The Adaptive Control of Saccades in Normal and Abnormal Children and Adults

Laura Elisabeth Mezey

A thesis submitted for the degree of
Doctor of Philosophy

Institute of Child Health
University College London Medical School
London
Abstract

This thesis examines the metrics of saccadic eye movements and the adaptive gain control of saccades to test the saccadic flight-time minimisation (SFM) hypothesis (Harris 1995, Vision Res. 35(5):691-701). The SFM hypothesis proposes that saccadic gain is determined by the drive to minimise saccadic flight-time and provides an explanation for the well-known undershoot bias of saccades. The level of undershoot in any individual is predicted to depend intimately on both the standard deviation of the error after the primary saccade, and the main sequence for duration for each individual. Experimental data to support both of these predictions of the SFM hypothesis are presented in the first section of this thesis.

Children with homonymous hemianopia were found to produce primary saccades with low gains and high standard deviations into their blind hemifield, but not into their seeing hemifield. The retained bias to undershoot, despite the high standard deviation, is proposed to be an adaptive strategy to prevent excessive overshoot and minimise saccadic flight-time when the exact target position is unknown. A similar relationship between the gain and standard deviation of saccades is reported for antisaccades made by normal adults. Between-subject comparisons in a separate experiment revealed a strong correlation between gain over a range of eccentricities and the main sequence for duration to further support the SFM hypothesis.

To maintain the gain of saccades at an optimal level the saccadic system is under constant adaptive control. The active functioning of the adaptive control system is demonstrated using an intrasaccadic target displacement paradigm in which the target position is consistently altered during the primary saccade, necessitating a change in saccade amplitude. Gain changes indicate that the goal of the adaptive process is not to minimise average retinal error over time, but is consistent with the SFM hypothesis.

The adaptive control paradigm was applied for the first time to children with Dancing Eye Syndrome. These patients are suspected to have defective adaptive control by virtue of proposed neuropathology in the vermis of the cerebellum. All patients but one were able to adaptively adjust the gain of their saccades suggesting no persistent effects of this disorder on the adaptive control system. Explanations are proposed for the single case in which adaptive control was absent.

The characteristics of gain in the situations outlined in this thesis support predictions made by the SFM hypothesis. The assumption that minimisation of retinal error is the sole driving force of the adaptive control process is not supported.
Acknowledgements

My thanks go to all the members of the Ophthalmology department at Great Ormond Street Hospital who’ve given me support and friendship during my time here. In particular my thanks go to Chris Harris without whom of course, this thesis could not have been started, let alone finished and who has tried so hard to share his knowledge! My sincere thanks also go to David Taylor whose kindness and support throughout my time at Great Ormond Street has been greatly appreciated; particularly for the financial assistance that allowed me to finish this PhD. Extra special thanks go to Fatima who has listened and helped me all the way and also been a good friend. Thanks also to Peter West for computing and general help; to Tony, for looking out for me, and his unfailing good humour; to Debbie, Nichola and Angela in the office for their help with my many and varied requests over the years; to Dorothy for help, humour and advice; Isabelle Russell-Eggitt for her enthusiasm and remembering my need for patients; and last but by no means least to Chris Timms and Jane Walker, again for remembering my need for patients and particularly for their orthoptic expertise with the hemianopic children. Additional thanks to my partners in the Lamb over the years, Mark, Siobhan, Peter & Chris, and Tony for always being ready to buy ‘one for the road’.

My fellow PhD students Mark and Siobhan deserve an extra special mention for being good friends and such constant and uncomplaining subjects in repeated experiments. Particularly to Mark for having such reliable and text-book worthy saccades and who, I think, began to feel rather at home with his head on the chin rest, wearing that fetching headset! Extra thanks to Mark too for all the help with this thesis, for being a fellow foodie, and in general for seeing me through all the trials and tribulations of PhD life and listening sympathetically over many a lunch and always being willing to laugh!

Thanks must go also to all the subjects, and in particular the children and their parents who were willing to spend their time to take part in this research.

My family and friends should really have come first as they are the ones who have given me the out-of-work support that I needed to make it through. I would love to mention everyone by name as they all deserve it, but in short, thanks especially to Mum, Dad and Matthew and my dear dog Jesse (RIP) who didn’t quite make it; to Claire, who has been waiting incredibly patiently to go globetrotting; to Angus for weekends off and always trying to find the light at the end of the tunnel; Charlotte, my culinary companion, for constant interest and being a willing subject; Alison and Beth who are my role models and showed me how a PhD should be done; Jane and Martina for being Jane and Martina; Marie for good friendship and wise advice every step of the way; Katherine for having so much faith in my abilities; Willy for light relief; and finally Elfine who never forgot to ask how the equipment was coming along!

Thanks also to Bob Taylor in Biomedical Engineering who helped with the careful mounting of the optical instrumentation, John Hackett who helped with the construction of the equipment, Rob Hart for computing assistance and Bill who made the earmuffs!

This PhD is dedicated to my family and friends who can be forgiven for thinking they would never see the day........
## Contents

**Abstract**

**Chapter 1. Introduction**

1.1 An overview  
1.2 Types of saccades  
1.3 Saccade dynamics and timing properties  
1.4 Saccade metrics  
  1.4.1 What is gain?  
  1.4.2 Measurement of gain  
  1.4.3 The undershoot bias  
  1.4.4 The range effect  
  1.4.5 Other effects on gain  
  1.4.6 How does gain develop?  
1.5 Why saccadic undershoot?  
  1.5.1 The hemispheric facilitation hypothesis  
  1.5.2 Other theories  
  1.5.3 The saccadic flight-time minimisation hypothesis  
1.6 How is gain controlled?  
  1.6.1 Adaptive control  
  1.6.2 Lesion studies  
  1.6.3 Experimental studies on humans  
  1.6.4 Characteristics of adaptive control  
1.7 The neural generation of saccades  
  1.7.1 The nature of the premotor signal and the neural integrator  
  1.7.2 The brainstem saccade generator  
  1.7.3 The superior colliculus  
  1.7.4 Cortical areas  
  1.7.5 The basal ganglia  
  1.7.6 The pulvinar and the intramedullary lamina of the thalamus  
1.8 The Cerebellum  
  1.8.1 The anatomy and physiology of the cerebellum  
  1.8.2 The cerebellum and dysmetria  
  1.8.3 The cerebellum and adaptive control  
  1.8.4 How the cerebellum might work?  
  1.8.5 Other areas that could be involved in adaptive control

2  
15  
15  
16  
17  
19  
19  
20  
23  
25  
26  
27  
28  
28  
30  
30  
33  
33  
34  
34  
35  
42  
43  
44  
45  
47  
51  
52  
52  
53  
54  
55  
56  
58
Chapter 2. Methodology

2.1 Introduction

2.2 Equipment design and construction 62
2.2.2 Eye movement recording 66
2.2.3 Set up 67
2.2.4 Stimulus control program 68
2.2.5 Analysis program 68

2.3 Testing the experimental set-up 71
2.2.1 Subjects and methodology 71
2.2.2 Results 71
2.2.3 Discussion 75
2.2.4 Conclusions 78

Chapter 3. The Gain of Saccades in Children with Hemianopia

3.1 Introduction

3.1.1 Saccadic gain in hemianopia 80
3.1.2 Pilot study 81

3.2 Methodology

3.2.1 Subjects 84
3.2.2 Experimental set-up 87
3.2.3 Experimental paradigm 88

3.3 Results

3.3.1 Control subjects 90
3.3.2 Hemianopic patients 91

3.4 Discussion

3.4.1 Effect of predictability 100
3.4.2 Effect of target eccentricity 102
3.4.3 Adaptive effects in the seeing hemifield 103
3.4.4 Variability 104
3.4.5 Saccadic strategies 105

3.5 Conclusion 109
Chapter 4. Antisaccades

4.1 Introduction

4.2 Subjects and Methods

4.3 Results

4.3.1 Prosaccades - metrics

4.3.2 Antisaccades - error rate

4.3.3 Antisaccades - metrics

4.3.4 Latency characteristics

4.4 Discussion

4.4.1 Error rate

4.4.2 Why low gain?

4.4.3 Hypermetric antisaccades

4.4.4 Corrective saccades

4.5 Conclusion

Chapter 5. Saccadic Gain and the Main Sequence

5.1 Introduction

5.1.1 The undershoot bias

5.1.2 Robinson’s hemispheric facilitation theory

5.1.3 Pre-programming theories

5.1.4 The flight-time minimisation hypothesis

5.1.5 Aims

5.2 Methodology

5.2.1 Subjects

5.2.2 Experimental set-up

5.2.3 Characterising the range effect

5.2.4 Characterising the main sequence

5.3 General parameters

5.3.1 Results

5.3.2 Discussion

5.4 Robinson’s hemispheric facilitation theory

5.4.1 Results

5.4.2 Discussion

5.5 The flight-time minimisation hypothesis

5.5.1 Results
Chapter 6. The Adaptive Control of Gain

6.1 Introduction

6.1.1 What is adaptive control? 163
6.1.2 How is adaptive control studied? 164
6.1.3 What is the adaptive controller controlling? 165
6.1.4 What is the goal of the adaptive controller? 166

6.2 Methodology

6.2.1 Subjects 168
6.2.2 Experimental set-up 168
6.2.3 Experimental paradigm 168
6.2.4 Data analysis 171

6.3 Results

6.3.1 Control condition 172
6.3.2 Gain increasing and gain decreasing paradigms 172
6.3.3 Random paradigm 176
6.3.4 Express saccades in Subject DS 179

6.4 Discussion

6.4.1 Support for the SFM hypothesis 182
6.4.2 Previous studies 183
6.4.3 Separate adaptive control elements? 187
6.4.4 Alternative explanations for our results 188
6.4.5 The error signal 188
6.4.6 Express saccades 190

6.5 Conclusions 192

Chapter 7. Adaptive Control in Patients with Dancing Eye Syndrome

7.1 Introduction

7.1.1 Saccadic dysmetria in clinical populations 195
7.1.2 Dancing eye syndrome (DSE) 196

7.2 Methodology

7.2.1 Subjects 198
7.2.2 Experimental set-up 198
7.2.3 Experimental paradigm
7.2.4 Data analysis

7.3 Results
  7.3.1 Saccade metrics
  7.3.2 Adaptive capabilities

7.4 Discussion
  7.4.1 Saccade metrics in patients with DES
  7.4.2 Is adaptive control affected in DES patients?
  7.4.3 Neuroanatomical substrates of saccadic dysmetria
  7.4.4 Neuroanatomical origin of opsoclonus
  7.4.5 Cognitive deficits and the vermis

7.5 Conclusions

Chapter 8. Final Discussion and Conclusions

References

Appendix A. Supporting publications and presentations
# List of Figures

## Chapter 1. Introduction

- Figure 1.1 A schematic representation of a saccadic eye movement. 22
- Figure 1.2 A typical main sequence for duration. 31
- Figure 1.3 Diagram to compare the flight-time of undershooting and overshooting saccades. 31
- Figure 1.4 Diagram to show hypothetical affects of variation in the standard deviation of gain. 32
- Figure 1.5 Areas of the brainstem involved in saccade control. 45
- Figure 1.6 Cortical areas involved in the generation of saccades. 48
- Figure 1.7 The cerebellum. 53

## Chapter 2. Methodology

- Figure 2.1 Photograph of a subject seated in the experimental set-up. 62
- Figure 2.2 Photograph of the laser and deflection system on the baseplate. 64
- Figure 2.3 Diagram to show the parameters used by the analysis program to determine the saccade amplitude. 69
- Figure 2.4 Latency histograms for three subjects. 72
- Figure 2.5 Main sequence plots for duration and peak velocity for three subjects. 73-4
- Figure 2.6 Plots to show the average gain at each target eccentricity, for three methods of determining gain. 74-5

## Chapter 3. Gain of Saccades in Children with Hemianopia

- Figure 3.1 Diagram to show the optic pathways. 79
- Figure 3.2 Diagram to show typical multiple hypometric eye movement trace. 80
- Figure 3.3 Schematic diagram to show hypermetric and hypometric strategies. 81
- Figure 3.4 Goldmann field results for hemianopic children. 85-6
- Figure 3.5 The neglect tasks, completed by a hemianopic child. 84
- Figure 3.6 Graph to show the mean saccadic gain to each target eccentricity in each phase. 90
- Figure 3.7A Eye movement traces of multiple hypometric saccades to 15° targets. 91
- Figure 3.7B Eye movements traces of multiple hypometric saccades to 5° targets. 92
- Figure 3.8A Multiple hypometric saccades with variation in the initial amplitude. 92
- Figure 3.8B Multiple hypometric saccades with overshooting final saccades. 92
Figure 3.9A Eye movement traces of hypermetric saccades to 15° targets. 93
Figure 3.9B Eye movement traces of hypermetric saccades to 5° targets. 93
Figure 3.10 Eye movement traces of saccades into the seeing field by 94
hemianopic subjects.
Figure 3.11 Diagram to show the mean gain of saccades for hemianopic patients 94
and control subjects in each phase of the experiment.
Figure 3.12 Bar chart to compare the mean gains for the different target 95
eccentricities in each phase.
Figure 3.13A Latency distributions in the random phase. 97
Figure 3.13B Latency distributions in the semi-predictable phase. 98
Figure 3.13C Latency distribution in the predictable phase. 99

Chapter 4. Antisaccades
Figure 4.1 An eye movement trace of a typical reflexive prosaccade. 115
Figure 4.2 Gain histogram for reflexive prosaccades. 116
Figure 4.3 Eye movement traces of typical antisaccade errors. 117
Figure 4.4 Representative eye movement traces of correct antisaccades. 118
Figure 4.5 Graph to compare the mean gain of pro- and antisaccades. 119
Figure 4.6 Gain distribution histograms for all subjects. 121
Figure 4.7 Graph to compare the gain distributions of pro- and antisaccades. 125

Chapter 5. Saccadic Gain and the Main Sequence
Figure 5.1 Histogram to show the latency characteristics of primary and 144
secondary saccades.
Figure 5.2 Graph to show the variation of latency with target eccentricity. 145
Figure 5.3 The main sequence for duration for 20 subjects together. 145
Figure 5.4 Graphs to show the dynamic properties of saccades from 20 subjects. 146
Figure 5.5 Graphs to show the relationship between target eccentricity and gain 147
or each different method of calculating gain.
Figure 5.6 Bar charts to show the relative amounts of overshooting and 147
undershooting.
Figure 5.7 Graph to show the relationship between gain and target eccentricity 152
from the data of Kapoula and Robinson (1986).
Figure 5.8 Graph to show the mean latency and amplitude of onwards and 153
backwards correctives.
Figure 5.9 Scatterplots to show the relationship between the main sequence intercept and the slope and intercept of the range effect.

