are at increased risk of long-term physical disabilities and sensory impairments. This could

potentially have important consequences for their psychological well-being. Studies with a variety of populations consistently report higher levels of behavioural and psychological problems in children who have motor difficulties, visual impairments or speech and language deficits (Davis, Ford, Anderson & Doyle, 2007; Lavigne & Faier-Routman, 1992; van Daal, Verhoeven & van Balkom, 2007). Recent studies have shown that children who have motor problems as a result of a central nervous system disorder or disease are at increased risk of behavioural problems (Hendriks, De Moor, Oud, Franken, & Savelberg, 2001), making this an important factor to consider.

In conclusion, it is clear that there is a gap in the research that examines psychological and behavioural outcomes for children who have received treatment for a brain tumour. Since treatment protocols for brain tumours in young children were altered to minimise the use of radiotherapy, there appear to have been no studies examining behavioural and psychological outcomes in those children diagnosed and treated for brain tumours under the age of three. This is an important group to study as research examining neuropsychological outcomes consistently points to a younger age at time of diagnosis as a significant risk factor for deficits (Mulhern et al., 2004). Furthermore, children diagnosed under the age of 3 are unlikely to have received cranial radiation and are therefore a good group to study as conclusions can be drawn about the relationship between treatment/tumour related factors, neuropsychological functioning and behavioural and psychological outcome without the confounding effects of radiation therapy.

Aims & Hypotheses

The aims of the current study will therefore be to:

- Document the longer-term behavioural and psychological outcomes of children treated for brain tumours under the age of 3.
- Investigate the relationship between neurological factors, neuropsychological functioning and behavioural and psychological outcome.

The main hypotheses will be:

- Young children who have been treated for brain tumours will exhibit high levels of internalizing, but not externalizing, problems.
- Young children who have been treated for brain tumours will have significantly lower executive functioning scores than would be predicted on the basis of available test and questionnaire norms.
- Deficits in cognitive functioning will be significantly related to worse behavioural and psychological outcomes.
- Location of tumour will be significantly related to behavioural and psychological outcomes.
- Physical and sensory impairments will be significantly related to worse behavioural and psychological outcomes.

Method

Participants

The research was undertaken at Great Ormond Street Children's Hospital and was based in the Psychosocial & Family Services department. Children who were diagnosed with a brain tumour at Great Ormond Street Hospital between the years of 1994 and 2002, and who were aged three or under at the time of diagnosis, were approached to participate in this study. Participants were aged 7-14 at the time of the study and were five years or more post-treatment. Children were excluded from the study if: i) they had received cranial radiotherapy iii) they did not speak English iv) they were receiving treatment for a recurrence. In total 44 children matched the study criteria. We were able to contact 38 of these, and 30 agreed to participate. Non-participants did not differ significantly from participants in terms of age $t(43) = .58$, $p > .05$, or gender $\chi^2(1, N = 44) = 0.17$, $p > .05$. Characteristics of participants are shown below in Table 5.

Table 5

Characteristics of Participants

	Mean (S.D.)	Range
Age at diagnosis	1.69 (0.84)	0.02-2.83
Age at testing	11.08 (2.23)	7-14.80
Time since diagnosis	9.39 (2.59)	5.10-14.22
	Frequency	Percentage
Gender:		
Male	17	56.7%
Female	13	43.3%
Ethnicity:		
White	22	73.3%
Other	8	26.7%
Socio-economic Status:		
Lower Working Class	4	13.3%
Upper Working Class	14	46.6%
Lower Middle Class	10	33.3%
Upper Middle Class	2	6.7%
Tumour Type:		
Astrocytoma	13	43.3%
Choroid Plexus	5	16.7%
Papilloma	4	13.3%
Ependymoma	8	26.7%
Other		
Tumour Location:		
Posterior Fossa	17	56.7%
Other	13	43.3%
Treatment:		
Surgery-only	20	66.7%
Surgery & chemotherapy	10	33.3%
Number of Surgical Interventions:		
One	21	70%
More than one	9	30%
Hydrocephalus:		
Present	19	63.3%
Absent	11	36.7%
Epilepsy*:		
Present	2	6.7%
Absent	28	93.3%
Surgical Complications:		
Present	21	70%
Absent	9	30%

*Judged to be present in children who are currently taking medication to control epilepsy and/or have had a seizure in the past two years.

Procedure

Children who met the inclusion criteria were identified and their parents were sent information packs about the study. They were contacted two weeks later and asked if they would like to participate. Families who agreed to participate in the study were assessed at Great Ormond Street Children's Hospital or at home. Parents were asked to complete the CBCL whilst neuropsychological testing was undertaken with their child. Assessments lasted between 2-3 hours. Parents were asked to give written consent for the child's class teacher to be sent the teacher version of the CBCL. If these were not returned, teachers were given one reminder telephone call. Copies of information sheets, invitation letters and teacher letters can be found in appendix I, II, and III.

The recruitment and testing procedure is outlined in Figure 3 below.

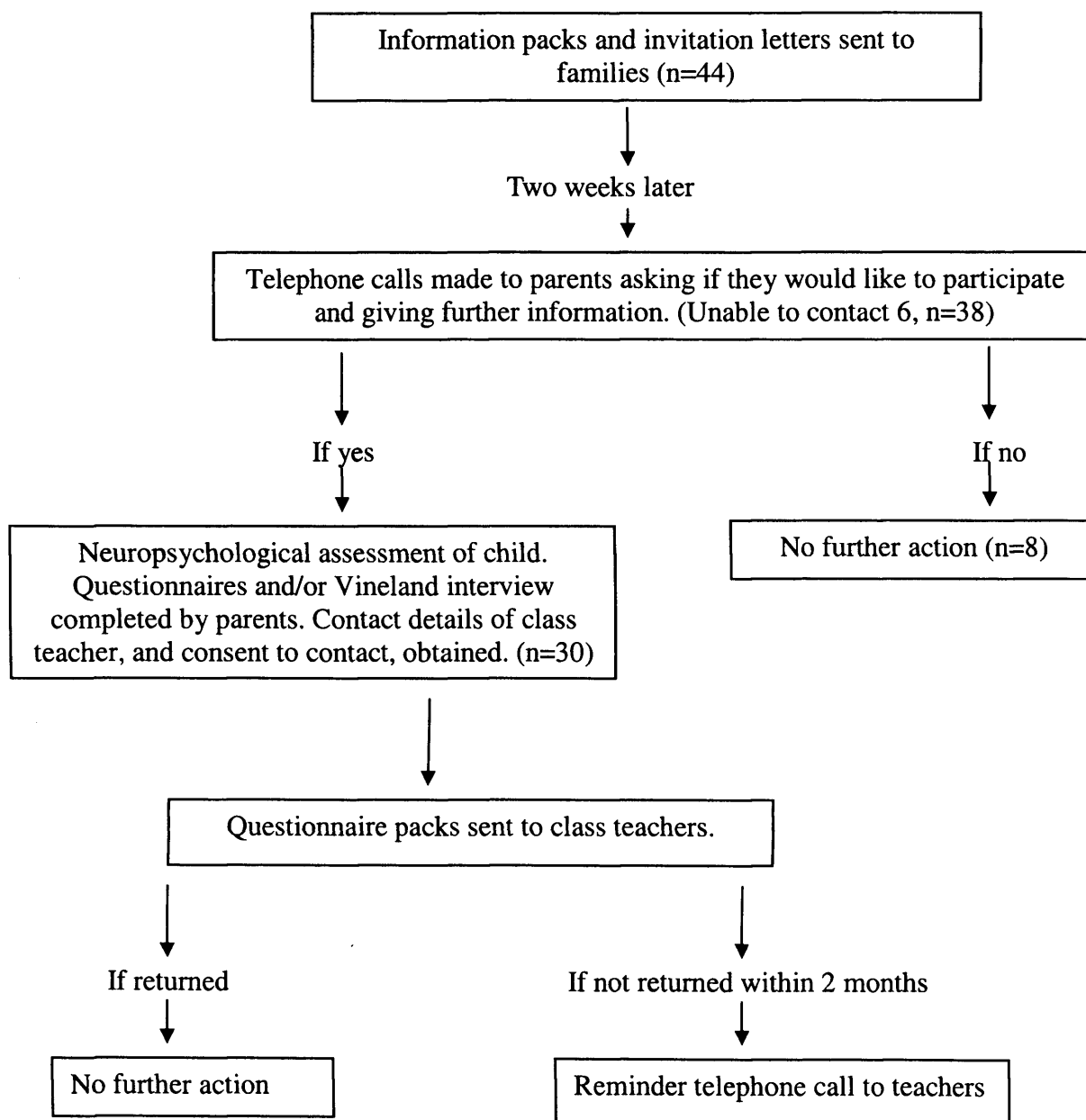


Figure 3 – Flow diagram to show the recruitment and testing procedure

Measures

Wechsler Abbreviated Scale of Intelligence (WASI) – This is a well-validated and reliable brief IQ test that has norms for people aged 6 to 89 and includes both verbal and performance IQ scales. A total of four sub-tests are administered. Two of these tests (Vocabulary and Similarities) are designed to assess the child's ability for verbal expression and grasp of verbal concepts and abstract reasoning. The sum of the scores obtained on the verbal sub-tests produces a verbal intelligence quotient. The two performance subtests (Block Design and Matrix Reasoning) consist of tasks that require the child to 'do' things (e.g. puzzles) within a time limit. These tests help to assess visual and spatial organisation and perceptual ability. The sum of the scores obtained on the performance sub-tests produces a performance intelligence quotient.

Children's Memory Scale (CMS) – This test is a valid and reliable measure of learning and memory functioning in children. It consists of eight indexes, which include: immediate and delayed recall of visually presented items (Visual Memory Immediate and Visual Memory Delayed Indexes), immediate and delayed recall of verbally presented information (Verbal Memory Immediate and Verbal Memory Delayed), recognition of verbally presented information after a delay (Verbal Memory Delayed Recognition), recalling and sequencing of verbally presented information (Attention/Concentration), ability to learn new verbal or visual information presented over a series of trials (Learning), overall learning and memory

ability (General Memory). Norms are available for children aged 5 to 16 years.

Behavioural Assessment of Dysexecutive Syndrome for Children (BADS-C) – A neuropsychological test that assesses executive functioning, including flexibility & perseveration, novel problem solving, sequencing, using feedback, planning, impulsivity and the ability to follow instructions. Four sub-tests were used in this study; the Key Search Test, Zoo Maps Tests 1 & 2 and the Six Parts Test. Several studies have supported the reliability and validity of this test and norms are available for children aged 7 - 16 years of age.

Child Behaviour Checklist (CBCL) – This questionnaire assesses behavioural and psychological functioning in 4-18 year olds. Multi-rater versions are available and this research included the use of both parent and teacher questionnaires. The CBCL is a valid, reliable and comprehensive measure that includes several scales for the assessment of a child's competence, in terms of activities, academic and social performance and syndrome scale scores which are based on DSM criteria. It also includes eight problem scales, Anxious/Depressed, Withdrawn/Depressed and Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-Breaking Behaviour and Aggressive Behaviour, which make up a Total Problems score. Three of the scales, Anxious/Depressed, Withdrawn/Depressed and Somatic Complaints also combine to make up an Internalising Problems score and two of the scales, Rule-Breaking Behaviour

and Aggressive Behaviour, make up an Externalising Problems score. For the purpose of this research the problem scale scores were judged to be the most useful and so the other scales were not included in the analysis.

Parents were also asked questions relating to their socio-economic status, whether the child has any psychiatric diagnoses, if the child had any deficits in motor functioning, vision or speech and language problems. Medical records were used to determine tumour location and type, treatment received, presence/absence of surgical complications or hydrocephalus, and age at diagnosis.

Ethical Considerations

The Great Ormond Street Ethics committee granted approval for the study. See Appendix VI for a copy of the approval letter.

Design & Statistical Analysis

The study can be split into 2 parts: Part 1 was largely exploratory and aimed to identify what the effects of brain tumour treatment are on the behavioural and emotional functioning of the children. This was measured via their performance on the neuropsychological tests administered, and the questionnaires completed by their parents and teachers. Analysis involved the use of descriptive statistics and t-tests to compare the participants' scores to population norms given for each test/questionnaire. Part 2 aimed to examine the relationship between neurological and neuropsychological variables and behavioural and psychological functioning using appropriate statistical tests.

Results

Visual inspection and preliminary analyses were conducted to check for normality of data. Data for all of the cognitive variables was continuous and met the assumptions for parametric analysis. Child Behaviour Checklist data was bi-modal, rather than continuous, with the result that non-parametric analysis was conducted on this variable. Outcomes of the sample in terms of physical impairments, psychiatric diagnoses, educational and social functioning are given in Table 6 below.

Table 6

Outcomes of the Sample

Factor	Frequency (%)
Motor Problems	58%
Speech and Language Difficulties	29%
Visual Problems	45%
Registered as Disabled	33%
Psychiatric/Neurodevelopmental Diagnoses (or currently undergoing assessment for suspected disorder). *	20%*
One close friend or less.	38%
Special Educational Placement	13%
Statement of Educational Needs	27%

**Including five children with diagnoses of /undergoing assessment for Autistic Spectrum Disorders/Aspergers Syndrome, one with ADHD, one diagnosed as having Oppositional Defiant Disorder and one with Gross Developmental Delay.*

It should be noted that two of the participants were unable to complete neuropsychological testing due to significant physical and cognitive impairments.

This meant that 28 children completed an IQ assessment. One further child was unable to complete the memory and executive functioning assessments, and two refused to complete the memory assessment. This meant that 27 children completed an assessment of executive functioning and 25 children underwent memory testing. We were able to obtain parent perspectives on the behavioural and psychological functioning of all 30 children. The teachers of 18 of the children completed behavioural and psychological questionnaires.

Part 1 – Descriptive Statistics and T-tests to assess divergence from test norms.

Cognitive Outcomes. Mean group scores are given in Table 7 below. One-sample t-test were performed and showed that IQ and memory index scores did not differ significantly from the test means of 100. Executive functioning, as assessed by the BADS-C, was significantly below the test mean of 100 $t(26) = -3.22, p=.003$.