Figure 5.10 Graph to show the mean number of corrective saccades in each trial for each target eccentricity.

Figure 5.11 Graph to show the mean gain of primary saccades depending on the number of corrective saccades made.

Chapter 6. Adaptive Control of Gain

Figure 6.1 Graph to show average gain of saccades before and after adaptation. 174
Figure 6.2 Graph to show the average gain in 10 trial averages over the course of the experiment for each subject separately. 175
Figure 6.3 Scatterplot to show the relationship between the magnitude of gain change in the gain increasing and decreasing paradigms. 176
Figure 6.4 Graph to show average gain before and after adaptation in the random paradigm. 177
Figure 6.5 Scatterplot to show the relationship between the magnitude of gain change in the three different paradigms. 178
Figure 6.6 Latency histograms for each subject separately. 179
Figure 6.7 Latency histograms for Subject DS in each paradigm. 181
Figure 6.8 Graph to show average gain of express and non-express saccades. 181
Figure 6.9 Graph to show the average gain of express and non-express saccades before and after adaptation in each paradigm for Subject DS. 182
Figure 6.10 Schematic representation of target and eye movement in the Deubel paradigm adapted from Wallman and Fuchs.(1998) 189

Chapter 7. Adaptive Control in Patients with Dancing Eye Syndrome

Figure 7.1 Eye movement traces from DES patients with hypermetria. 203
Figure 7.2 Eye movement traces from DES patients with hypometria. 204
Figure 7.3 Mean gain before and after adaptation in DES patients. 206
Figure 7.4 A schematic representation of the connections of the brainstem saccade generator. 216
List of Tables

Chapter 2. Methodology
Table 2.1 Latency and main sequence parameters for three subjects. 72

Chapter 3. Gain of Saccades in Children with Hemianopia
Table 3.1 Patient details. 87
Table 3.2 Patient details continued. 87
Table 3.3 Mean gain of saccades for control subjects. 90
Table 3.4 Mean gain of saccades for hemianopic patients. 94

Chapter 4. Antisaccades
Table 4.1 Mean gain and error rates of prosaccades and antisaccades. 115
Table 4.2 To show the percentage of hypometric, hypermetric and single pro- and antisaccades. 119
Table 4.3 Latency characteristics of pro- and correct and incorrect antisaccades. 122

Chapter 5. Saccadic Gain and the Main Sequence
Table 5.1 To show the mean latencies and amplitudes of onwards and backwards correctives. 152
Table 5.2 To show the mean latencies and amplitudes of amplitude-matched corrective saccades. 153
Table 5.3. Correlation coefficients between main sequence parameters and range effect parameters (full range effect). 156
Table 5.4. Correlation coefficients between main sequence parameters and range effect parameters (Limited range effect). 156

Chapter 6. Adaptive control of Gain
Table 6.1 Average gain before and after adaptation for the gain increasing and gain decreasing paradigms. 173
Table 6.2 To show the mean gain before and after adaptation in the random paradigm for all subjects. 177
Table 6.3 To show the magnitude of gain change for subjects in each paradigm. 178
Chapter 7. Adaptive Control in Patients with Dancing Eye Syndrome

Table 7.1 Summary of patient details. 198

Table 7.2 Mean primary gain and percentage of overshooting saccades for DES patients and control subjects. 202

Table 7.3 The magnitude of gain change for control subjects. 205

Table 7.4 The mean gain and percentage of hypermetric saccades before and after adaptation. 207
Abbreviations

CT: computed tomography
DES: dancing eye syndrome
EOG: electro-oculography
EOM: extra-ocular muscles
FEF: frontal eye fields
FOR: fastigial oculomotor region
LED: light emitting diode
LIP: lateral intraparietal area
MRI: magnetic resonance imaging
PEF: parietal eye field
PPRF: paramedian pontine reticular formation
riMLF: rostral intersitial nucleus of the medial longitudinal fasciculus
SEF: supplementary eye field
SFM: saccadic flight-time minimisation
SNpr: substantia nigra pars reticulata
SPECT: single proton emission computed tomography
VOR: vestibulo-ocular reflex
Chapter 1. Introduction

1.1 An Overview

Saccades are conjugate rapid eye movements that shift the direction of gaze in order to align a new visual target on the fovea. While in primitive vertebrates and afoveate animals eye movements are intimately tied in with head movements and vestibular stimulation, the evolutionary emergence of the fovea necessitated an independent means of rapidly changing the line of sight in order to exploit this high acuity region of the retina optimally.

The foveola, the region of highest acuity at the centre of the fovea, constitutes just under 1° of the central visual field and is less than 1mm in diameter (Cohen, 1992). Visual acuity rapidly falls off from the fovea in humans (Ludvig, 1941). It is expected therefore that the optimal behaviour of the saccadic system would be to generate highly accurate saccades that would place a visual target on the high acuity area in a single step, thus minimising post-saccadic retinal error. Remarkably, this does not seem to occur. There is a robust tendency to undershoot the target (the undershoot bias), in spite of a highly sensitive adaptive control system for saccades.

This thesis interprets data in the context of the saccadic flight-time minimisation (SFM) hypothesis (Harris, 1995), which proposes that, in order to maximise the time of clear vision, the system attempts to minimise saccadic flight-time across sequences of saccades. This hypothesis provides an alternative explanation for undershoot bias to those that have been proposed before (eg Robinson, 1973; Kapoula and Robinson, 1986, de Bie et al., 1987).

It is important that the saccadic control system is able to adapt its behaviour to maintain optimal performance in the face of both internal and external changes. Internal changes result naturally from the effects of growth and ageing, or from trauma and
disease processes affecting the visual or saccadic systems. External changes may result from the use of lenses in front of the eyes. Saccades have a duration that is too short to be under direct feedback control; instead they are under adaptive control. This is the process of controlling motor behaviour by monitoring performance and compensating for any errors by adjusting parameters to refine subsequent behaviour on the basis of these errors.

In this thesis the behaviour of the saccadic system under normal and abnormal circumstances is analysed in the context of the SFM hypothesis and the active functioning of the adaptive control system is also directly tested.

1.2 Types of saccades

Saccades have been classified in various ways by different researchers. Whittaker et al. (1991) suggest that two types of saccades can be distinguished behaviourally: 'foveating saccades' which direct the fovea to salient targets in the visual field; and 'non-foveating saccades' such as the quick phases of nystagmus, and saccades made without visual stimuli. Further behavioural classifications have been made which, in general, fit in this basic division of foveating and non-foveating saccades, for example by Becker (1989). According to Becker, foveating saccades can be either goal-directed saccades, or reorienting saccades. Goal-directed saccades are those such as reflexive saccades evoked by sudden changes in the extrafoveal visual field; refixation saccades, which direct the eye at pre-selected objects from the visual environment; scanning saccades used to explore the visual environment, attracted to objects on the basis of their salient features; and catch-up saccades which make up for any lag when smoothly tracking a moving object. Reorienting saccades, on the other hand, are usually very large saccades, which combine with head movements, to bring areas from the very periphery of the visual field, or beyond, to the fovea. Non-foveating saccades in Becker’s (1989) division would be those such as micro-saccades and the quick phases of nystagmus.
Divisions can also be made on the basis of how the saccades are elicited. Research suggests that these differences in classification may also be reflected in the actual pathways involved in eliciting the different types of saccades. Tusa et al. (1986) draw a distinction between reflexive saccades to suddenly appearing novel stimuli, usually in the peripheral visual field, which are said to be ‘externally triggered’, and intentional saccades which are more volitional in their generation, ‘internally triggered’, and shift gaze to a predetermined visual target. Internally generated saccades to stationary targets have been shown to be more accurate than externally generated saccades to jumping targets (Collewijn et al., 1988; Lemij and Collewijn, 1989). Differences in the amplitude-peak velocity relationship have also been reported (Smit and van Gisbergen, 1987). Such differences appear to reflect true functional distinctions, as there is evidence that these two types of saccades have distinct adaptive control mechanisms (Erkelens and Hulleman, 1993; Deubel, 1995). It is important to consider these differences when planning experiments and dealing with data as different response strategies may produce conflicting results.

1.3 Saccade Dynamics and Timing Properties

The dynamic properties of saccades (duration and peak velocity) and timing properties will be outlined briefly here but expanded upon with respect to experimental data in Chapters 2 and 5.

Saccades are notable for their short durations and high accelerations. Most saccades are completed within 100 msec (Bahill et al., 1975a) and their peak velocity may reach up to 700°/sec for large saccades (Wolf et al., 1984). Accordingly, a typical 10° saccade in a human lasts approximately 50 msec and has a peak velocity of just under 350°/sec. Both the duration and velocity of saccades can be characterised by their stereotypical relationships with respect to saccade amplitude. For saccades above about
4°, the duration increases linearly with amplitude, forming a remarkably consistent relationship across and within individuals. This relationship is known as the main sequence, a term borrowed from astronomy by Bahill et al. (1975b), and was originally used to refer primarily to the amplitude-velocity relationship, but has since been used for the ‘main sequence for duration’ too. Although these dynamic properties of saccades cannot be voluntarily controlled, there is further evidence that peak velocity, in particular, is susceptible to the context in which the saccade is elicited. Predictive or centrifugal saccades have been shown to have lower peak velocities than reflexive or centripetal saccades (Bronstein and Kennard, 1987, Collewijn et al., 1988). The amplitude-duration relationship is discussed further in Section 1.5.3 in the context of the saccadic flight-time minimisation hypothesis.

Saccades have recently been shown to exhibit also a ‘spectral main sequence’ in the frequency domain which is essentially independent of recording set-up and calibration (Harwood et al., 1999). This may provide a better method for characterising saccade dynamics, that takes into account the whole saccade trajectory and not just the zero and peak velocity points.

The average latency of a primary saccade is approximately 200msec with a standard deviation of 25 to 50msec (Carpenter, 1988). Fischer et al. (1997) have classified primary saccades into a number of groups according to their latencies: slow regular saccades (180-220msec); fast regular saccades (140-180msec); express saccades (80-135msec); anticipatory saccades (<80msec).

The latency of corrective saccades is reported to be lower than that of primary saccades, in the order of 130msec. This varies with the size of the corrective (Becker, 1972; Prablanc and Jeannerod, 1975; Henson, 1978). Becker and Fuchs (1969) and Becker and Jürgens (1979) have reported that the latency of a corrective saccade depends on the mode in which it is generated and that primary saccades that are grossly inaccurate may be followed almost immediately by corrective saccades.
1.4 Saccade Metrics

The metrics of a saccade refers to its amplitude and direction. Saccadic gain is a measure that quantifies saccadic amplitude, traditionally in relation to the target eccentricity. Gain is particularly relevant to this thesis and is discussed fully in this introduction. The total amplitude range of saccades is between a few minutes of arc and 100° (Bahill et al., 1975a). They do not usually exceed 40°, and most naturally occurring saccades are found to be less than 15° (Bahill et al., 1975a). Target eccentricities greater than 20° regularly involve combined eye and head movements (Becker, 1989). For this reason, the largest target eccentricity used in the experiments in this thesis was limited to 20° to minimise the likelihood of inducing head movements as well as saccades. The direction in which saccades are made was not found to make any significant differences to the data collected in this thesis, apart from in the context of patients with homonymous hemianopia in Chapter 3. Directional differences have been reported however by Barnes and Gresty (1973) and were interpreted to result from a bias due to the typical patterns of scanning from left to right in western culture.

1.4.1 What is Gain?

The term ‘gain’ is used to denote the accuracy of the saccadic system. Gain refers to the magnitude of the saccade with respect to the visual goal. The visual goal is generally represented by a visual stimulus (i.e. the visual target), though there are some cases, such as the antisaccadic task, where the visual goal and visual stimulus are not at the same location. Primary saccades to a visual target are rarely accurate. A secondary ‘corrective’ saccade is often required to make up for any overshoot or undershoot of the target made by the primary saccade. It is a well-known phenomenon that most primary saccades undershoot a visual target. This is known as the undershoot bias and is discussed further below.
1.4.2 Measurement of Gain

Gain is traditionally defined as the ratio of the primary saccade amplitude, to the eccentricity of the visual target. This method of determining gain is highly dependent on the calibration for each subject, and the ability to keep the head absolutely static for the duration of the experiment. Any small movement of the head with respect to the target, or the eyes with respect to the eye-movement recording sensors (in the case of the infra-red reflection technique as used in this thesis) can greatly affect the reliability of the measurement. A small head shift with respect to the target of \(-1^\circ\) when assessing gain to targets of \(5^\circ\) could give the impression of a 20\% change in gain when in fact the actual behaviour of the eye with respect to the target has not changed.

The experimental set-up used in the experiments contained within this thesis was designed and built with the ability to test both normal and abnormal children in mind. It was felt that a bite bar, which is the most effective means of ensuring head stabilisation for the duration of an experiment, would not be suitable. ‘Ear-muffs’ were made as an alternative means of head stabilisation, although these could not to used for some children, and for adults experienced in oculomotor research they were not found to assist head stabilisation.

A further drawback of the traditional means of determining gain is due to a phenomenon known as expectation drift (Kowler and Steinman, 1979). Expectation drift is a presaccadic movement of the eyes away from the initial fixation target. This has been reported to be as large as \(1.5^\circ\) using the accurate search coil technique (Lemij and Collewijn, 1989). This drift would decrease the size of the saccade required to fixate the target and so affect the gain of the saccade when determined according to the target amplitude.

The traditional method also depends on the subject foveating different targets with the same retinal locus throughout the duration of an experiment. The visual goal for an identical stimulus is assumed to be constant and equivalent to the target location.
However, it has been suggested that the saccadic system may be lazy. Kapoula and Robinson (1986) suggested that a target may not be accurately foveated if enough information regarding the visual stimulus can be obtained by examining the target slightly off-fovea. Such a theory may be particularly relevant to experiments such as those in this thesis in which the visual stimulus was simple and unchanging, and no detailed analysis of its features was required. Barnes and Gresty (1973) suggested that small angular displacements may rely on the object of fixation having fine or contrasting features. They also suggested that for small retinal errors in the order to $\frac{1}{2}$–$1^\circ$, no attempt would be made to bring the image directly onto the fovea because adequate fixation could be achieved if it rested in the region of the central macular. If such a lazy strategy were true to some extent, the visual goal would not necessarily coincide with the visual stimulus, and furthermore, the visual goal may change over the course of the experiment as the subject becomes aware of the lack of information to be acquired from the target stimulus.

A final drawback of the traditional method is that a less than ideal calibration may sometimes have to be accepted, particularly in children, in order to move on quickly and record as much data as possible before the subject tires or drops out.