Table 7

Mean group scores by area of cognitive functioning

Area of Cognitive Functioning	Mean (S.D)	Range
WASI IQ Scores (n=28)		
Full Scale IQ	98.96 (16.12)	63-131
Verbal IQ	100.29 (15.36)	69-136
Performance IQ	98.57 (15.90)	59-127
CMS Memory Scores (n=25)		
General Memory	98.40 (22.90)	54-138
Visual Immediate	98.44 (17.15)	57-131
Visual Delayed	99.36 (18.99)	57-138
Verbal Immediate	98.84 (19.62)	60-127
Verbal Delayed	97.24 (18.35)	57-131
Attention & Concentration	97.68 (19.95)	57-134
Delayed Verbal Recognition	97.00 (16.41)	60-125
Learning	99.40 (16.66)	72-134
BADS-C Executive Function Score (n=27)		
BADS-C Total Scaled-Score	87.88 (19.53)**	range 49-133

*p<.01, **p<.005

Behavioural & Psychological Outcomes. The percentage of parents and teachers reporting clinical range CBCL problem scale scores are shown in Table 8 below. The CBCL normative sample suggests that the rate of clinical range behavioural and psychological problems in the normal population is around seventeen-eighteen percent.

Table 8

Percentage of Clinical Range Scores Reported by Parents and Teachers

CBCL Problems Scale	Parent Version Percentage	Teacher Version Percentage
Total Problems	43%	32%
Internalising Problems	47%	47%
Externalising Problems	40%	26%

Chi-squared analysis indicated a significant difference in the frequency of clinical range Total Problem scores $\chi^2(1, N = 18) = 6.92, p = .02$, as reported by parents and teachers.

Part 2 – Factors relating to behavioural and psychological outcome

Visual inspection of the data revealed a bi-modal, rather than continuous, distribution in terms of CBCL Total Problems scores. This can be seen in the graph (Figure 4) below.

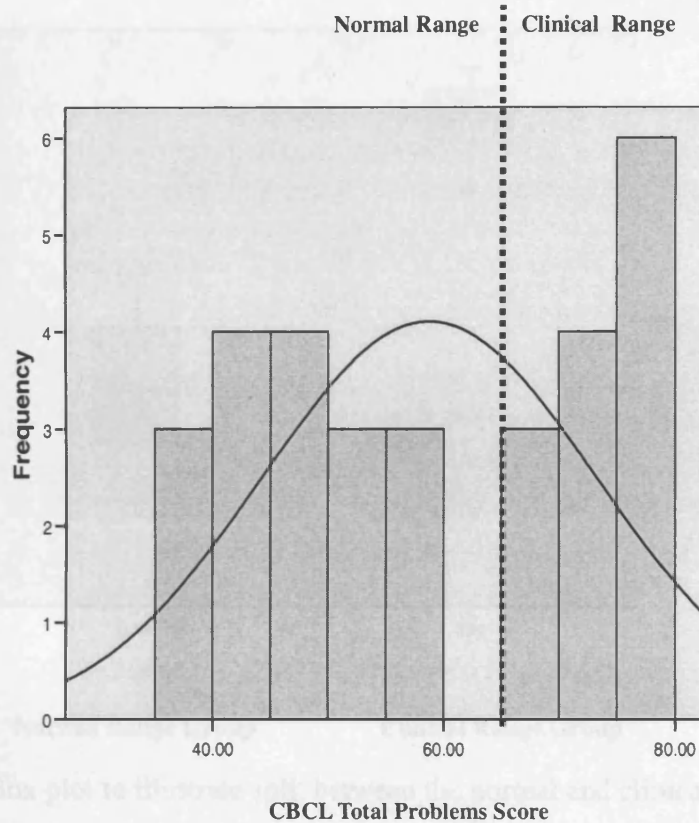


Figure 4 – Graph to show the distribution of CBCL Total Problems Scores

This pattern of results is interesting as it appears that the participants can be split into two distinct groups, consistent with the CBCL cut off point for clinically significant behavioural and psychological difficulties. One group of children are clearly functioning within the clinical range (scores of 65 or more) and the other group are clearly functioning within the normal range (scores of less than 60). The box plot below (Figure 5) further illustrates this distinction.

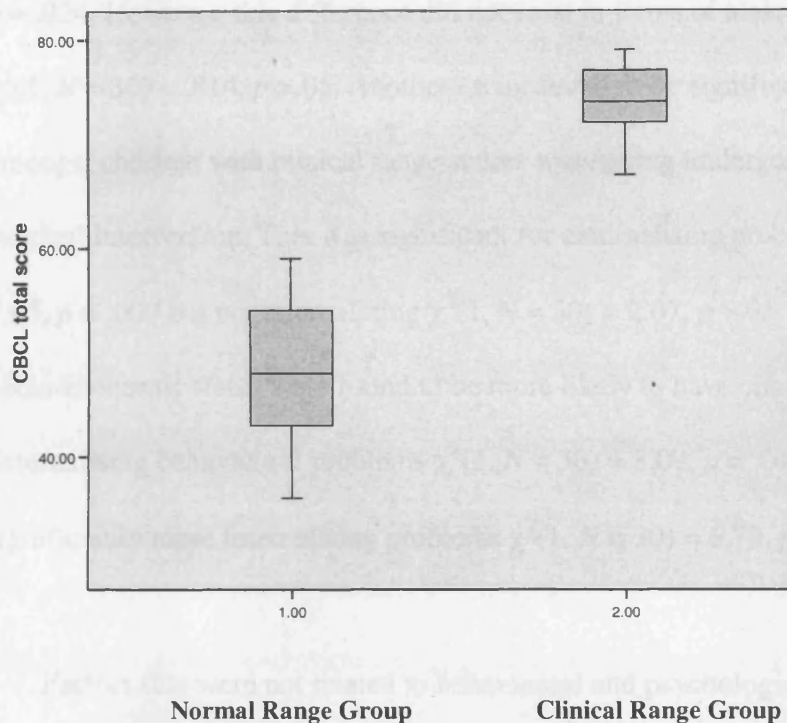


Figure 5 – Box plot to illustrate split between the normal and clinical range groups

As a result of this bi-model distribution the most appropriate method for statistical analysis was to split the sample into two groups (clinical versus normal) and use exact chi-squared tests to assess associations with presence/absence of characteristics such as physical impairments and tumour location with clinical range CBCL scores. T-test were used to assess differences between those with clinical and normal range CBCL scores in terms of continuous variables such as IQ, memory and executive functioning.

Children with clinical range CBCL scores had a higher frequency of reported motor problems $\chi^2(1, N = 30) = 9.98, p = .002$ and speech and language difficulties $\chi^2(1, N = 30) = 6.212, p = .018$. In terms of gender, the frequency of male children within the clinical range internalising scores group was significantly higher than the number in the normal range internalising scores group $\chi^2(1, N = 30) = 5.13,$

$p = .024$. However, this difference did not exist in terms of male externalising scores $\chi^2(1, N = 30) = .814, p >.05$. Another factor found to be significantly more frequent amongst children with clinical range scores was having undergone more than one surgical intervention. This was significant for externalising problems $\chi^2(1, N = 30) = 7.65, p = .009$ but not internalizing $\chi^2(1, N = 30) = 2.07, p >.05$. Those of lower socio-economic status were found to be more likely to have clinical range externalising behavioural problems $\chi^2(1, N = 30) = 8.09, p = .04$ but did not have significantly more internalising problems $\chi^2(1, N = 30) = 6.79, p > .05$.