Given the drawbacks of the traditional method of determining gain, we introduce two alternative methods. These alternatives are both independent of calibration. They use eye position information, not target position information, to determine the visual goal and are thus independent of target amplitude. This means that gain is determined according to the internal goal of the saccadic system, rather than the external goal defined solely by the target position.

The first alternative method we call ‘component gain’. This determines the visual goal by totalling the (directionally signed) amplitudes of all the saccadic movements made within one trial in order to reach the target. This method disregards the role of non-saccadic eye movement components such as slow phases or drift that may occur while acquiring the visual target. This method also introduces a bias towards a gain of 1.0 in
that any trial without any corrective saccades will, by default, have a gain of 1.0, and thus be deemed, ‘on target’. It is important that primary saccades with a gain of 1.0 using the ‘component gain’ are interpreted with caution. A gain of 1.0 does not necessarily indicate that these primary saccades are accurate, merely that for whatever reason, no corrective saccades were made. This method of determining gain has been used by other researchers (e.g. Wolf et al., 1984; Semmlow et al., 1989) but is less popular than the traditional means of determining gain.

A third method of determining gain, used only in Chapters 2 and 5, we call ‘net gain’. In this method, the eye position at the end of the data collection period (900 msec after target movement unless specified) is taken to be the desired final eye position. Net gain is similar to the component gain but takes into account any non-saccadic components that may occur while acquiring the target.

Barnes and Gresty (1973) have reported that slow phase movements were rare when making reflexive saccades, only being apparent when making small angular displacements. We did not observe significant slow phase components in general; however, when tired, some subjects made large saccades with glissadic endings which may have fallen below the velocity threshold for saccade detection.

The three methods of determining gain are summarised below in Figure 1.1. As can be seen, these three measures differ only in the way in which the target amplitude (the denominator) is determined.

![Figure 1.1](image_url)

**Figure 1.1.** A schematic representation of a saccadic eye movement. The dotted line represents the movement of the target by an amplitude of A. The solid line represents the movement of the eye. The primary saccade is of an amplitude a, the corrective saccade an amplitude b, and the total displacement an amplitude of c. As suggested by this figure, the amplitude of the total eye movement (c) may not be exactly the same as the target movement (A). This may influence the calculation of traditional gain, but not component or net gain.
Traditional Gain = \frac{\text{primary saccade amplitude}}{\text{target amplitude}} = \frac{a}{A}

Component Gain = \frac{\text{primary saccade amplitude}}{\text{total saccadic component}} = \frac{a}{a + b}

Net Gain = \frac{\text{primary saccade amplitude}}{\text{net eye displacement}} = \frac{a}{c}

Given a perfect calibration, no non-saccadic eye movement components, and no signal drift in the instrumentation, we would expect \( a + b = c \). Additionally, given perfect foveation of the target by the eye we would expect \( c = A \). If these relationships were true, all three methods of calculating gain would produce identical values. However, the reliability of the calibration, instrumentation and non-saccadic eye movement components cannot be consistently predicted or guaranteed. For these reasons, we have considered the different methods of characterising gain as outlined above. The component gain was felt to be the most reliable and suitable for characterising the eye movement data in this thesis, particularly the data from children. Consequently, this form of gain has been used throughout this thesis and will be referred to simply as gain, not as component gain. The exception is in Chapters 2 and 5 when all three forms of gain are compared.

1.4.3 The Undershoot Bias

Given a highly developed oculomotor system, one would expect goal-directed saccades to land on target. This would give a gain of 1.0 (however gain is measured). This is the optimal level of gain in order to minimise post-saccadic retinal error. However, most saccades slightly undershoot the target, requiring one or more corrective saccades to make up the difference. Although the amount of undershoot is small, usually around 10% of the total target amplitude (Becker, 1972; Barnes and Gresty, 1973), it is reasonably consistent. The undershoot bias was noted in some of the very earliest investigations into saccadic eye movements (Clark, 1936; Hyde, 1959), and quantified by many researchers
since (Becker and Fuchs, 1969; Weber and Daroff, 1971, 1972; Henson, 1978, 1979; Collewijn et al., 1988; Lemij and Collewijn, 1989; Bötzel et al., 1993)

The undershoot bias is clearest with large eccentricities as both the frequency and the magnitude of undershoot are often found to be roughly proportional to the target eccentricity (Hyde, 1959; Weber and Daroff, 1971, 1972; Henson, 1979; Lemij and Collewijn, 1989). Undershoot has however been recorded consistently to target eccentricities of as low as 4° (Henson, 1979).

Saccadic overshoots, when they occur, are not found to show the same dependence on target eccentricity as saccadic undershoots. Both the frequency and magnitude of overshoots were found to be approximately the same across a range of target eccentricities (Henson, 1979). Early studies in which eye movements were recorded with electro-oculography (EOG) may have under-estimated the amount of both undershoots and overshoots, and over-estimated the number of saccades without correctives, due to the poor resolution of EOG (eg Weber and Daroff, 1971).

The undershoot bias is not however inevitable. Kapoula and Robinson (1986) demonstrated that when presented with a range of target eccentricities, the saccadic system tends to increase the frequency and magnitude of overshoots to the smallest target eccentricity, thus decreasing the frequency of undershoots. The opposite trend is observed for the largest target eccentricities. This phenomenon is known as the range effect and is discussed below.

The undershoot bias is known to be a deliberate strategy as shifting the target back slightly during the primary saccade, to induce more overshoot, causes an adaptive change which eliminates the induced overshoot to re-establish the undershoot bias (Henson, 1978). Similar adaptive changes have since been repeatedly demonstrated using various techniques (eg Wolf et al., 1984; Deubel et al., 1986; see below, Section 1.5)
1.4.4 The Range Effect

Simply put, the range effect is the over-estimation of small target eccentricities and the under-estimation of large target eccentricities. This means that small target eccentricities will elicit high gain saccades, which may even consistently overshoot the target, while large target eccentricities will elicit saccades with a lower gain than normal. This occurs when a range of target eccentricities are presented together in the same experimental paradigm. The range effect is a fundamental characteristic of motor skills (Poulton, 1981) and was first comprehensively reported in the case of saccadic eye movements by Kapoula (1985).

Kapoula and Robinson (1986) demonstrated that given the appropriate experimental conditions, any target eccentricity could be over- or undershot. Using a range of targets from 5° to 20° they found that the average frequency of overshoot in their 5 subjects to the 10° target eccentricity was 15(±10)%.

In contrast, Henson (1979) used a range of target eccentricities, with the 10° target eccentricity being the greatest. The frequency of overshoot, again averaged across 5 subjects, was in the order of 2% (Henson, 1979, see Figure 4, p60). Both paradigms involved reflexive saccades, the main difference being that saccades were elicited only centrifugally by Kapoula and Robinson (1986) but both centrifugally and centripetally by Henson (1978). Centripetal saccades are known to be more likely to overshoot the target (Collewijn et al., 1988), thus the inclusion of centripetal saccades in the data of Henson (1979) is not likely to be a confounding factor. If anything, centripetal saccades would be expected to increase the percentage of overshooting saccades.

While Henson (1978) has shown that consistent overshoot to single targets is eliminated (by adaptive control), the consistent overshoot seen to small target eccentricities in the context of the range effect is not eliminated. This suggests that the saccadic system operates in a global sense, in both space and time, rather than responding to each event separately.
A notable consequence of the range effect is that the saccades in the middle of the range presented have an almost perfect accuracy, while the overall accuracy to targets is not improved. Hence the functional significance of the range effect in the natural environment, if it exists, has still not been pin-pointed, but could be to refine accuracy to parts of the visual environment holding the most important information, while sacrificing a degree of accuracy in the areas peripheral to this.

The range effect establishes itself quickly (Kapoula and Robinson, 1986), although initially the familiar undershoot to all target eccentricities is observed. The strength of the effect can be increased by the use of a visual discrimination task (Kapoula and Robinson, 1986).

1.4.5 Other Effects on Gain

Like the range effect, the global effect (Findlay, 1982) describes a phenomenon in which saccadic accuracy can be influenced by the background or arrangement of targets. For example, a saccade will often land in an intermediate position between two simultaneously presented peripheral targets on the same side of the point of visual fixation on the horizontal axis, the exact position depending on the properties of the visual targets. A saccade will land nearer the stimulus with more salient properties (Findlay, 1982; Ottes et al., 1984).

The exact amount of undershoot or overshoot (i.e. post-saccadic error) is affected by many other factors that arise from the conditions in which saccades are elicited, as well as of course individual differences in performance.

As mentioned, absolute error is affected by the target amplitude, not just in the context of the range effect as discussed above. Both the mean amplitude of the error, and the standard deviation of the error, increase with target eccentricity (Henson, 1979; Lemij and Collewijn, 1989). The amount of error also depends on whether saccades are centrifugal or centripetal. Centrifugal saccades are found to have a greater mean
amplitude and standard deviation of error than centripetal saccades (Becker, 1972; Kapoola, 1985; Collewijn et al., 1988).

The type of saccade generated also affects accuracy. Voluntary saccades between stationary targets are reported to show less error than reflexive saccades to suddenly appearing targets (Lemij and Collewijn, 1989; Becker, 1989).

The accuracy of reflexive saccades is compromised if saccades are initiated before or within approximately 80msec of the target movement (Findlay, 1981; Bronstein and Kennard, 1987). Such saccades are known as anticipatory or predictive saccades and are distinct from normal reflexive saccades, not just in their timing properties and metrics, but also in their dynamics (Bronstein and Kennard, 1987; Smit and van Gisbergen, 1989) and it is thus important to distinguish them in experimental data.

1.4.7 How does Gain Develop?

While saccadic eye movements are present from a young age, their accuracy is very poor in infants up to about 4 months of age (Harris et al., 1993). Saccades to visual targets are difficult to elicit in the young infant. Large visual targets with an additional auditory stimulus are generally required (Jacobs et al., 1992). Infant saccades are found to show gross undershoot (extremely low gain) and a large standard deviation of the error (Alsin and Salapatek, 1975; Harris et al., 1993). Many separate saccades are required to fixate the target. Such sequences of small saccades have been called 'staircase saccades', or 'multiple hypometric' saccades (Meienberg et al., 1981; Harris et al., 1993). Although such saccades are a common feature in infants, Troost et al. (1974) reported their frequency in adults to be less than 2%.

The gain of infant saccades increases over the first few months of life. Accuracy is still not quite up to adult levels by 7 months of age (Harris et al., 1993) but by around one year of age a normal amount of saccadic undershoot and deviation of the error is generally observed (personal communication, C. M. Harris).
The development of the infant visuo-motor system undergoes very rapid change in these first few months of life. Not only does a basic improvement of accuracy have to be achieved, but also compensation for rapid development of other parts of the visual system. Changes occur in optical magnification due to growth of the eyeball, lens and cornea, and photoreceptor migration (Yuodelis and Hendrickson, 1986), and the ocular plant due to growth in eyeball size and of the extraocular muscles.

These intense changes in early life require a highly plastic system, able to learn quickly in order to adapt to such rapid changes and achieve an acceptable degree of accuracy in a relatively short amount of time. The adaptive control system, which is known to be very efficient in the human adult (Deubel et al., 1986), would be able to subserve such changes in infants, if indeed it were present from birth.

1.5 Why Saccadic Undershoot?

It has already been mentioned that saccadic undershoot is a robust phenomenon. However, relatively few theories have been put forward to explain this. The saccadic system is highly adaptive (see below, Section 1.6), and greater accuracy is certainly within the adaptive capabilities of the system. The robust undershoot bias however suggests that there may be some sort of penalty for overshooting and that the system does not wish simply to minimise retinal error, but possibly to implement an alternative goal for the system.

1.5.1 The hemispheric facilitation hypothesis

An early and persistent theory proposes that targets are undershot in order to maintain the representation of the visual target in the same hemisphere. In doing so, the visual system is facilitated in re-identifying and re-locating the target after the end of the primary saccade. This would in turn mean that any subsequent saccade could be elicited with a shorter latency than if the representation had switched to the opposite hemisphere.
This theory was first proposed by Robinson (1973) in relation to the data of Young et al. (1968) and has been called the 'Hemispheric facilitation hypothesis' (Henson, 1978).

Young et al. (1968) reported that the latency for backward corrective saccades, after an overshooting primary saccade, was double that of onward corrective saccades after an undershooting primary saccade.

A number of researchers have since investigated latency differences between onwards and backwards corrective saccades. Results have not been conclusive and the methodology is crucial. It is important that the amplitude of the corrective saccades is taken into account as saccadic latency is known to increase as amplitude decreases (Becker, 1972; Henson, 1978; Kapoula and Robinson, 1986). Additionally, the amount of overshoot, and thus the magnitude of the backwards corrective saccade, is generally less than the magnitude of undershooting saccades and their onwards correctives (Weber and Daroff, 1972; Kapoula and Robinson, 1986). Weber and Daroff (1972) reported that the latencies for onwards and corrective saccades were the same, though they do not specify their methods for determining this. Becker (1972) reported the same result. Henson (1978) on the other hand reported a highly significant difference between the latency of onwards and backwards corrective saccades. He stressed the importance of comparing latencies from within the same experimental session in order to prevent day-to-day variations affecting the results. He did not however specify the relative amplitudes of the onwards and backward saccades that he compared. We postulate in Chapter 5 that differences in amplitude were the reason behind the reported differences in latency.

Kapoula and Robinson (1986) reported that there were no significant differences between onwards and backward corrective latencies, though once again they did not fully compensate for differences in amplitude. In Chapter 5 within-subject (and within-session) comparisons of amplitude-matched corrective saccades reveal that there is indeed no significant difference in the latencies of onwards and backwards corrective saccades. This finding contradicts the predictions of the hemispheric facilitation hypothesis.
1.5.2 Other theories

De Bie et al. (1987) suggested that the probability of an overshoot is kept below a fixed value in order to maintain the stability of the system. However, it has been pointed out by Harris (1995) that stability would only be an issue if the gain were very high (eg at or above 2) which is not likely in a healthy adult.

Kapoula and Robinson (1986) proposed that undershoot is indicative of a ‘lazy strategy’ in natural scanning which is carried over to the laboratory context. When scanning, they propose that the system does not make the effort to be accurate as the significance of objects can be determined slightly peripheral to the fovea. If this were the case however, one would expect a relatively constant amount of undershoot to all target eccentricities. This is not the case (Henson, 1979; Lemij and Collewijn, 1989).

1.5.3 The saccadic flight-time minimisation hypothesis

The most recent theory to address the undershoot bias is the saccadic flight-time minimisation (SFM) hypothesis (Harris, 1995). This theory predicts that undershooting is an economical strategy for maximising the time of clear vision by minimising saccadic flight-time. Such an idea was first suggested, but not expanded upon, by Becker (1989) who proposed that saccadic undershoot was a ‘parsimonious strategy in terms of energy expenditure and the total time spent in fast travel’.