Factors that were not related to behavioural and psychological outcome included tumour location (infratentorial vs supratentorial) $\chi^2(1, N = 30) = 0.07, p >.05$, reported visual problems $\chi^2(1, N = 27) = 0.00, p >.05$, Full Scale IQ $t(26) = 1.30, p >.05$, General Memory $t(23) = 0.05, p >.05$ and Executive Functioning $t(25) = 0.32, p >.05$.

Discussion

The results of this study show that the majority of children who were treated for brain tumours during infancy have good outcomes in terms of general intellectual functioning and memory. This differs from the results of studies that have examined cognitive outcomes in young children treated using radiotherapy, which tend to report significant deficits in IQ and memory functioning (Moore et al., 1992) but is consistent with the results of research examining outcomes in older children treated using surgery-only (Mulhern et al., 1999; Ronning et al., 2005; Steinlin et al., 2003). As a group, children treated for brain tumours in infancy were found to have significant deficits in executive functioning, supporting our hypothesis and previous

research that reports executive function deficits in older children treated using surgery-only (Aarsen et al., 2004; Ronning et al., 2005; Steinlin et al., 2003).

Forty three percent of the sample of children treated for brain tumours showed clinical range behavioural and psychological difficulties, as reported by their parents. This is a very high number, particularly when compared to the CBCL normative sample in which only seven percent of children were reported to have clinical range behavioural and psychological problems. Moreover, our results suggested that internalising problems, such as anxiety and depression, as well as externalising problems, such as rule-breaking and aggression, are issues for this group of children. The finding that children treated for brain tumours have such high levels of internalising problems supports our hypothesis concerning these children's adjustment. However, the higher rates of externalising behaviour problems in these children, than would be expected on the basis of test norms, is surprising and was not predicted. Furthermore, this latter finding is in contrast to the literature on behavioural and psychological outcomes in children treated for brain tumours, which suggests that externalising behaviour problems are not over-represented amongst this population (Mulhern et al., 1993; Carpentieri, Mulhern, Douglas, Hanna & Fairclough, 1993). There may be several possible explanations for the inconsistency between our findings and those previously reported in the literature regarding externalising behaviour problems, including differences in sampling and measurement. For example, there are substantial differences between the participants in the current study and those in the studies of Mulhern et al. (1993) and Carpentieri et al. (1993) as their samples included children who were older at the time of treatment and who had received cranial radiation therapy as part of their treatment. It

is difficult to speculate about why these differences may lead to more externalising problems in our sample. One possibility is that children diagnosed at a younger age are more likely to experience speech and language and motor deficits, making them more susceptible to long-term externalising behavioural problems. Another option is that having a child who has undergone treatment for a life-threatening illness results in a change of parenting style, which affects the child's behaviour. Research has shown that the parents of chronically ill children are more likely to adopt an overly protective parenting style that includes excessive concern for their child's welfare, infantilisation, excessive physical and social contact, and over-control (Cappelli, McGrath, MacDonald, Katsanis, & Lascelles, 1989; Davies, Noll, DeStefano, Murkowski & Kulkarni, 1991; Holmbeck et al., 2002). Studies have linked this over protection to increased levels of externalising behavioural problems and depression in the child (Holmbeck et al., 2002) The results of this style of parenting may be more pronounced in children who are diagnosed during infancy as they will have had less exposure, if any, to parenting that is not over protective than children who are diagnosed at an older age. A final hypothesis relates to the literature on the effects of hospitalisation during infancy on the attachment relationship. Several studies have demonstrated that repeated or prolonged hospitalisation, particularly during the first three years of life, is significantly related to behavioural and emotional difficulties several years later (Fahrenfort, Jacobs, Miedema, & Schweizer, 1996; Shannon, Fergusson, & Dimond, 1984; Ludman, Lansdown, & Spitz, 1992), and that difficulties in the mother-child attachment relationship are significantly higher than in mother-child dyads who have not spent time in hospital (Ludman et al. 1992). These findings raise the possibility that the children in the current study may be more susceptible to behavioural problems as a result of difficulties in forming a strong

attachment to their mothers while hospitalised. The finding of the current study that children who had undergone more than one surgical intervention were more likely to have reported externalising behavioural difficulties also fits with this hypothesis as the implication of this is that these children spent a longer time in hospital than children who underwent only one surgical intervention. It is clear that further investigation in this area would be useful.

At this point it is important to note that parents reported significantly higher levels of behavioural and psychological difficulties in their children than teachers, particularly in terms of externalising behaviours. This is interesting and appears to be a common pattern in the literature (Noll et al., 1997; Radcliffe, Bennett, Kazak, Foley & Phillips, 1996). A number of possible explanations have been proposed to explain this difference. Radcliffe et al.(1996) suggest that the differences between parent and teacher reports may be due to the fact that family members are more likely to have known the child before their illness. Therefore they may rate the child's current functioning in relation to pre-illness functioning, whereas teachers are likely to have only had a post-illness relationship with the child. Another possibility is that parents are over-reporting difficulties, which could be the result of increased sensitivity to problems in their child due to the psychological trauma of their child having had a life-threatening illness, or because they are expecting their child to have more behavioural and psychological problems as a result of their brain tumour and treatment. At the same time it is feasible that teachers are under-reporting difficulties in these children. The majority of teachers will be aware of the fact that these children have undergone treatment for a brain tumour and, as suggested by Lavigne & Faier-Raitman (1992), sympathy may have resulted in them adopting an approach

of making allowances for the children's behavioural difficulties. As parents and teachers observe children in very different environments, and interact with them in different ways, it is also feasible that the discrepancy in scores is due to the fact that the children are displaying a higher level of behavioural problems at home than at school. This may be the result of parents finding it more difficult than teachers to set limits and rules for their child who has had a life-threatening illness and who may have consequent disabilities and health problems. Whatever the reason for this discrepancy, future researchers should consider the inclusion of researcher ratings on child behaviour and mental health as well as self-report measures to allow the children themselves to report on their perception of any difficulties. In particular, it may add to understanding if independent raters were able to observe the children's behaviour in both the classroom and home setting to enable investigation of the reasons behind the discrepancy in parent and teacher reports.