The evolution of saccades is presumed to facilitate the refixation of visual stimuli very rapidly. Visual perception during saccades is greatly degraded, not only due to the speed with which the image is moving across the retina (Barnes and Smith, 1981) but also due to a physiological process known as ‘saccadic suppression’ (Matin, 1974). As such it would seem logical to keep this time of lost vision i.e. saccadic flight-time, to a minimal level. Given the same magnitude of error, an overshooting saccade would involve a longer flight-time than an undershooting saccade to reach a target. This can be determined from the amplitude-duration relationship of saccades. This relationship is known as the main
sequence for duration (Bahill et al., 1975a) and has a stereotypical appearance. There is
an initial rapid rise in duration with amplitude, followed by a linear portion for saccades
>4°. See Figure 1.2. Linearity is lost at the larger amplitude end of the spectrum, but such
large saccades are not elicited in any of the experiments in this thesis.

![Graph showing duration vs. amplitude](image)

**Figure 1.2.** A typical main sequence
for duration (from one of the
subjects in Chapter 5). The linear
regression line, slope ($\beta$) and
intercept ($\alpha$) are marked.

Given this linear relationship, it is simple to see that the flight-time of an
overshooting sequence of saccades is greater than the flight-time of an undershooting
sequence of saccades by $2\beta(e)$, when the magnitude of error ($e$) is the same in each. See
Figure 1.3.

![Diagram showing flight-time for overshooting and undershooting saccades](image)

**Figure 1.3.** To demonstrate the increased
flight-time involved when making an
overshooting rather than an undershooting
saccade.

Thus, undershooting is best for minimising flight-time. However, due to the
natural random variation in saccadic error, the average gain would have to be quite low in
order to avoid any overshoot at all. How low would depend on the standard deviation. In
Figure 1.4A it can be seen that the mean gain is relatively high while still keeping the
number of overshooting saccades relatively low because there is little spread in the data. In Figure 1.4B however the mean gain becomes very low to prevent excessive numbers of overshooting saccades.

![Figure 1.4](image)

*Figure 1.4. The solid curve represents a gain distribution with an average gain of 1.0 in each graph. The dotted curve represents a hypothetical optimum in order to minimise saccadic flight-time. When the standard deviation of the gain is low as in A, an average gain of just below one reduces, though does not eliminate, overshooting saccades. In order to produce approximately the same percentage of overshooting saccades when the standard deviation of the gain is high, as in B, the average gain must become very low. The dashed reference lines indicates a gain of 1.0.*

Very low gain saccades are not however beneficial for minimising saccadic flight-time either. Low gain saccades require more corrective saccades to reach the target. From Equation 1 it can be seen that there is a penalty (α) for simply making a saccade so a greater number of saccades would increase the flight-time by $n(\alpha)$ where $n$ is the number of saccades made, regardless of their amplitude. The x-axis intercept represents the trade-off between $\alpha$ and $\beta$ has been called gamma ($\gamma = \alpha/\beta$).

In computer simulations using the main sequence data of Collewijn *et al.* (1988), Harris (1995) showed that when the standard deviation of the saccadic error is approximately 10% of the target distance, the optimal gain is 0.93-0.97. This fits with empirical evidence. The exact value in each individual depends on their main sequence for duration, with $\gamma$ predicted to be positively correlated with gain. For example, both $\gamma$ and average gain are increased in centripetal relative to centrifugal saccades (Collewijn *et al.*, 1988).
When the standard deviation is large, for example in infants, the optimal gain was predicted to be 0.6 which also agrees with empirical observations (Harris et al., 1993). In Chapters 3 and 4 we present further examples of situations in which a large standard deviation of saccadic error is associated with a low gain. In Chapter 5 we investigate the relationship between the main sequence for duration and gain in 20 subjects.

1.6 How is gain controlled?

In order to manipulate the optimal gain according to changing circumstances the saccadic system must have an efficient control system to detect errors and adjust gain appropriately. The saccadic system is known to be under adaptive control.

1.6.1 Adaptive control

Adaptive gain control is needed to maintain accuracy in systems where feedback is absent, or of too low a gain (Ito, 1984). These are known as open loop systems. Saccadic eye movements have a duration too short to enable direct feedback control by the relatively slow visual feedback signals. In order therefore to maintain a sufficient level of accuracy, the oculomotor control system must employ a method of control that can achieve proper calibration of the parameters. Adaptive control systems are self-correcting systems which continually monitor their own performance. In the event of an error, the system adjusts its own parameters so as to reduce the probability of such an error occurring again. Such constant monitoring of performance by an adaptive control system is important not only in infants and children, in their growth and development, but also throughout life in response to on-going development and ageing, as well as disease and injury.

Evidence for the capability of the saccadic system to compensate adaptively for pathological dysmetria has been gathered from both clinical and experimental lesion
studies (Kommerell et al., 1976; Optican and Robinson, 1980). Artificially induced
dysmetria has also demonstrated the impressive adaptive capabilities of the saccadic
system (Henson, 1978; Deubel et al., 1986). Several findings from lesion studies point to
the involvement of parts of the cerebellum, specifically the midline cerebellar vermis
lobules VI and VII, as being the site of the saccadic adaptive gain controller (Optican and
Robinson, 1980; Takagi et al., 1998) and thus essential for the production of accurate
saccades, probably by acting on the saccadic generator of the brainstem.

1.6.2 Lesion studies

Some of the first examples of the adaptive control of saccades were seen in
patients with ocular motor nerve palsies. Kommerell et al. (1976) noted that patients with
a unilateral nerve palsy could adjust the amplitude of their saccades depending on which
eye was forced to view. Abel et al. (1978) reported similar findings in a patient with a
partial third nerve palsy.

These early findings in human patients have been reproduced under controlled
conditions in monkeys. Optican and Robinson (1980) were the first to confirm the
existence of similar adaptive capabilities of the saccadic system in monkeys in response
to muscle tenectomy. Their seminal paper localised the adaptive controller to the vermis
of the cerebellum.

1.6.3 Experimental studies on humans

The adaptive control of saccades has been the focus of many investigations. These
generally artificially induce a greater number of overshooting saccades in order to
stimulate the adaptive control system to adjust the gain of saccades to restore the
undershoot bias. Henson (1978) used a contact lens-spectacle lens combination to induce
overshooting saccades. The most popular method has been to shift the visual target
slightly back towards its original position while the primary saccade is in progress. This is
known as intrasaccadic target perturbation, or intrasaccadic target displacement (McLaughlin, 1967; Vossius, 1972; Miller et al., 1981; Wolf et al., 1984; Deubel et al., 1986; Semmlow et al., 1989; Erkelens and Hulleman, 1993; Frens and van Opstal, 1994; Deubel, 1995; Straube and Deubel, 1995). By intrasaccadically displacing the target back slightly towards the fixation point during the primary saccade, an increased number of overshooting saccades is induced. This leads to an adaptive decrease in gain to restore the undershoot bias. We have called this the gain decreasing paradigm in this thesis. In contrast, by shifting the target onwards during the primary saccade, the magnitude of undershoot will be increased and the number of overshoots decreased. This leads to an adaptive increase in gain. We call this the gain increasing paradigm.

The characteristics of gain control have been a popular area of investigation. There are a number of features of the adaptive control of saccades that are generally agreed upon, while others have produced conflicting data and interpretations.

### 1.6.4 Characteristics of Adaptive Control

**Directional specificity**

Saccadic adaptation is directionally specific (Kommerell et al., 1976; Abel et al., 1978; Wolf et al., 1984; Deubel et al., 1986). Modification of gain for saccades in one direction does not affect the gain of saccades in the opposite direction. More specifically Deubel (1985) demonstrated that induced gain modifications are limited to an angle of +/-30° around the adapted direction. This finding fits in with the known lateralisation and symmetry of the oculomotor pathways in the central nervous system. It is also complementary to the arrangement of the extraocular muscles, in that it is sensible to have some degree of independent adaptation around each of the directions of action of the extraocular muscles in order to be able to deal with peripheral changes.
It has additionally been shown that the each eye may adapt by a different amount in the same direction. This was demonstrated by Lemij and Collewijn (1991a, b) in subjects who wore anisometropic spectacles. The ability to achieve such non-conjugate adaptation is also beneficial given that peripheral or central damage to the eye movement control systems will not necessarily affect both eyes symmetrically.

**Asymmetrical adaptation**

An asymmetry in the adaptive effect has been noted from the very first investigations of adaptive control (McLaughlin, 1967). Gain decreases are found to take place faster than gain increases. This distinction has been consistently reported since, in both experiments on monkeys (Optican and Robinson, 1980; Fitzgibbon et al., 1986), and in target perturbation experiments in humans (Miller et al., 1981; Wolf et al., 1984; Deubel et al., 1986). Miller et al. (1981) reported that gain decreases reached approximately 60% of completion while gain increases reached only 25% of complete adaptation over the same time scale. Similarly, Deubel et al. (1986) reported that the gain decreasing paradigm led to a reduction in gain within a few tens of trials, while the same change magnitude of change in a gain increasing paradigm took in the order of hundreds of trials. These biases are specific purely to the direction of adaptation, up or down, and not to the initial gain value. This is revealed by the time-scales for re-adaptation after the end of the adaptive phase. Re-adaptation after a gain decreasing paradigm shows the same slow rate as seen in a gain increasing paradigm, and vice versa (Deubel et al., 1986).

Two studies have reported trends in the opposite direction (Abel et al., 1978; Albano and King, 1989). There are no clear explanations for these discrepant findings. The results of Abel et al. (1978) were based on the findings of one patient who had suffered a probable brainstem stroke causing a partial third nerve palsy and ptosis, and thus other factors surrounding his neurological status may have affected his gain control mechanisms. Albano and King (1989) used a novel intrasaccadic target displacement
paradigm which has not reportedly been used before or since. Their findings may have been unique to their adaptive paradigm.

In spite of gain decreases taking place faster than gain increases, complete adaptation in the gain decreasing paradigm over the course of a standard length experiment has rarely been achieved. However, Deubel et al. (1986) extended the number of adaptive trials to 375 and reported that complete adaptation was possible.

Is adaptive control really parametric?

The adaptive control of saccadic eye movements has often been labelled ‘parametric’ (McLaughlin, 1967, Miller et al., 1981; Wolf et al., 1984; Deubel et al., 1986). This refers to the belief that adaptive changes of saccadic gain will affect saccades of all sizes (in the adapted direction) proportionally to their amplitudes. In retrospect, early experiments did not use enough target eccentricities to determine whether the adaptive effect was truly parametric, or was specific to a certain target eccentricity, or position in space (eg McLaughlin, 1967; Henson, 1979; Miller et al., 1981). Wolf et al. (1984) found that the size of adapted saccades was directly proportional to the size of the target step for a range of target eccentricities (10°-15°). This effect was also present when saccades to only one target eccentricity had been adapted. This supported the parametric nature of gain control. More recently it has been revealed that the parametric effect does not always affect saccades of all amplitudes in a specific direction, but is restricted to a range of saccadic vectors, centred around the adaptation saccade. This has been labelled a ‘restricted adaptation field’ by Frens and van Opstal (1994). The adaptation field is proposed to be quite broad, stretching at least 5° below the adapted eccentricity on the horizontal meridian (eccentricities above were not tested), and to angles at least ±30° above and below the adapted meridian (Deubel, 1985) which explains why previous
investigations which used a restricted range of target eccentricities did not report this restriction of adaptation to certain amplitudes.

**The dynamics of adapted saccades**

There has been little consistency in the reports of the dynamics of adapted saccades. No changes have been reported in the dynamics of adapted saccades by Albano and King (1989) or Frens and Van Opstal (1994) in humans, or by Optican and Robinson, (1980) in monkeys. However, Straube and Deubel (1995) have reported effects in humans. These were different in the gain increasing and gain decreasing paradigms. Gain increasing caused a decrease in peak velocity while gain decreasing showed changes in the peak acceleration/deceleration ratio. Takagi *et al.* (1998) also reported changes in peak velocity, acceleration and deceleration in monkeys while Fitzgibbon *et al.* (1986) reported that adapted saccades in a gain decreasing paradigm in monkeys had lower peak velocities than normal saccades of an equal size, while saccades in a gain increasing paradigm had longer durations due to multiple velocity maxima. A consistent change in saccade dynamics as a result of adaptation may suggest that adaptation has effects at the level of the burst generator in the brainstem.

**Latency characteristics of adapted saccades**

Changes reported in latency characteristics appear to be idiosyncratic and again are not consistent between experiments. Frens and van Opstal (1994) reported no effects of adaptation on the latency of primary or corrective saccades in humans. However, Fitzgibbon *et al.* (1986) reported that saccadic profiles indicated that corrective saccades may have been incorporated into the primary saccade, suggesting that they are generated with abnormally low intersaccadic intervals. Straube *et al.* (1997) on the other hand reported a significant increase in primary saccade latency in only two of four monkeys and that these increases in average latency appeared to be due to the loss of short-latency
express saccades from the latency distribution. The loss of express saccades and an increase in the primary latency has also been reported in monkeys by Takagi et al. (1998).

Two distinct types of adaptation? Fast and slow

Muscle weakening produces relatively slow adaptation in both humans and monkeys, with adaptive changes taking place over a time scale of days (Kommerell et al., 1976; Abel et al., 1978; Optican and Robinson, 1980). However, intrasaccadic perturbation experiments produce adaptive changes over a much faster time scale. Changes begin to take place over as little as a few tens of trials which takes only a few minutes (McLaughlin, 1967; Miller et al., 1981; Deubel et al., 1986). This suggests that there may be a distinction between the slow adaptation seen as a result of motor system impairment, and the rapid adaptation seen due to visual manipulation.

The possibility that fast adaptations are in fact the result of cognitive or even conscious strategies, rather than genuine oculomotor adaptions, is possible. However, Deubel (1995b) demonstrated that various context variables cannot be used to switch cognitively between different response parameters. Furthermore, the gradual change in gain, both initially when manipulating gain, and subsequently when restoring ‘normal’ gain, rather than a sudden change, does not support the use of a conscious strategy. On the other hand, experiments involving the adaptation of the gain of the vestibulo-ocular reflex (VOR) have suggested that humans can adaptively adjust their VOR gain depending on context (Shelhamer et al., 1992).

Deubel (1995) suggests that a fast adaptive mechanism might exist to rapidly adjust the magnitude of saccadic responses individually for each movement direction, while another, much slower adaptive process allows compensation for position-dependent effects. This is due to the finding that there are position-specific effects in slow adaptation (Optican and Robinson, 1980), but not in fast adaptation (Deubel, 1995). It may be relevant, however, that in the clinical studies involving paretic eye muscles, the gain of
saccades is initially very low and is required to increase substantially. As already
discussed, gain increases seem to take much longer than gain decreases and indeed have
not been seen to achieve anything near completion in any intrasaccadic target
displacement paradigm. Thus, the distinction between slow adaptation, as a result of
muscle weakening, and fast adaptation, seen in target displacement paradigms, may be an
artefact of the asymmetry of the adaptive effect.

The question remains however, if there are separate fast and slow adaptive
processes, whether the underlying mechanisms and anatomy are the same, or do different
time courses suggest also different mechanisms? Vermis lobules VI - IX and the fastigial
nuclei have been shown to be essential in the slow adaptation paradigms in monkeys
(Optican and Robinson, 1980) while lesions to the oculomotor region of the fastigial
nucleus and the interpositus nucleus in monkey result in a lasting inability to adaptively
adjust gain in the rapid adaptation paradigm (intrasaccadic target perturbation paradigm)
(Goldberg et al., 1993). In humans there is sparse data. Waespe and Baumgartner (1992)
reported that patients with Wallenberg’s lateral medullary syndrome, which affects the
olivo-cerebellar pathways, were unable to adaptively adjust the size of their saccades in a
target perturbation paradigm.

Context-Specific Adaptation

Erkelens and Hullemen (1993) and Deubel (1995a) have reported that internally
triggered saccades (voluntary saccades) can be adapted independently from externally
triggered saccades (reflexive saccades) in humans. Erkelens and Hullemen (1993) only
examined transfer from adapted voluntary saccades to reflexive saccades. Deubel (1995a)
examined transfer in both directions and reported no transfer from reflexive saccades to
voluntary saccades, but found a small but significant transfer of adaptation from voluntary
to reflexive saccades. Deubel (1995b) additionally reported that other context variables,
such as the spatial position of the target, the form and colour of the target, or the presence or absence of a background structure, were not used to trigger specific adaptive changes.

It is possible that the results of Erkelens and Hulleman (1993) could have been affected by the large intrasaccadic movement of the target. Bridgeman et al. (1975) has reported that intrasaccadic target steps of less than 33% of the target eccentricity are not detectable due to saccadic suppression. Frens and van Opstal (1994) have reported that three subjects who were aware of an intrasaccadic target jump of 33% backwards did not adapt as expected. In the paradigm of Erkelens and Hulleman (1993) the target moved backwards by 50% after the initial 17.5° target step. They reported that although the subjects did not notice the intrasaccadic displacement, they were aware that the position of the target after the saccade differed from before the saccade. This level of awareness may have affected the transfer of adaptation from internally to externally triggered saccades.

The results of Erkelens and Hulleman (1993) and Deubel (1995) suggest that reflexive and voluntary saccades may have at least partially different pathways and adaptive control mechanisms. This could be a consequence of the separate evolutionary development of these pathways, as the externally triggered reflex eye movements were the evolutionary forerunners to voluntary, internally triggered saccades. Systems with separate pathways would also be expected to have separate adaptive control mechanisms. Clinical evidence has suggested that the midline cerebellum is involved in the gain control of reflexive saccades but not voluntary saccades (Straube et al., 1995).

Species differences

It has been found that adaptation seems to take place faster in humans than in monkeys. Direct comparisons between experiments is difficult due to differences in experimental paradigms used in monkeys and humans by different researchers. Straube et al. (1997) have suggested that humans may adapt faster because they use a strategic
component when adapting in addition to true plasticity. The possibility of cortical involvement in adaptation is discussed in Section 1.8.5.

Further species differences have been revealed in the transfer of adaptation between different types of saccade. As discussed above, Erkelens and Hulme (1993) and Deubel (1995) both reported little or no transfer between voluntary and reflexive saccades. In contrast, Fuchs et al. (1996) found substantial transfer from reflexive saccades to voluntary saccades in monkeys. These contrasting findings suggest that saccadic gain adaptation may involve different pathways in humans and in monkeys. This finding also means that care should be taken when extrapolating lesion data from monkeys to interpret experimental findings in humans.

A dissociation between the anatomical areas involved in saccade control in humans and monkeys has already been suggested with respect to the basal ganglia (Petit et al., 1993, see Section 1.7.5).

1.7 The Neural Generation of Saccades

The areas involved in the generation of saccades are spread diffusely throughout the cortex and subcortex. The final common pathway for all saccades involves burst neurons in the pontine and mesencephalic reticular formations. These neurons provide the immediate premotor command signal, the pulse, which is sent to the oculomotor nuclei. There are many different cortical areas that are believed to be involved in saccade generation under distinct circumstances. These are mainly located in the frontal and parietal areas.

Although the adaptive control of saccades has been attributed primarily to the cerebellum, it is still unknown exactly where along the saccade generating pathway the adaptive control signal is able to influence the oculomotor signal. The brainstem saccade generating areas in the pons and the superior colliculus are known to be the two most
important subcortical structures involved in the generation of saccades, and potential sites of signal convergence due to their widespread afferent pathways.

In this section an overview of the different areas involved in saccade control will be given, and in the next section the cerebellum in particular will be discussed along with its role in adaptive control.

1.7.1 The Nature of the Premotor Signal and the Neural Integrator

The pattern of innervation sent from the premotor circuitry in the brainstem (the pulse generator) to the extra-ocular muscles (EOM) is known to consist of a pulse and a step (Robinson, 1964; Robinson and Fuchs, 1969). The pulse of activity sent to the agonist muscles is required to give high acceleration in the face of the viscous resistance of the eye in the orbit. The intensity of the firing rate determines the velocity of a saccade, and together with the duration of the pulse, this determines the amplitude of the saccade. The step component is a change in the tonic innervation of the EOM to hold the eyes steady at the new direction of gaze, in order to balance the elastic forces of the EOM, which would otherwise return the eye to its primary position in the orbit.

In order to obtain this step signal, the eye velocity signal is integrated by the 'neural integrator' (Skavenski and Robinson, 1973). Cannon and Robinson (1987) proposed that the job of the neural integrator is performed by cells in the region of the prepositus nucleus and medial vestibular nuclei; this is generally agreed, at least with respect to horizontal saccades. However, the brainstem does not appear to be the only site of neural integration; lesions of the cerebellum have also been found to affect the neural integration process. The time constant of the neural integrator is effectively infinite in the intact brain in photopic conditions. Ablation of the brainstem integration nuclei reduces this time constant to approximately 200msec (Cannon and Robinson, 1987), effectively eliminating any integration capacities, while ablation of the cerebellum makes the integrator 'leaky', reducing the time constant to >1300msec (Zee et al., 1981). The neural
integration apparatus of the brainstem and the cerebellum appear to supplement each
other, the cerebellum improving the performance of the inherently leaky neural integrator
of the brainstem (Leigh and Zee, 1991). Ideally, with an intact neural integrator, the new
level of tonic activity, the step, should exactly match the new position to which the eye
was driven by the preceding pulse. A leaky neural integrator will result in a ‘pulse-step
mismatch’ and the eye will drift from the position it was driven to by the pulse, to the new
resting position determined by the step.

1.7.2 The Brainstem Saccade Generator

Burst cells in the paramedian pontine reticular formation (PPRF) in the pons
provide the immediate pre-motor pulse signal for all ipsilateral horizontal saccades. This
is the saccadic velocity command which is sent in parallel to the oculomotor neurons and
the neural integrator (Keller, 1974; Sparks and Mays, 1990). The burst neurons for
vertical and torsional saccades lie in the rostral interstitial nucleus of the medial
longitudinal fasciculus (riMLF) of the midbrain. This thesis investigates only the
characteristics of horizontal saccades and so only the areas involved in the control of
horizontal saccades will be discussed here.

Single unit recordings in alert animals have revealed three types of saccade-related
neurons (Fuchs et al., 1985): 1) short-lead burst neurons which begin firing 8-12msec
before ipsilateral saccade onset and create the pulse of activity that is sent to the
extraocular muscles via the oculomotor neurons. These neurons were originally called
medium-lead burst neurons. They project directly to the ipsilateral abducens nucleus as
well as inhibitory burst neurons, the vestibular nuclei and other brainstem sites; 2) long-
lead burst neurons which show a change in activity more than 100msec before saccade
onset. These neurons are found in many parts of the pons and rostral medulla, as well as
the superior colliculus. Their exact role is unknown but they may help to encode saccade
direction and assist synchronisation; 3) pause neurons in the nucleus raphe interpositus
whose tonic discharge ceases before and during saccades. A subset of these neurons are known as the omnipause neurons as they respond for saccades in all directions. They are believed to have control over the short-lead burst neurons.

The brainstem also contains inhibitory burst neurons, located in the nucleus paragigantocellularis dorsalis in the dorsomedial rostral medulla. They inhibit the contralateral abducens nucleus during ipsilateral saccades.

There is an area of the brainstem, the nucleus reticularis tegmentis pontis, which receives projections from the frontal eye fields and superior colliculus, and projects to the cerebellum, particularly to vermis lobules VI and VII (Ito, 1984). This area, about which relatively little is known, may be important for the adaptive control process by providing input to the cerebellum about intended saccadic behaviour.

The relationship between the brainstem areas is shown below in Figure 1.5.

![Diagram of brainstem areas](image)

**Figure 1.5.** To show the relationship between the saccade-related brainstem areas, the thalamus and the cerebellum in the rhesus monkey. From Miller (1985). The areas of primary relevance are:
- PPRF - paramedian pontine reticular formation
- iMLF - interstitial nucleus of the medial longitudinal fasciculus
- SC - superior colliculus
- III - oculomotor nucleus
- IV - trochlear nucleus
- VI - abducens nucleus

### 1.7.3 The Superior Colliculus

Lesion studies in monkeys have indicated the importance of the superior colliculus in saccade generation. Acute lesions cause delayed, hypometric saccades with abnormal directions and speeds (Wurtz and Goldberg, 1972; Schiller *et al.*, 1980; Hikosaka and Wurtz, 1985, 1986). Recovery from these profound deficits occurs but still leaves subtle deficits in latency and accuracy. Superior colliculus lesions also eliminate short-latency ‘express saccades’ (Schiller *et al.*, 1987). The recovery from lesions of the superior
colliculus is believed to be due to parallel pathways to the brainstem saccade generator from the frontal eye fields (FEF). Combined lesions of the superior colliculus and FEF cause a long-lasting inability to make saccades (Schiller et al., 1980; Keating and Gooley, 1988). Isolated lesions of the superior colliculus have rarely been reported in humans.

Each superior colliculus contains a retinotopic map of the contralateral hemifield (Robinson and McClurkin, 1989; Sparks and Harwich-Young, 1989) The metrics of a saccade are spatially encoded in the superior colliculus by the site of activity. The superior colliculus projects directly to the brainstem saccade generator where the characteristics of the saccade are encoded in the temporal properties of the signal. It is believed that the superior colliculus makes the transformation of the signal from spatial coding to the temporal coding. The way in which the superior colliculus achieves this has been proposed by Munoz and Wurtz (1995a, b).

The superior colliculus is fundamental to the generation of most saccades and receives many converging inputs. Visual attentional excitation is received from the posterior parietal cortex, motor command excitation from the FEF, while tonic inhibition from the substantia nigra gates the ability of the superior colliculus to respond to excitation from the cortex.

The superior colliculus has a distinct anatomy of seven layers with widespread input and output relations. The dorsal layers receive retinotopic projections from the retina and striate cortex, and contain a visual map. The intermediate layers contain a motor map and at least three different types of cells: burst neurons, build-up neurons and fixation neurons. Burst neurons have distinct ‘movement fields’, they fire only in relation to a saccade that will move to a certain part of the visual field (Schiller and Stryker, 1972). As such they encode the desired change in eye position. The movement fields of burst neurons are large, so the actual saccade generated is determined by the weighted activity of many tectal neurons (McIlwain, 1982; Ottos et al., 1986). Such population coding minimises the effects of noise. Although the motor map in the intermediate layers,
and the sensory map of the superficial layers, are aligned, visually induced activity in the superficial layers does not necessarily lead to movement activity in the intermediate layers (Leigh and Zee, 1991).

The deep layers of the superior colliculus receive inputs from other sensory modalities which are represented in further sensory maps (Leigh and Zee, 1991).

The superior colliculus is clearly a highly important relay stage for the generation of saccades. In fact, there is evidence that there may be a purely subcortical route for eliciting goal-directed saccades in the absence of conscious visual perception, in which the superior colliculus can provide the visual input necessary for making accurate saccades. This is known as blindsight (see Cowey and Stoerig, 1991), and is a controversial topic which is not addressed in this thesis.

1.7.4 Cortical Areas

Many different cortical areas are involved in the generation of saccades. See Figure 1.6. There are however just three cortical areas capable of triggering saccades: the frontal eye fields, the parietal eye fields and the supplementary eye fields (Pierrot-Deseilligny et al., 1995). The influence of the frontal and parietal areas on the control of saccades appears to be by two parallel pathways. The pathway from the frontal cortex passes, either directly, or indirectly via the basal ganglia, to the superior colliculus and is related to internally generated saccades. The pathway from the parietal cortex passes directly to the superior colliculus and is particularly involved in generating reflexive saccades and reorienting to novel visual stimuli. These pathways and their proposed roles are not completely separate though; there are strong interconnections between them. [See over for diagram to show the cortical areas believed to be involved in saccade generation.]
The Frontal eye Fields

The frontal eye fields (FEF) (Brodmanns Area 8) are part of the prefrontal association cortex and lie on the posterior segment of the anterior bank of the arcuate sulcus (Bruce et al., 1985). Electrical stimulation of Area 8 leads to contralateral eye movements in monkeys (Robinson and Fuchs, 1969) and humans (Goday et al., 1990). Experimental lesions to the FEF in monkeys causes particular deficits in saccadic tasks involving the generation of voluntary, or internally generated saccades. Similar impairments with voluntary saccades are seen in humans with frontal lesions. Such lesions can additionally produce saccade slowing and hypometria saccades (Leigh and Zee, 1991). Imaging studies have also supported the role of the FEF in voluntary eye movements (Melamed and Larsen, 1979; Fox et al., 1985; Petit et al., 1993).

The FEF receive widespread connections from the thalamus and other cortical areas including the saccade-related areas of the parietal lobe and the visual areas of the occipital cortex. The largest projection from the FEF is topographically to the ipsilateral superior colliculus but they also send a direct projection to the ipsilateral brainstem
saccade generator (Stanton et al., 1988), as well as to the basal ganglia and thalamus. The
direct projection from the FEF to the brainstem saccade generator is supported by the
finding that ablation of the superior colliculus does not prevent elicitation of saccades by
stimulation of the FEF (Schiller et al., 1972; Keating et al., 1983; Shibutani et al., 1984).
The frontopontine tract (bundle of Arnold) provides the means by which the frontal eye
fields can communicate with the cerebellum.