The results of this study also revealed that children whose parents reported clinical range behavioural and psychological problems were more likely to have physical difficulties such as motor and speech and language impairments. These findings support our hypotheses and fit with several studies in the literature, which consistently show significant rates of both internalising and externalising disorders in children with motor functioning (Lavigne & Faier-Routman, 1992) and speech and language deficits (van Daal et al., 2007). There are several possible explanations to account for the associations found between physical difficulties and behavioural outcomes. For example, numerous studies have found a link between social competencies and behavioural and psychological problems (Asarnow & Callan, 1985; Dodge, Laird, Lochman, & Zeli, 2002) and Yaghoub-Zadeh, Im-Bolter &

Cohen (2007) have recently demonstrated that speech and language functioning mediates the relationship between social competency and externalising behaviour problems. They hypothesise that children with speech and language problems find it difficult to effectively communicate due to problems in understanding others and in expressing themselves. This may then lead to an increase in the use of less appropriate forms of emotional expression such as physical aggression. Children with motor problems may have similar difficulties with social functioning in the sense that their problems may be visible to other children, which could lead to social isolation and consequent internalising and externalising psychological difficulties. A further possibility links in with the literature on over-protective parenting in chronically ill children that is discussed above. It is feasible that children who are left with significant physical difficulties following tumour treatment are perceived as more vulnerable by their parents than children who do not suffer long-term physical consequences. These parents may be more likely to adopt an over-protective style of parenting, increasing the likelihood of their child developing behavioural and psychological problems. Again, further studies are required to investigate these possibilities.

Analyses also showed that male children were more likely to fall in the clinical range in terms of internalising psychological problems such as anxiety and depression. In contrast there was no significant difference in the number of male children who were reported to be in the clinical or normal ranges in terms of externalising difficulties. This finding is interesting as, in the normal population, male children are typically found to have a higher level of externalising disorders than female children. The CBCL questionnaire norms take this into account, with the

result that the scaled scores we used in the analysis were calculated in relation to the level of difficulties that parents would be expected to report in their male children. This indicates that male children who have received treatment for a brain tumour are particularly susceptible to long-term internalising psychological problems.

The finding that children from families of lower socio-economic status had a higher frequency of reported externalising behaviour problems is consistent with the literature on child psychopathology that has frequently demonstrated that children of lower socio-economic status are more likely to experience behavioural problems (Pike, Iervolino, Eley, Price, & Plomin, 2006). Given that the current study relied on comparison with population norms, rather than a control group, it is important to consider the distribution of socio-economic status in the sample. As can be seen in Table 1, the number of children classified as belonging to the various socio-economic groups is broadly in line with normal population distributions. In this respect, it is unlikely that over representation of lower socio-economic groups inflated the rates of behavioural and psychological problems in this sample compared to population norms.

Significant relationships between location of tumour and outcome were not found and therefore did not support our hypothesis concerning these variables. The lack of relationship between tumour location and behavioural and psychological outcomes found in this study is not surprising given the crude nature of the division of location into infratentorial and supratentorial areas. Research that has demonstrated a difference has tended to report that children who have tumours occurring in the supratentorial region have worse outcomes. However, as Fuellmeller

et al.(2002) point out, these children are more likely than those with infratentorial tumours to have received radiotherapy as part of their treatment, making the effects of localisation difficult to disentangle from the effects of exposure to whole brain radiation. The current study was an opportunity to investigate whether any differences in psychological and behavioural outcome were related to tumour location, without the confounding effects of sequale resulting from cranial radiation. The finding of no significant difference in functioning between those children with supratentorial and those children with infratentorial tumours suggests that differences in child functioning found in other studies (Fuelmeller et al., 2002) may be related to treatment factors, rather than tumour location.

In relation to this complex issue, studies that have focused on cerebellar and hypothalamic/chiasmatic region tumours have tended to report increased levels of behavioural and psychological difficulties as compared to normal population functioning (Ellenberg et al., 1987; Riva et al., 1998; Steinlin et al., 2003;), which they have hypothesised are the result of neural connections between these regions and the frontal lobes (Riva et al., 1998; Steinlin et al., 2003). In the current study children with cerebellar tumours were classified as infratentorial, whereas those with hypothalamic/chiasmatic region tumours were surpratentorial. This raises the question of whether the behavioural problems of children with tumours in the cerebellum, and those of children with tumours located in the hypothalamic/chiasmatic region have, effectively, balanced each other out. Clearly we cannot conclude from this that there is no effect of tumour location on behavioural and psychological outcome, as these broad classifications include such diverse regions that any differences in the function of location are as likely to exist

within the broad regions as between them. Future studies that aim to assess for differences in terms of tumour location will need to recruit larger sample sizes to allow for division into more specific localisation groups.

The findings from our study showed no difference between children with clinical and normal range behavioural and psychological functioning in terms of IQ, memory and executive functioning. These results do not support our hypothesis and are in contrast with earlier literature in this area, which reports a significant relationship between cognitive functions and behavioural and psychological difficulties (e.g. Holmquist & Scott, 2002; Mulhern et al., 1993). One possible reason for this is that a limited number of children in the current study were found to be functioning below the average range in terms of IQ and memory, with the result that the power required to detect a difference may not have been reached. However, this explanation does not hold for the lack of relationship between executive functioning and behavioural and psychological outcome as a significant proportion of the children in this study had deficits in executive functioning. Furthermore, research on other populations indicates a strong link between executive function and behaviour, which fits with the conceptualisation of executive function as a collection of processes that are responsible for guiding, directing and managing cognitive, emotional and behavioural functions. Further research is required to help clarify relationships between executive functioning and psychosocial adjustment in young children treated for brain tumours.

Conclusions & Future Directions

The current study represents the first attempt in the literature to document the long-term incidence of behavioural and psychological difficulties in children who have received chemotherapy and/or surgical treatment for a brain tumour during infancy. Analyses indicate that these children are functioning at the expected level in terms of IQ and memory but have significant difficulties in terms of executive, behavioural and psychological functioning. Teachers reported significantly lower levels of behavioural and psychological problems than parents.

Children who have motor and/or speech and language difficulties, those who have undergone more than one surgical intervention, male children and those of lower socio-economic status are at greater risk of behavioural and psychological deficits. Neuropsychological test performance and location of tumour were not related to behavioural and psychological functioning. As with other studies in this area a small sample size was the main methodological limitation and may have led to the occurrence of type two errors. Future research would certainly benefit from including a larger number of participants, which may require the undertaking of multi-centre research trials.

Future studies may wish to further examine the reasons for the discrepancy in parent and teacher report of behavioural and psychological difficulties, perhaps by the use of independent raters to assess a child's behaviour. It would also be interesting to investigate the link between early hospitalisation, quality of attachment, parenting style and long-term behavioural and psychological functioning in this population of children. Several recent studies have contributed to our understanding of the impact of physical difficulties on a child's psychological well-

being and behaviour as well as the factors that mediate this relationship. It would be useful to further investigate the reasons for the link between physical and psychological problems in children who have undergone treatment for a brain tumour in order to allow appropriate interventions and support packages to be developed for this population.

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Part 3: Critical Appraisal

Introduction

The present study examined long-term behavioural and psychological outcomes in children treated for brain tumours during infancy. The specific aim was to assess the outcomes of those children who had not received radiotherapy as part of their treatment and examine the relationship between neuropsychological functioning, tumour/treatment factors and behavioural and psychological functioning. Results indicated that a high proportion of the sample were experiencing significant behavioural and psychological difficulties. Compared to parents, teachers reported a smaller proportion of children as having clinically significant difficulties.