The FEF also contain a motor map, similar to that described in the superior
colliculus. Visual cells, movement cells, and fixation cells have been identified in the FEF
(Bruce and Goldberg, 1985) and are thought to have two major influences on the
generation of saccades via the superior colliculus: they indicate to the superior colliculus
the amplitude and direction of an imminent saccade and they assist in the control of
fixation.

The Parietal Eye Fields

The posterior parietal cortex (Brodmann’s Area 7a) is known to be important in
spatial-attentional processes and thus it is difficult to distinguish saccadic deficits
secondary to visual neglect from primary deficits resulting from the parietal lesion.
Nevertheless, an area of the posterior parietal cortex has been identified that has a specific
role in the generation of saccades. This area is found in the lateral intraparietal area (LIP)
of the intraparietal sulcus (Andersen, 1992) and is known as the parietal eye field (PEF).
Stimulation in the LIP elicits contralateral saccades (Shibutani et al., 1984) and it is found
to have strong anatomical connections to other saccade-related areas including the FEF
(Andersen et al., 1985), the superior colliculus (Lynch et al., 1985) and the dorsal
pontine nuclei (May and Andersen, 1986) though not directly to the brainstem saccade
generator. Lesions of the parietal lobe produce saccade latency and metric deficits (Lynch
and McLaren, 1989) and combined parietal and frontal lesions produce severe saccade
deficits while frontal lesions alone do not.
The influence of LIP is funnelled through the superior colliculus; thus stimulation of the LIP will not elicit saccades if the superior colliculus has been lesioned (Keating et al., 1983). The LIP is believed to localise targets in a head-centred craniotopic system.

**The Supplementary Eye Field**

The supplementary eye fields (SEF) are located at the anterior part of the supplementary motor area in monkeys (Schlag and Schlag-Rey, 1987). Stimulation in monkeys elicits saccades (Goldberg and Segraves, 1989). Imaging studies in humans have shown increased cerebral blood flow in this area during saccadic tasks (Fox et al., 1985, Petit et al., 1993).

The SEF projects to the FEF, LIP, superior colliculus, basal ganglia and directly to the pause cell region in the pons (Leigh and Zee, 1991). This area appears to be particularly involved in the organisation of sequences of saccades (Gaymard et al., 1990).

**Other Cortical areas**

The anterior cingulate cortex has recently been implicated in the control of voluntary, particularly remembered, saccades as a result of functional imaging studies (Petit et al., 1993; O’Sullivan et al., 1995). Previous studies with positron emission tomography (PET) have shown that activation in the anterior cingulate is associated with selection for action and attention (Pardo et al., 1990; Corbetta et al., 1991). The suggestion of higher-order cognitive oculomotor functions for the anterior cingulate ties in with the ideas of Pierrot-Deseilligny. Pierrot-Deseilligny (oral communication, BOMG, 1996) reported that lesions in the area of the anterior cingulate cortex cause dysmetria in memory-guided saccades. He suggested that perhaps there is another ‘eye field’ in the anterior cingulate cortex which could be a part of an ‘anterior attentional network’ involved in the control of motivation and intentional spatial exploration.
The dorsolateral prefrontal cortex shows activity related to the memory of target locations (Leigh and Zee, 1991). Lesions cause deficits in remembered saccades.

1.7.5 The Basal Ganglia

The basal ganglia are a group of nuclei located bilaterally deep within each cerebral hemisphere. Hikosaka et al. (1989) showed in the monkey that the basal ganglia contribute to the suppression and initiation of saccadic eye movements through a tonic inhibition on the superior colliculus by the caudate-nigral system. The substantia nigra pars reticulata (SNpr) exerts control over the superior colliculus with a high level of tonic discharge. When the SNpr is itself inhibited by the caudate, this disinhibits the superior colliculus, allowing the saccadic processing to proceed. The output of the superior colliculus feeds back to the caudate via the intramedullary lamina of the thalamus. The FEF, as well as many other cortical areas, also send a direct projection to the caudate.

Conflicting results regarding the influence of the basal ganglia have been found in clinical and imaging studies on humans. Patients with basal ganglia dysfunction such as Parkinson’s or Huntington’s diseases, have been shown to display distinct oculomotor disorders (Evarts et al., 1984; Albin et al., 1989; Kennard and Lueck, 1989). Imaging studies in normal volunteers have revealed no significant changes in the basal ganglia during sensory-guided saccades (Melamed and Larsen, 1979; Fox et al., 1985) but bilateral changes in the putamen, globus pallidus and lentiform (lenticular) nuclei during large amplitude voluntary saccades (Petit et al., 1993). This suggests that the basal ganglia may have a different influence on saccades according to how they are generated. The absence of caudate activation in Petit’s study was interpreted to indicate that the exact areas of the basal ganglia involved in voluntary saccade generation in humans may be slightly different to monkeys, perhaps involving the putamen-pallidal system.
1.7.6 The Pulvinar and Intramedullary Lamina of Thalamus

Electrophysiological studies have shown the involvement of two thalamic areas in the control and execution of saccades: the internal medullary lamina (Schlag-Rey and Schlag, 1989) and the pulvinar (Robinson et al., 1986).

The pulvinar is the largest of the thalamic nuclei and forms the most posterior part of the thalamus. It receives inputs from the deep layers of the superior colliculus and retina and primary visual cortex, and both sends and receives projections from the parietal cortex and frontal eye fields (Robinson and McClurkin, 1989). As such it is believed to play a role in integrating sensory information, especially in mediating visual attention and visual processing, rather than in oculomotor control itself.

The intermedullary lamina of the thalamus is connected with just about every important area of the cerebral hemispheres concerned with generating saccades, except the brainstem. Its exact functions are not known.

1.8 The Cerebellum

The importance of the cerebellum in motor control has long been known, and was first described in detail by Holmes (1939). The involvement of the cerebellum in saccadic eye movements specifically has since been indicated by many studies on both humans and in monkeys (Ritchie, 1976; Selhorst et al., 1976; Optican and Robinson, 1980, Vilis and Hore, 1981; Sato and Noda, 1992; Bötzel et al., 1993; Robinson et al., 1993, Goldberg et al., 1993; Büttner et al., 1994; Vahedi et al., 1995; Straube et al., 1995). Experimental work on animals has revealed three specific cerebellar areas that are involved in the generation of eye movements: the floccular region which is involved mainly with smooth pursuit and gaze-holding (Zee et al., 1981); the nodulus and uvula with vestibular related eye movements (Waespe et al., 1985); and the oculomotor vermis and the fastigial
nucleus with saccades and also smooth pursuit. Functional imaging results have also indicated that the cerebellar vermis is involved in oculomotor tasks, particularly voluntary tasks (Petit et al., 1983; Fox et al., 1985). Patients with cerebellar lesions are not reported to have any problems with initiating saccades, and saccades have apparently normal main sequence relationships and latency characteristics in monkeys with cerebellar lesions (Optican and Robinson, 1980; Fitzgibbon et al., 1986). Evidence suggests that the primary effect of cerebellar lesions is on the size of a saccade with respect to the target.

1.8.1 Anatomy and Physiology of the Cerebellum

The cerebellum is divided into several functionally independent lobes, each of which makes connections with different areas of the brain. The most important area of the cerebellum in relation to saccadic eye movements is the vermis, a thin longitudinal strip along the midline. The area of the vermis that is specifically related to eye movements is known as the oculomotor vermis and is made up of lobules VI and VII (Sato and Noda, 1992). These are located in the posterior part of the vermis which consists of lobules V-IX, although the term ‘posterior vermis’ is often used to refer specifically to lobules VI and VII.

![Diagram of the cerebellum](image)

*Figure 1.7. Diagram to show the anatomy of the cerebellum. From Rao (1993).*

The output nucleus of the vermis is the fastigial nucleus. The oculomotor vermis projects primarily to the ipsilateral caudal fastigial nucleus (Yamada and Noda, 1987;
Noda and Fujikado, 1987; Noda et al., 1990) which projects bilaterally to cortical and
brainstem regions involved in motor control. This area of the fastigial nucleus is known as
the fastigial oculomotor region (FOR) as it is the only part to contain saccade related
neurons (Batton et al., 1977; Ohtsuka and Noda, 1991).

Efferents from the FOR immediately cross the midline and travel within the
contralateral rostral fastigial nucleus before terminating in the premotor saccade
generating areas of the brainstem (Noda et al., 1990).

Both the Purkinje cells in the vermis, and cells in the FOR show saccade-related
activity. Saccade-related Purkinje cells in the oculomotor vermis are all spontaneously
active, and generally burst with all types of saccade (Kase et al., 1980; Helmchen et al.,
1994a). A few Purkinje cells pause with saccades (Kase et al., 1980). The FOR contains
intermingled saccade and smooth pursuit neurons which are spontaneously active and
burst with each saccade (Büttner et al., 1991).

1.8.2 The Cerebellum and Dysmetria

Both clinical reports of cerebellar patients, and experimental studies on animals,
have revealed the association between saccadic dysmetria and damage to the cerebellar
vermis. Dysmetria may represent a passive effect of the failure of the adaptive control
system.

Studies in monkeys have revealed that cooling the fastigial nucleus (Vilis and
Hore, 1981), ablating the caudal cerebellar vermis and surrounding areas (Ritchie, 1976),
and more specifically lesions of vermis lobules VI and VII (Sato and Noda, 1992), or the
FOR (Robinson et al., 1993), make saccades dysmetric. Unilateral lesions of the
oculomotor vermis lead to contralateral hypermetria and ipsilateral hypometria (Aschoff
and Cohen, 1971). The opposite relationship is observed when the FOR is lesioned, due to
the inhibitory input to the FOR from the oculomotor vermis (Robinson et al., 1993).
Differences are reported according to whether saccades are centrifugal or centripetal (Ritchie et al., 1976).

Studies in humans have revealed a similar pattern of deficits to those formally determined in monkeys, although patients with unilateral, localised lesions to the vermis and/or deep fastigial nuclei are not commonly reported. This is probably due to the midline position of these structures making them particularly susceptible to bilateral lesions. Saccades are well-known to be dysmetric in cerebellar patients (Brandt and Buchele, 1983; Uno et al., 1989; Leigh and Zee, 1991; Bötzler et al., 1993; Straube et al., 1995; Vahedi et al., 1995). Specifically, Leigh and Zee (1991) report a patient with a tumour involving the dorsal (posterior) vermis whose only neurological abnormality was dysmetric saccades. A general hypometria is reported for lesions to the posterior vermis (Vahedi et al., 1995). Bötzler et al. (1993) reported a complex pattern of saccadic dysmetria in a variety of cerebellar patients. There was further evidence however that lesions of the oculomotor vermis induce ipsilateral hypometria and contralateral hypermetria, whereas lesions to the caudal fastigial nucleus induce ipsilateral hypermetria and contralateral hypometria.

1.8.3 The Cerebellum and Adaptive Control

The involvement of the cerebellum in particular in the adaptive control of saccades was suggested by early clinical studies of patients with enduring dysmetria in association with cerebellar degeneration (Zee et al., 1976; Dichgans and Young, 1975). However, the specific role of the cerebellum, in particular the vermis, in the adaptive control of saccades was revealed in monkeys by Optican and Robinson (1980). They surgically weakened the lateral and medial recti of one eye and demonstrated the expected adaptive compensation according to which eye was forced to view. Total cerebellectomies then completely abolished the ability of the saccadic system to adaptively compensate for the muscle weakness. Partial cerebellectomies, of the vermis and paravermis (lobules IV-
and fastigial nuclei, however abolished the adaptive control only of the size of saccades, the pulse component, but not of the step component. Thus the neural integrator was still intact in monkeys with partial cerebellectomies. This adaptation took place over a time scale of a few days, and thus may represent a fundamentally different form of adaptation to the fast adaptation that is witnessed in intrasaccadic target perturbation experiments. The involvement of the fastigial nuclei (and the interpositus nuclei) in the fast form of adaptation has also been demonstrated (Goldberg et al., 1993). The distinction between fast and slow adaptation has been discussed in Section 1.6.4.

A specific examination of the adaptive control capabilities of cerebellar patients has rarely been made. Waespe and Baumgartner (1992) examined the adaptive control capabilities of patients with Wallenburg’s Lateral Medullary Syndrome. These patients have lesions in the dorsolateral aspect of the medulla which are believed to interrupt olivo-cerebellar pathways. Experimental evidence suggests a crucial role for these pathways for the adaptive control of motor performance by the cerebellum (Llinas, 1975). These patients displayed enduring dysmetria, and showed a reduced ability to readjust saccadic amplitude to induced retinal error. Saccadic dysmetria has not however been shown in animals after destruction or inactivation of the inferior olive, or in patients with inferior olivary nucleus degeneration.

1.8.4 How the cerebellum might work?

The role of the cerebellum in motor learning and classical conditioning is well known (Dow and Moruzzi, 1958). This has been particularly well characterised for the conditioned eye-blink reflex (McCormick and Thompson, 1984). The uniform cytoarchitecture of the cerebellum suggests that it may perform a similar function on a wide variety of inputs. The Marr-Albus model provided a framework for understanding the role of the cerebellum in modifying the response of its major output cells, the Purkinje
cells, to inputs from mossy fibres. Ito et al. (1982) proposed a mechanism by which this
learning at the Purkinje cell may happen. This has been called long-term depression.

The inputs and outputs of the cerebellum indicate that it is able to compare
internal feedback signals that represent the intended movement (for example, from the
FEF and superior colliculus), with external feedback signals regarding the actual
movement. It is uncertain exactly what form this external feedback signal may take.
Wallman and Fuchs (1998) have proposed that it is primarily a visual error signal,
although they could not rule out a role for a motor error signal. Alternatively, in the
context of the SFM hypothesis, the error signal may take on a more abstract form. The
comparison of external and internal signals would allow a system error signal to be
determined and then used to manipulate the gain of saccades in order to optimise
performance.