Those children who were experiencing problems with motor functioning and speech and language difficulties were most at risk for behavioural and psychological problems. Male children and those who had experienced surgical complications were more likely to have significant difficulties in terms of internalising problems, such as anxiety and depression, and children who had undergone more than one surgical intervention were more likely to have externalising behaviour problems such as aggression and rule-breaking behaviour. Being of lower socio-economic status also increased the likelihood of behavioural and psychological problems. In terms of neurological factors and neuropsychological functioning, analysis indicated that location of tumour, IQ, memory and executive functioning were not related to behavioural and psychological outcome.

This review will reflect on the process of the present research, beginning with a discussion of the origins and development of the idea, limitations of the study that

may be useful for other researchers in this field to consider and implications of the study's findings and ideas for future research will then be discussed.

Origins and development of the study

I chose to complete a study in the area of paediatric oncology because I have an interest in neurological conditions and how these impact on cognitive and emotional functioning. As an Assistant Psychologist I worked with children who had received treatment for a childhood brain tumour, which meant that I was aware of the significant difficulties that they face in terms of physical, social, cognitive and emotional functioning. I was also aware of the deleterious effects of cranial radiotherapy as the majority of the children I worked with had received it as part of their treatment. On reflection I feel that these children had much greater long-term difficulties than the children who participated in the current study, possibly as a result of the fact that they had not received radiotherapy as part of their treatment. The majority of the children who participated in the study had not had any involvement with the psychologists at Great Ormond Street Hospital. I think that this was because they had received treatment at such a young age that, by the time any cognitive and/or psychological problems became evident, the family were no longer in regular contact with health professionals at the hospital with the result that they accessed support through local services. This made them a particularly interesting group to study as there was a general feel of a lack of feedback on their progress amongst members of the paediatric neuro-oncology team. However, the difficulty with this was that I was uncertain about the number of children who would be able to complete neuropsychological testing, as we had limited knowledge about long-term functioning in this group of children. As the main focus of the study was exploratory

I felt that, if a significant number of children could not complete neuropsychological testing, this would at least give us some indication about the severity of cognitive impairments in this group. Furthermore, it would still allow us to make conclusions about the behavioural and psychological functioning of these children on the basis of parent and teacher reports, which was one of the principal aims of the study.

I developed the idea for the study by collaborating with my supervisor and medical staff who belonged to the paediatric neuro-oncology team. They raised the possibility of focusing on this group of children because, as mentioned above, they were relatively un-informed about their outcomes. They are also a good group to study due to the recent treatment guidelines that limit the use of radiotherapy with this population, making it easier for us to make conclusions about the relationship between neurological factors and functioning. I then developed the idea further by deciding to focus on behavioural and psychological outcomes, which I feel are as important as cognitive outcomes but are much less frequently considered in the literature on childhood brain tumour survivors.

Selection of measures was largely dependent on the availability of standardised test norms, due to the lack of a control group in the study. I reviewed the validity and reliability of measures that had been utilised in similar studies and opted for the Weschler scales for IQ and memory and the BADS-C as the assessment of executive function. These appeared to be the most reliable and valid measures for these respective constructs and included norms for use with a wide range of ages. The CBCL was selected as it provides measures of both internalising and externalising disorders, is the gold standard in terms of assessment of behavioural and

psychological functioning in clinical practice, and is frequently used in research.

During my initial meetings with members of the paediatric neuro-oncology team I was aware that there may be an issue with sample size, as only a limited number of children had received treatment for a brain tumour in infancy. Furthermore, we felt that it was important to assess children who were at least five years post-treatment to allow time for recovery of functions and to ensure that all of the children were old enough to be assessed using the same neuropsychological measure. This meant that the potential pool of participants was limited to those who were aged seven to sixteen years, had received treatment under the age of three and had been off treatment for at least five years. In total 44 children matched the study criteria, which meant that I would need a 70% recruitment rate in order to meet the required level of power for the study. I was concerned that this was far from realistic and so decided to undertake preliminary telephone calls to a random sample of twenty two of the families to ask if they might be interested in participating if the study went ahead. Of the twenty two families twenty felt that they would like to be involved, which is a 91% response rate. In reality the response rate was not that high, with 79% of the families I was able to contact agreeing to participate. However, this did provide enough power to allow detection of some significant results.

Limitations of the current study and implications for future research

Small sample size is a common issue in this field due to the rare nature of childhood brain tumours. I chose to focus on children who had been diagnosed in infancy, and had not received radiotherapy as part of their treatment, which further limited the pool of potential participants. In total forty four children met the inclusion

criteria for the study but I was only able to contact thirty eight families. This was probably due to the length of time that had passed since treatment, which was at least five years, and in some cases as long as fourteen. During this time several families had moved house, often relocating to another country, with the result that I was unable to locate them. Of those families that I was able to contact, 30 agreed to participate. This is an acceptable number but leaves a question mark over the characteristics of the eight children who did not participate. Reasons for non-participation tended to be related to time constraints on the family or the child's wishes not to undergo testing. Other than demographics, on which non-participants and participants did not differ significantly, I was unable to gather any further information about the non-participants.

The final sample size of 30 children is rather small and raises a number of statistical issues. Firstly, smaller sample sizes increase the risk of type two errors occurring, which makes non-significant findings unreliable. For example, in the current study mean group scores on some of the memory indices were between two and three points lower than mean test norms. This difference was not significant with a sample size of only 25 children who had completed a memory assessment but may have reached the level of significance if the same mean scores occurred in a larger sample. Secondly, I was unable to perform multivariate analysis on my data as the number of variables was too large to allow reliable analysis of only 30 cases. This was disappointing as it meant that I was unable to further my understanding of the relationship between the various independent variables and behavioural and psychological functioning in brain tumour survivors. In particular I would have liked to investigate possible mediating factors and/or developed a predictive model for

functioning in these children.

Another issue with the current study was that two children were unable to complete neuropsychological testing due to significant physical and cognitive impairment, with the result that statistical analysis of differences in IQ, memory and executive function between the group and test norms does not include any data on them. Other studies in this field have often faced the same issue and have tended to exclude these children from the research (e.g. Steinlin et al., 2003, & Beebe et al., 2005). This raises questions about the ability of these studies, and the current study, to make conclusive statements about the cognitive outcomes in *all* children treated for brain tumours as statistical analysis of difference from control groups or norms consequently excludes these very low functioning individuals. There are few options available to overcome this difficulty as measures of cognitive function that can be used with children with such significant deficits and with children with normal range functioning appear to be non-existent.

Ideally a control group matched for age, gender and socio-economic status would have been included in the current study. Unfortunately the need for me to undertake comprehensive neuropsychological testing with each child, often requiring me to travel long distances to their family home, meant that I did not have enough time to recruit and test a control group. In an attempt to overcome the limitations of comparing participants scores to test norms I chose well standardized, reliable and valid measures. All of these measures allow for calculation of scores on the basis of age, and sometimes gender. The distribution of the sample children in terms of socio-economic status was in line with the normal population, with the result that I was

able to be more confident in the validity of comparison with the test norms. A number of studies in this area have found significant relationships between family functioning variables and behavioural and psychological difficulties (Fuemmeler, Elkin & Mulins, 2002). On reflection it would have been useful to assess for differences on the basis of family function or include a group of sibling controls to control for the influence of family environment on functioning.