Apart from anatomical evidence regarding the input and output connections of the
cerebellum, which support its potential to play a fundamental role in the adaptive control
process, there is also more recent physiological evidence. It has been shown that the
temporal firing properties of neurons in the cerebellum are consistent with its ability to
influence the premotor generation of a saccade. Saccade-related burst neurons in both the
vermis (Sato and Noda, 1992) and in the FOR (Ohtsuka and Noda, 1990) have a lead time
which would allow them to modify the characteristics of an impending saccade. The lead
time of the burst neurons in the FOR is shorter than that of the burst neurons in the
superior colliculus, but, at approximately 15-20 msec, longer than the short-lead burst
neurons in the PPRF. This suggests that any modification being effected by inputs from
the cerebellum would not arrive early enough to affect the outputs of the superior
colliculus, but would be early enough to modify the collicular signal before the beginning
of a saccade once it has been passed into the brainstem. The burst of activity in the FOR
begins earlier for contralateral saccades than ipsilateral saccades (Ohtsuka and Noda,
1991; Fuchs et al., 1993; Helmchen et al., 1994). It has been suggested that the FOR may
be involved in the acceleration and deceleration of saccades, more specifically the
deceleration of ipsilateral saccades and the acceleration of contralateral saccades (Büttner
et al., 1984; Helmchen et al., 1994; Robinson, 1993; Fuchs et al., 1993).

The FOR neurons could modify saccades by directly influencing the acceleration
and deceleration of individual eye movements by direct input to the neurons of the
saccade generator in the brainstem, though the FOR neurons probably do not directly
encode acceleration or deceleration. Thus, increased peak burst activity of FOR neurons
would lead to higher acceleration and deceleration and in turn a larger amplitude for a
given duration. If this was the case one would predict a change in the main sequence for
duration. FOR neurons are more active in the light than the dark, explaining why saccades
in the dark have a lower amplitude than saccades in the light of the same duration
(Helmchen et al., 1994a). It is not known whether the altered FOR output to the brainstem
saccade generator alone causes the dysmetria, or whether the output to the superior
colliculus also has to be considered (May et al., 1990).

1.8.5 Other areas that could be involved in adaptive control

There are many possible areas that may play a role in saccadic adaptation given
the diversity of the saccadic pathways. The brainstem saccade generator is unlikely to be
one such site as its role as the final common generator for all saccades would suggest that
adaptation should affect all saccades. This has not been found to be the case. Adaptation
of one type of saccade may not affect other types of saccades. Fuchs et al. (1993)
reported that gain changes induced to reflexive saccades in monkeys were not transferred
at all to the quick phases of nystagmus which are reported to share the same saccade
generator as other types of saccade (Ron et al., 1972). These gain changes did however
transfer to express saccades, suggesting that the locus of such adaptation is subcortical.
The superior colliculus itself is not thought to be the site of adaptation either (Fuchs et al.,
1993). Stimulation studies have been contradictory, indicating that saccadic adaptation
may take place either upstream (Fitzgibbon et al., 1986) or downstream (Goldberg et al., 1993) of the superior colliculus.

Adaptation is not generally thought to involve cortical areas, and no direct evidence has been produced to support cortical involvement. The fact that lesions to the cortex can cause lasting dysmetria (hypometria only though, not hypermetria) (Lynch and McLaren, 1989; Leigh and Zee, 1991) suggests that cortical areas may play a role in adaptive control. Furthermore, the cortex, and certain areas in particular, are known to be very plastic and thus potentially capable of adaptive learning.

1.9 Abnormal saccades in clinical populations

Due to the widespread nature of the control systems for saccades both cortically and subcortically, it is not surprising that saccades are often affected by neurological problems. Some effects may be subtle and require careful eye movement analysis to detect, such as slow saccades in Gaucher’s Disease (Lengyel et al., 1999) and merosin-negative congenital muscular dystrophy (Mezey et al., 1999). Other effects may be more prominent. The effects of cerebellar and cortical lesions have already been discussed above and may involve gross dysmetria, and clear deficits on certain saccadic tasks such as the antisaccade task.

In some diseases there is an absence of saccades due to an inability to initiate saccades. This is traditionally known as Congenital Oculomotor Apraxia (Cogan, 1952) but has more recently been labelled as ‘saccade initiation failure’ (Harris et al., 1996). In contrast, there may be an excess of saccades. These may be ‘intrusive saccades’ as observed in Huntington’s Disease which affects the basal ganglia, or more extreme opsoclonus in which there are spontaneous, chaotic, involuntary bursts of back-to-back saccades in all directions. Such a series of saccades may last up to a few hundred milliseconds and are often precipitated by refixation saccades or blinking. Opsoclonus is a
feature of Dancing Eye Syndrome which has an onset usually under the age of two years. This syndrome is believed to involve the vermis of the cerebellum (Tuchman et al., 1989; Oguro et al., 1997) or the FOR (Shawkat et al., 1993). In Chapter 7 we investigate the adaptive control capabilities of children with Dancing Eye Syndrome.

Lesions that do not affect the saccade generating pathways themselves may also cause abnormal saccades. The loss of one visual hemifield due to a lesion at any point along the optic pathways resulting in homonymous hemianopia causes low gain ‘multiple hypometric’ saccades (Meienberg et al., 1981, Mezey et al., 1998). Children with homonymous hemianopia are examined in Chapter 3.

1.10 Aims

The studies in this thesis aim to document how adaptive mechanisms manipulate the gain of saccades in both normal and abnormal circumstances in children and adults. The gain of saccades in children has rarely been explicitly reported. This is probably due to the difficulty in recording saccades from children using high resolution eye movement equipment such as an infra-red limbus eye tracker.

The initial experiments investigate the relationship between the gain of saccades and both the standard deviation of the gain and the main sequence for duration within individuals. The characteristics of gain are interpreted according to the saccadic flight-time minimisation (SFM) hypothesis (Harris, 1995). Few hypotheses have been put forward to describe the characteristic changes in gain in different circumstances and the adaptive control of saccades in response to abnormal circumstances. The SFM hypothesis provides a framework for understanding these changes, and particularly the undershoot bias.

The characteristics of saccades are first investigated in children with homonymous hemianopia. Results from a pilot study indicate that saccades into the blind hemifield are
typically low gain in such children. In this experiment we aim to quantify the gain and standard deviation of saccades made into both the blind and seeing hemifields, and investigate the effect of target predictability on the gain of saccades made by these children.

Another situation in which there are reported to be characteristic effects on gain is in the antisaccade task. This is a novel oculomotor task that involves making a saccade in the opposite direction to the movement of the target. This task is investigated in a group of normal adults, again to quantify the gain and standard deviation of saccades and relate findings to predictions made by the SFM hypothesis.

The relationship between the gain of saccades and the main sequence for duration is investigated in the following chapter in a group of 20 normal adults to determine whether there are correlations between the gain of saccades across a range of target eccentricities, and the main sequence for saccades amongst these individuals. The hemispheric facilitation hypothesis proposed by Robinson (1973) to explain the undershoot bias is also investigated using the data from this experiment.

The final section of this thesis investigates the active functioning of the adaptive control system using an intrasaccadic target displacement paradigm. Predictions of the SFM hypothesis regarding the nature of the adaptive change in different experimental protocols are made and tested. Finally, we apply the intrasaccadic target displacement paradigm to children and young adults with Dancing Eye Syndrome (DES). This disorder is believed to involve the vermis of the cerebellum, an area that is intimately tied in with the adaptive control of saccades. Our investigation of children with DES is the first time an intrasaccadic target displacement paradigm has been used in children.

The experiments within this thesis all provide evidence to support predictions made by SFM hypothesis. However, the results are of course open to interpretation. Alternative explanations for the results are discussed within each chapter.
Chapter 2. Methodology

2.1 Introduction

The experimental set-up used in these investigations was designed and assembled as part of the work of this PhD. In brief, the stimulus was a red laser spot, front-projected on to a large white screen. Two dimensional movement was enabled by a 2-mirror, 2-axis laser deflection system. Subjects were seated on a height-adjustable chair attached to a mobile platform facing the screen. Subjects’ heads were supported by an adjustable chin rest with further optional stabilisation provided by ear muffs. Eye movements were recorded using the infra-red reflection technique and were viewed off-line by the experimenter before being scored and analysed by in-house computer software.

![Figure 2.1](image) to show a subject in position in the equipment.

2.1.1 Equipment Design and Construction

A laser deflection system was chosen as the most suitable means of dynamic stimulus generation, with the greatest degree of resolution and flexibility for the purpose of our experiments. Video systems are limited in both temporal resolution by the frame rate, and, to a lesser extent, spatial resolution by the number of pixels across the screen.
The video screen also imposes field limitations and provides an unwanted frame of reference during experiments. Similarly, a light-emitting diode (LED) board would not have been able to provide the spatial or temporal resolution required, especially if the position of unlit LEDs were to be concealed. The laser deflection system provides a spatial resolution of 1248 units across its dynamic range.

A laser diode module (Vector Technology, Gwent, UK. Model Beta CW106812CO.6) with an output aperture of 0.6mm diameter was used. This had a nominal wavelength of 670nm and a single element lens of aspheric design which produced a high quality collimated beam. When viewed on the screen however, the red spot was found to have a diameter of closer to 1 mm. The laser was housed in a centring mounting plate (Spindler and Hoyer, Milton Keynes, UK).

Two-dimensional laser deflection was enabled with the commercially available X-Y scan head (General Scanning, Banbury, England. Model XY0507). These 2-mirror, 2-axis galvanometer scan heads produce extremely high torque to inertia ratios and useful angles of ±20° optical. Feedback control is established by a rotation sensor attached mechanically to the galvanometer shaft, and electronically to the drive coils via the servo drive amplifier. The accuracy of the angular position at rest is ±0.3% of full field. For a ±20° scan, the maximum error is quoted as being ±7 min. arc, or ±2 milli-radians in each axis.

Precise optical alignment of the laser with respect to the X-Y scan heads was required. The laser and scan heads were permanently mounted to a solid metal baseplate. An adjustable front-surface mirror was used to reflect the laser beam through 90°. This mirror was adjustable to enable the precise alignment of the laser beam on the centre of the input mirror of the X-Y deflection system. See Figure 2.1.
As it is important that both the scanner drivers and mirrors are protected from dust accumulation or accidental damage they were enclosed in a metal box with a suitable aperture cut for the exit of the laser light.

The scanner heads were driven by the DAD2 dual axis scanner driver card that was purchased along with the scan heads from General Scanning (Banbury, England).

The dynamic range of the laser deflection system was $\pm 20^\circ$ given an equal distance of the subject and laser system from the screen. In order to increase the dynamic range, the viewing distance of the subject had to be less than the distance of the laser from the screen. However, it was not possible to mount the laser system either directly over the head of the subject, or behind the subject, due to logistical reasons. Thus, within the confines of the space available, the extra distance required from the screen by the laser relative to the subject was achieved by deflecting the laser beam through $90^\circ$ and mounting the laser system between the subject and the viewing screen, though displaced to one side. This can be seen in Figure 2.1. This enabled us to achieve a slightly greater angular range than $\pm 20^\circ$. 

Figure 2.2 to show the mounting of the laser, mirror and X-Y deflection system on the baseplate. A - the laser in the centring device; B - the front surface mirror to reflect the laser through $90^\circ$; C - the x-y deflection scan head.
A front-surface mirror (Vacuum Coating Ltd, London) of suitable dimensions to accommodate the full range of the laser deflection system was used to deflect the laser beam through 90°. To maintain precise alignment between the laser system and this front surface mirror they were both mounted on a baseplate with the mirror at 45° to the output angle of the deflection system. Due to the angle of the mirror with respect to the laser system, the optical centre of the mirror did not coincide with the geometric centre of the mirror and thus it was important to make sure that the optical centre of the mirror was aligned to the binocular viewing position of the subject.

Given that the laser deflection system had to be mounted between the subject and the viewing screen it was necessary for it to be mounted some distance below the eye level of the subject to ensure that it did not significantly intrude into the field of view. Thus the whole laser system had to be fixed at such an angle that the laser spot was projected upwards along a horizontal meridian approximately in the centre of the screen.

The adjustable chin rest had a vertical range of 10cm which could be adjusted, either by the experimenter, or the subject themselves to a comfortable position in which they felt the central target spot to be straight ahead.

Attached to the chin rest were a pair of ‘ear muffs’ that could be optionally used to provide further stabilisation of the head if necessary. However, in comparisons of data made with or without the ear muffs, no differences were noted.

The laser-mirror system and the chin rest were both attached to a table-like construction that was secured to the floor and stabilised by heavy wooden inserts to prevent movement. As such the apparatus was fully stable and no shifting was expected to occur. This was checked regularly.

The screen onto which the laser was projected was required to be a large, white, non-reflective flat surface that could be wall mounted. Plain white ‘contiboard’ (chipboard with a white coating) was found to be most effective, as well as cheap and
easy to clean if it became dirty. This was wall-mounted and was large enough (157 x 117 cms) that it filled the majority of the visual field at the viewing distance of 89cm.

A draftsmans chair was the only type of chair, within budget, that could provide the adjustment range necessary to accommodate both young children and tall adults. This chair was attached to a mobile platform with lockable wheels so that the subject could be rolled into place after they had positioned themselves comfortably on the chair.

2.1.2 Eye Movement Recording

There are many techniques available for recording eye movements, varying greatly in the resolution they can provide and the cost and effort in acquiring and setting up the equipment. For the following experiments the infra-red reflection technique was used. The technique depends on the differential reflection of infra-red radiation by the iris-sclera boundary (the limbus) of the eye. It provides a compromise between the ease of use yet poor resolution of electro-oculography (EOG) and the very high resolution but the expense, complexity and invasive nature of the scleral coil technique.

Infra-red eye trackers have been commercially available for a number of years, and are regularly used for eye movement research, though not as regularly as EOG in a clinical context. Few reports have been published of their use in children, in either a research or clinical context. This may be due to factors of co-operation and head size.

The IRIS infra-red light eye tracker (Skalar Medical, Delft, The Netherlands. Model 6500) was used. This system consists of a light-weight helmet attached to which are two infra-red light transducers, one in front of each eye. The transducers can be oriented to record either horizontal or vertical eye movements. Only horizontal eye movements were recorded for these experiments. The transducers do not impede the field of view horizontally. The system has a dynamic recording range of ±30° horizontally.
although linearity within 3% was only guaranteed within ±25°. The optimal resolution is reported to be 2minarc.

The infra-red light transducers consist of an array of 9 infrared LEDs (type Siemens LD269) and 9 photodiodes (type Siemens BPX89). The infrared light of the emitter is converted in to a narrow beam and focused on the eye with a cylindrical lens in front of each emitter array. The detector array is positioned underneath the LED array. To reduce the influence of ambient light, a black infra-red filter covers the detector array.

For optimal alignment of the transducers, so that their ‘receptive’ fields match the iris-scleral transition, both transducers can be adjusted independently in three perpendicular directions. With proper pre-adjustment, preparation and calibration times could be minimised which was important when testing children.