The current study highlighted the importance of the relationship between physical difficulties, in particular motor problems, and behavioural and psychological difficulties. This finding is not surprising and fits with other studies that report higher levels of behavioural and psychological problems in children with functional impairments or disabilities (Mulhern, Carpentieri, Shema, Stone, & Fairclough, 1993, & Greenberg, Kazak, & Meadows, 1989). It was not possible to consider what factors may mediate the relationship between motor functioning and behavioural and psychological difficulties in the current study. However, this is an important consideration for future research if children who are at particular risk are to be identified and offered appropriate support and interventions. Wallander and Varni (1998) have developed a disability-stress-coping model and have conducted several studies with paediatric oncology patients as well as other chronically ill patients, that lend support to their model. They highlight the importance of factors such as the severity and visibility of disease/disability related factors, cognitive impairment, level of functional independence (including ambulation and communication skills), personality, family environment, social support, psychosocial stressors relating to their disease/disability, stress as a result of major life events and cognitive appraisal on psychological and behavioural adjustment. Future studies with

childhood brain tumour survivors may wish to investigate the relationship between some of these factors and behavioural and psychological functioning in these children. In terms of the development of appropriate interventions for childhood brain tumour survivors, research examining the contribution of their cognitive appraisals of physical impairments and appearance and other disease/disability related factors to behavioural and psychological functioning would be particularly useful as this could potentially lead to the development of effective cognitive-behavioural programmes for these children.

Wallander and Varni's (1998) model highlights the importance of severity and visibility of the disease/disability, something that was not considered in the current study. In fact, the current study was limited by the lack of standardised measures of motor, visual and speech and language problems. I chose to rely on parent report alone and to code their responses as presence vs. absence of difficulties. The result of this was that children with very different types of motor problems, for example minor difficulties with fine motor skills and significant impairment of gross motor functioning, were placed in the same group for the purpose of analysis. My reasoning for not including specific tests of physical and sensory impairment was because I felt that the participants would already have to undergo a significant amount of assessment and I did not want to overload them. Also, the inclusion of physical factors as a possible variable that might relate to behavioural and psychological outcome was something that was decided upon later in the planning process. On reflection, I did not think it would be as important a variable as neuropsychological functioning and tumour/treatment factors and so did not give as much consideration to the best ways of measuring the childrens' physical functioning. As a result I am

unable to comment on the severity of the children's motor, visual and speech and language difficulties and how these might relate to outcome. This is an important factor as other research has demonstrated differences in behavioural and psychological outcome depending on severity of deficit. For example, Hendriks, De Moor, Oud, Franken, & Savelberg (2001) found that children with very severe motor deficits actually exhibited the least externalising behaviour problems. In terms of speech and language impairment research has shown that certain types of deficit, such as expressive language difficulties, are predictive of a greater risk of particular behavioural and psychological problems such as, attention deficits (Snowling, Bishop, Stothard, Chipchase, & Kaplan, 2006). The current study was not able to investigate whether this pattern is also present in a paediatric brain tumour population as classification of impairment was not undertaken.

Conclusion

I feel that the current study makes a valid contribution to research in the field of paediatric neuro-oncology. Behavioural and psychological outcomes of children treated in infancy have not been examined before. The findings of the current study highlight the difficulties faced by these children, which are significant and long-lasting. There are a number of limitations and methodological issues with the current study, which other researchers in this field should consider when designing future studies. In particular there is a clear need for studies involving larger sample sizes. There is also a need for research to further examine the factors that relate to outcome for these children so that recommendations about supportive and preventative strategies for those who are at the most risk can be made.

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Appendix 1: Parent, Child & Young Persons Information Sheets

Parent Information Sheet

We would like to invite you and your child to participate in a research study. The study aims to investigate the behaviour, emotions and social lives of children who have been treated for brain tumours at a young age. Before you decide whether you would like to participate it is important that you understand why the research is being done and what you and your child would be asked to do. Please read the information below carefully. Ask us if there is anything you are unsure about or if you would like to know more.

What is the purpose of the study?

The study aims to investigate the behaviour, emotions and social lives of children who have been treated for brain tumours. This study will focus on children who were diagnosed under the age of 3 and who have not received radiotherapy as part of their treatment. This is a group that has not been studied before. It is important to find out what, if any, the effects of being treated for a brain tumour at such a young age are. The study will also look at the things that influence outcome for these children. For example, whether a tumour located in a certain part of the brain increases the chance of a child having behaviour problems.

Why have we been invited to take part?

You have been invited to take part because your child was treated for a brain tumour at Great Ormond Street Hospital. You have also been invited because your child was diagnosed when they were aged 3 or younger and did not receive radiotherapy as part of their treatment. There are 52 children who meet these criteria and are now between the ages of 7 and 16. They are all being approached to take part in this research.

Do I have to take part?

No, it's up to you and your child to decide whether you would like to participate. We have sent you this information sheet to give you a chance to read it and think about whether you would like to participate. You will receive a telephone call from us asking if you would like to be involved. If you would then you will be asked to sign a consent form to show you have agreed to take part. If your child is over the age of 10 they will also be asked to give written assent by signing a children's assent form. You are free to withdraw at any time. This would not affect the standard of care your child receives.

What will we have to do if we do agree to take part?

A time will be arranged for you both to meet with a researcher who will assess your child using neuropsychological tests. These are not invasive. They involve the researcher asking the child to complete tasks such as puzzles and remember things such as lists of words. It is expected that the average time this will take is 2 hours. If your child gets tired it will be fine to take a break in the middle.

While your child is being assessed you will be asked to complete some questionnaires that will ask about your child's behaviour, social life and emotions. You will also be asked questions about your family life for example, whether you are

a single parent, what your job is and how old you are. These should take no longer than 1 hour to complete.

You will also be asked to give your consent for your child's medical records to be seen. This is so that we can find out information about the treatment they received and if there were any complications. Your consent will also be needed to enable us to write to your child's teacher and ask him or her to complete some questionnaires about your child's behaviour, emotions and social life at school.

If your child is due to attend Great Ormond Street for a medical appointment we will try to organise to meet with you at the hospital that day. Otherwise we are happy to arrange to come to your home to do the assessment. We do not expect your child to miss school to take part in the research and so would be happy to arrange a time during the school holidays.

What are the possible risks and disadvantages of taking part?

There are no risks from taking part in this study. The only inconvenience is that you and your child will have to give 2-3 hours of your time in order to participate. Your child may find the neuropsychological assessment tiring, although many children enjoy completing the tasks.

What are the possible benefits of taking part?

The main benefit is that you will receive a summary report of your child's performance on the neuropsychological tests. If there is a problem identified we can refer you on to an appropriate person. We cannot promise the study will help your child but the information we get might help other young people and children who are treated for brain tumours in the future.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (0207 8298679). If you remain unhappy and wish to complain formally, you can do this through the NHS complaints procedure. Details can be obtained through the hospital.

Will my taking part in the study be kept confidential?

Information which is collected about you and your child during the course of the research will be kept strictly confidential. In exceptional cases, for example if there is a concern about your child's safety, we may have to share some information with other professionals. However, we will do our best to discuss this with you first. Any information about you or your child that leaves the hospital will have identifying information, such as name and address, removed. We will write to your child's GP to inform them of your child's involvement in the research.

What will happen if we don't want to carry on with the study?

You can withdraw from the study at any time. This will not affect your child's medical care. If you do withdraw you may be asked if we can still use the data collected up to that point in the study. If you do not wish any of your child's data to be used it will be destroyed.

What will happen to the results of the research study?

It is intended that the results of the study will be published in a scientific journal. All families who participate in the research will be sent a summary report, discussing the results and conclusions of the study.

Who is organising and funding the research?

The research is being undertaken as part of the requirements for an educational qualification. The department of Clinical Health Psychology, University College London is funding the study.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by Great Ormond Street Hospital Research Ethics Committee.

Further information and contact details

If you require any further information or have any concerns about the study please contact Dr Dianne Gumley, Clinical Psychologist on 0207 8298679.

Child Information Sheet (ages 6–10)

What is Research? Why is this project being done?

Research is a way we try to find out answers to questions. We want to see if having a brain tumour affects children's behaviour.

Why have I been asked to take part?

You have been asked to take part in this research because you were treated for a brain tumour when you were younger.

Did anyone else check the study is ok to do?

Before any research is allowed to happen it has to be checked by a group of people called a Research Ethics Committee. They make sure that the research is fair. This project has been checked by Great Ormond Street Research Ethics Committee.

Do I have to take part?

No, it's up to you if you want to take part or not.

What will happen to me if I take part in the research?

A researcher will come to your house or you will come to Great Ormond Street Hospital. You will be asked to do some tasks such as remembering lists of words and jigsaw puzzles. This will take about 2 hours. If you feel tired we will take a break in the middle.

Your parents and teacher will answer some questions about your behaviour.

Will joining in help me?

We cannot promise that the study will help you but the information we get might help children who have brain tumours in the future.

Will anyone else know I'm doing this?

We will write to your GP to let them know that you are taking part. We will keep your details private but if we are worried about you we may need to share some information with other people such as your parents or other health professionals.

What if I don't want to do the research anymore?

If you don't want to do the research anymore tell your parents or the researcher at anytime. They will not be cross with you. It is ok to stop at anytime.

Young Persons Information Sheet (11-16)

We are asking if you would take part in research project to find out what effect being treated for a brain tumour has on a person's behaviour and emotions. Before you decide if you want to join in it's important to understand why the research is being done and what it will involve. Please consider this information sheet carefully and talk about it with your family, friends, doctor or nurse if you want to.

Why are we doing this research?

The study aims to investigate the behaviour, emotions and social lives of children who have been treated for brain tumours. This study will focus on children who were diagnosed under the age of 3 and who have not received radiotherapy as part of their treatment. This is a group that has not been studied before. It is important to find out what, if any, the effects of being treated for a brain tumour at such a young age are. The study will also look at the things that influence outcome. For example, whether a tumour located in a certain part of the brain increases the chance of a child having behaviour problems as they get older.

Why have I been invited to take part?

You have been invited to take part because you were treated for a brain tumour at Great Ormond Street Hospital. You have also been invited because you were diagnosed when you were aged 3 or younger and did not receive radiotherapy as part of your treatment. There are 52 children who meet these criteria and are now between the ages of 7 and 16. They are all being approached to take part in this research.

Do I have to take part?

No, it's up to you to decide whether you would like to take part. Your parent(s) will receive a telephone call from us asking if you would like to be involved. If you would then you will be asked to sign an assent form to show you have agreed to take part. As you are under 18, your parent(s) will also be asked to sign a consent form. You are free to stop taking part at any time during the research without giving a reason. If you decide to stop **this** will not affect the care you receive.

What will I have to do if I do agree to take part?

A time will be arranged for you and your parent(s) to meet with a researcher who will assess you using neuropsychological tests. Neuropsychological tests involve the researcher asking you to complete tasks such as puzzles and remember things such as lists of words. It is expected that the average time this will take is 2 hours. If you get tired it will be fine to take a break in the middle.

While you are being assessed your parent(s) will be asked to complete some questionnaires that will ask about your behaviour, social life and emotions. They will also be asked questions about your family life.

You will also be asked to give your assent for your medical records to be seen. This is so that the researcher can find out information about the treatment you received

and if there were any complications. Your assent will also be needed to enable us to write to your teacher and ask him or her to complete some questionnaires about your behaviour, emotions and social life at school.

What are the possible risks and disadvantages of taking part?

There are no risks from taking part in this study. The only inconvenience is that you will have to give 2-3 hours of your time in order to participate. You may find the neuropsychological assessment tiring, although many people enjoy completing the tasks.

What are the possible benefits of taking part?

The main benefit is that you will receive a summary report of your performance on the neuropsychological tests. We cannot promise the study will help you but the information we get might help other young people and children who are treated for brain tumours in the future.

What if there is a problem?

If you or your parent(s) have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (0207 8298679). If you remain unhappy and wish to complain formally, you can do this through the NHS complaints procedure. Details can be obtained through the hospital.

Will anyone else know I'm doing this?

We will keep your information in confidence. This means we will only tell those who have a need or right to know. We will remove your name and address from any information that is taken outside of the hospital. We will write to your GP to let them know that you are taking part in the study.

Who is organising and funding the research?

The department of Clinical Health Psychology, University College London is funding the study.

Who has reviewed the study?

Before any research goes ahead it has to be checked by a Research Ethics Committee. They make sure that the research is fair. This research has been checked by Great Ormond Street Hospital Research Ethics Committee. Thank you for reading this – please ask any questions if you need to.

Further information and contact details

If you require any further information or have any concerns about the study please contact Dianne Gumley, Clinical Psychologist on 0207 8298679.

Appendix 2: Invitation Letter

Dear (parents name)

We are writing to ask you, and (child's name), if you would like to participate in a research study. The research is being conducted at Great Ormond Street Children's Hospital and aims to identify what effect treatment for a brain tumour has on a child's behaviour, emotions and social life. We are also hoping to discover the factors that effect these things, for example whether the location of the tumour and/or a child's ability to remember new things has any effect.

Please read the parent information sheet enclosed and take time to think about whether you would like to participate. We have also enclosed a children's version for (child's name) to read. You will receive a telephone call within the next few weeks asking whether you would like to take part or not. You will be given the opportunity to ask any questions about the study during this telephone conversation. However, if you wish to contact us before then please call us on 0207 8298679.

Yours sincerely,

Catherine Ward
Trainee Clinical Psychologist

Dr Dianne Gumley
Clinical Psychologist

Appendix 3: Teacher Letter

Dear (teacher's name)

We are writing to ask you to complete the enclosed questionnaires with reference to (child's name and dob). We are researching the effects of receiving treatment for a brain tumour at a young age. (Child's name) and his/her parents are participating in the study and have given their consent for you to be approached. (Please see separate copy of consent form signed by them).

We hope that you will have time to complete these questionnaires. Please feel free to call us on 0207 8298679 with any questions or concerns.

Yours sincerely,

Catherine Ward

Trainee Clinical Psychologist

Dr Dianne Gumley

Clinical Psychologist

(version 2, 07/05/07)

Appendix 4: Letter of Ethical Approval