2.1.3 Set Up

The subject was first seated in the chair at a suitable height and the chin rest adjusted until the subject reported that the central target spot was straight ahead. The wheels of the platform were then locked so that no movement of the chair or platform could occur during the experiment.

Extra padding for the headset was occasionally required for young children with small heads. With the experimenter standing directly in front of the subject and the subject looking straight ahead, the sensors were then independently positioned centrally over each eye.

All experiments were performed in dimmed lighting conditions (2 cd/m²).

The initial calibration was made by asking the subject to fixate in turn the central target and targets at 20° to the left and right of the centre. The offset and gain controls were then adjusted for each eye independently to produce a symmetrical displacement of the eye position LEDs on the control module.
2.1.4 Stimulus Control Program

The laser deflection system was controlled by a computer program which could be modified according to the needs of the experiment. Protocol files containing the trial to trial movement of the target, details of any intrasaccadic target steps, and timing parameters were used to run the experiments.

In order to compensate for the small increase in viewing distance at more eccentric target positions by virtue of the flat surface of the viewing screen, and the 45° upwards projection of the laser, a compensatory equation was included in the control program.

2.1.5 Analysis Program

The data for each subject were viewed in graphic form off line and all trials containing blinks directly associated with saccades were rejected, as well as, in most experiments, predictive saccades with latencies <80msec. The remaining trials were saved. Predictive saccades were removed as they have been reported to show an altered main sequence and decreased gain in comparison to reflexive saccades (Bronstein and Kennard 1987; Smit and van Gisbergen 1989). The number of trials that had to be rejected from each data set varied greatly between subjects; this was sometimes as much as 20%. This also generally depended on the length of the paradigm and the age of the subject. The longer the experiment and the younger the subject, the more trials were likely to be lost in total from the data.

A computer program was used to determine the characteristics of the eye movements in each trial. A trial consisted of the movement of the target from the centre to the periphery, and then after a pause back to the centre again. The recording period over which positional information was collected was set at 1500msec: 500msec pre-stimulus and 1000msec post-stimulus. The length of the post stimulus recording period of 1000msec in which saccades were sought by the analysis program could be manipulated. In our analyses this was usually set at 900msec as this provided enough time for all
foveating saccades to be completed (except in the case of hemianopic subjects) but also often discounted blinks or return saccades that often occurred at this late post-stimulus stage.

Saccades were detected by their peak velocity calculated via a 2-point central difference algorithm with 3 dB point at 111Hz. The beginning and end of the saccade was defined by the points at which the velocity fell below 5°/sec. This threshold measure was found to be effective in detecting very small saccades yet filtering out noise and non-saccadic artefacts. This was confirmed by visual comparison of the eye movement traces to the saccade parameters contained in the data file. The data length over which averaging took place (‘b’, see Figure 2.3) to obtain positional information could also be selected, as well as a gap (‘a’) between the end of the detected saccade and the point at which this averaging took place. For all experiments this gap was set as 20msec, and the averaging window set at 5msec. The gap was imposed in order that the positional information would be gathered after any post-saccadic drift or dynamic overshoot was completed and that the amplitude of the saccade cannot be erroneously shortened thus affecting the gain.

![Figure 2.3. To show the parameters used to determine the amplitude of each saccade.](image)

Care was taken that the small return movements associated with dynamic overshoot (see Bahill et al., 1975c) were not scored as corrective saccades. This was achieved not only by the gap discussed above, but also by imposing a minimum intersaccadic interval of 30msec in most experiments. Detection and exclusion of these
elements on the basis of dynamic characteristics is not possible as they have been shown to lie on the same duration-amplitude profile as saccades not associated with dynamic overshoot (Bahill et al., 1975c).

The computer program produced all the timing, velocity and amplitude parameters for each saccade made within the recording period of each trial, and the gain of the primary saccade determined in each of the different ways outlined in the introduction. Thus, the primary saccade, and a varying number of correctives saccades were recorded in each trial. The data was imported into SPSS and all manipulations and statistical analyses were made using this software package.

In order to test all parts of the equipment in combination to ensure that the data obtained fell within the normal ranges as reported previously we recorded saccades to a range of target eccentricities from three subjects.
2.2 Testing of Experiment Set-Up

2.2.1 Subjects and Methodology

Three normal, healthy, male subjects were recorded (ages 25, 35 and 44). None had a history of squint or eye problems, nor required compensation for refractive errors. Two of the subjects were experienced in oculomotor research.

Subjects were presented with 100 trials at 5 different eccentricities to the left and right of the central target. The eccentricities presented were (± 2.5, 5, 10, 15, 20 degrees). The central target stimulus moved instantaneously after a randomised time delay of 1100-2500msec to a peripheral position where it remained for 1500msec before returning to the centre for the beginning of the next trial.

A calibration procedure consisting of 10 different eccentricities presented in positional order along the horizontal meridian was performed before the experiment began. Each trial was examined on-line by the experimenter to confirm a 500msec period of stable fixation, and then either accepted, or rejected and repeated. A linear regression was produced on-line after the calibration was completed, and again either accepted, or if necessary the apparatus was re-adjusted and the calibration procedure repeated until an acceptable linear relationship between eye position and target position was obtained.

2.2.2 Results

100 trials were recorded from each subject. A number of trials were lost from each data set due to blinks, these numbered 2 (Subject MH), 6 (CH) and 10 (RH).
<table>
<thead>
<tr>
<th>Subject</th>
<th>Primary Latency (msec)</th>
<th>Intersaccadic interval (msec)</th>
<th>Main Sequence (&gt;5°)</th>
<th>Ratio PV/MV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>n</td>
<td>Mean</td>
</tr>
<tr>
<td>MH</td>
<td>181.23</td>
<td>23.88</td>
<td>98</td>
<td>125.53</td>
</tr>
<tr>
<td>CH</td>
<td>161.63</td>
<td>27.51</td>
<td>94</td>
<td>115.25</td>
</tr>
<tr>
<td>RH</td>
<td>186.06</td>
<td>21.39</td>
<td>90</td>
<td>146.10</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>176.31</strong></td>
<td><strong>12.94</strong></td>
<td><strong>94</strong></td>
<td><strong>128.96</strong></td>
</tr>
</tbody>
</table>

Table 2.1. The main saccadic parameters for each of the three subjects tested are shown.

Latency

The latency distributions of primary and secondary saccades are displayed for each subject in Figure 2.4 below. There was no evidence of bimodality in the primary saccadic reaction times for any of these three subjects.

Figure 2.4. Latency histograms of primary and secondary saccades for all three subjects.
Saccade Dynamics

The main sequences for both duration and peak velocity showed the stereotypical relationships. Subject CH made a number of saccades with abnormally long durations. They were found, on examination of the eye movement profile, to be due to saccades with glissadic endings. These saccades were attributed to fatigue. The relationship for the main sequence for duration was quantified for each subject by regression analysis for saccades with a magnitude of greater than 4°, as described in Section 1.5.3. The results are shown in Table 2.1.

The ratio of peak velocity to mean velocity is represented for each subject in Figure 2.5 below. This relationship is remarkably linear and can be quantified by linear regression (see Table 2.1) to enable comparisons with previous data.

Main sequence for duration

![Graphs showing saccade amplitude vs duration for Subject MH, CH, and RH.](Image)

Saccade amplitude (degrees)

Main sequence for peak velocity

![Graphs showing saccade amplitude vs peak velocity for Subject MH, CH, and RH.](Image)

Saccade amplitude (degrees)

**Figure 2.5.** Scatterplots showing the dynamic characteristics of saccades for all three subjects.
Peak velocity/mean velocity plots

Figure 2.5 cont. Scatterplots showing dynamic characteristics of saccades for all three subjects.

Saccadic Gain

The mean gain for primary saccades to each target eccentricity was calculated for each subject for the three different types of gain. These are displayed below. Subject CH showed the clearest range effect and consistency across all three types of gain. Subject MH and RH also showed a range effect, though for Subject RH the gains at the extreme eccentricities were not as would have been predicted by the range effect.

Traditional gain (saccade amplitude/target amplitude)

Component gain (saccade amplitude/total saccadic component)

Figure 2.6 continued overleaf.
Net gain (saccade amplitude/net eye displacement)

![Charts](image)

Target amplitude (degrees)

**Figure 2.6.** The average gain at each target eccentricity for the three different types of gain, for each subject.

### 2.7.3 Discussion

The average latency of all primary saccades made by these three subjects was 176.31 msec. This is relatively short compared to reaction times reported before for similar unpredictable reflexive saccade paradigms. It lies just below the average range reported by Becker (1989) of 180-220msec though within the wide range (170-350msec) reported by Findlay (1981) and also within the ‘short latency regular saccades’ range of 140-180msec as classified by Fischer *et al.*, (1997).

Spatial and temporal predictability were not expected to affect our paradigm. Ten eccentricities were used to minimise spatial predictability, while the delay at the central target position was randomised. Predictive saccades have been defined as having latencies of less than 80msec (Becker 1989) while Findlay (1981) and Bronstein and Kennard (1987) have used a threshold of 100msec. It can be seen in Figure 2.4 that only one predictive saccade (<80msec) was elicited. This confirms that our paradigm was unpredictable as intended.

The latency of all secondary saccades was 128.96 msec which, as expected, is less than that of the primary saccades. This is again relatively low, though within the previously reported range of 120-160 msec (Becker 1989). A reciprocal relationship
between the latency and saccade amplitude was found, as has been previously reported (Becker 1972; Prablanc and Jeannerod 1974; Henson 1978).

The main sequence for duration for each of these three subjects produced slope values (average 3.03) that were somewhat higher than previously reported values which have been in the order of 2.5° (see Becker 1989) while the intercept values (average 23.04) varied in both directions from the 20-30msec range quoted by Becker (1989).

The high slope and reciprocally reduced intercept value for Subject CH was probably partly due to the saccades of this subject being relatively fast but featuring a few large amplitude saccades with extra long durations. There is no such explanation for the slightly high slope value obtained from Subject MH, however this subject’s value did not diverge excessively from the previously reported ranges.

The main sequence for peak velocity, as plotted for each subject in Figure 2.5, shows variation that is reported to be typical of this relationship between peak velocity and saccade amplitude (Schmidt et al., 1979; Jürgens et al., 1981), as well as the stereotypical profile. Subject CH only showed a marked divergence between abducting and adducting saccades, which was also reflected in his main sequence for duration plot, although less markedly. Abducting saccades were faster than adducting saccades. Collewijn et al. (1988) has reported an abduction-adduction asymmetry when comparing the left and right eye where saccades of the abducting eye had a higher peak velocity, however, he did not specify whether a similar asymmetry was noted for adducting and abducting saccades in the same eye, although one would expect this to be the case, unless the differences were related to the eye itself rather than its trajectory.

The ratio of peak velocity to mean velocity was close to the value (1.64) reported by Becker (1989) for Subjects MH (1.66) and RH (1.69). The value for Subject CH lay just outside the 95% range reported by Becker for this data, although once again the explanation lies with the glissadic large amplitude saccades.
The gain plots for each subject show a great variation in the range effect between subjects. Subject CH showed the clearest range effect, in the manner predicted, with overshooting saccades to the smaller target eccentricities and undershooting saccades to the large target eccentricities. This same pattern was seen for all three different ways of determining gain in Subject CH and was within approximately the same range of values. These consistencies probably result from not only a good calibration but also eye movement trials which were very ‘clean’ with a lack of any obvious slow eye movement components or drift.

Subject MH also showed a typical range effect, across all but the largest eccentricity. The gain for saccades to the 20° target eccentricity was greater (ie less undershooting) than the gain for the 15° target eccentricity. This pattern was seen across each different type of gain, although the level around which the gain values were placed varied between the different methods of determining gain. For traditional gain, all the mean values lay below 0.8, suggesting a high degree of undershoot for saccades to all eccentricities. On the other hand, the component gain and net gain measurements both showed gains of greater than 1.0 to the smallest eccentricity and a lowest gain of around 0.9°. These differences suggest either an element of centripetal drift, or perhaps movement during the experiment which affected the validity of the calibration. The traditional gain measurement is the only measurement that is affected by the calibration.

Subject RH showed a clear range effect across the 3 middle eccentricities but the gain to the smallest target eccentricity was unexpected low and the gain to the greatest eccentricity targets was unexpectedly high.

These results suggest that the pattern of the range effect is highly idiosyncratic and unpredictable.
2.7.4 Conclusions

It has been show in this initial recording session that this newly assembled experimental set-up and analysis program can produce saccadic data that has parameters which are consistent with previously reported results. Also implied from these preliminary results is the importance of the different means of measuring gain, and the idiosyncratic nature of the range effect.

Using this experimental set-up as described we have been able to successfully record saccades from co-operative children as young as 6 years old. An experimental protocol of 100 saccades takes approximately 7 minutes. This could be achieved in children with encouragement though given an inevitable amount of movement. Tolerant adults were able to endure paradigms with as many as 400 trials, this took approximately 1/2 an hour to complete. By this time the headset would generally be feeling quite uncomfortable.
Chapter 3. Gain of Saccades in Children with Hemianopia

3.1 Introduction

Homonymous hemianopia is the loss of conscious visual perception in one visual hemifield as a result of a lesion anywhere along the optic pathways from the optic chiasm to the visual cortex. See Figure 3.1. Due to overlap in the cortical mapping around the vertical midline of the visual field there may be a certain amount of sparing of the macular region. In adults, late-onset hemianopia can be severely debilitating, causing problems with crossing roads, finding objects and bumping into objects in the blind field (Kerkhoff et al., 1994). In contrast, children cope remarkably well with visual field deficits and both the child and parents may sometimes be completely unaware of any problems until a restricted visual field is picked up by chance in visual testing. These differences may reflect the use of distinct compensatory strategies in adults and children, particularly with regard to saccadic eye movements. Saccadic eye movements are the most important type of eye movements for scanning the visual environment and fixating objects within the visual field for more detailed analysis.

Figure 3.1. To show the optic pathways and the decussation of the optic nerve fibres from each eye at the optic chiasm causing stimuli in each visual hemifield to be processed by the contralateral hemisphere.
3.1.1 Saccadic gain in hemianopia

The gain of saccades to visual targets in the blind hemifield in adults with homonymous hemianopia has been reported to be low by many researchers (Gassel and Williams, 1963; Meenberg et al., 1981; Meenberg et al., 1986). This low gain is reflected in a distinctive pattern of eye movements that has been termed ‘multiple hypometric saccades’ (Harris et al., 1993) or ‘staircase saccades’ (Meenberg et al., 1981). As these terms suggest, this is the generation of many small saccades in order to reach the target (see Figure 3.2).

![Figure 3.2. Typical multiple hypometric (staircase) saccades to a 15° target in the blind (left) field made by one of the patients in this study with homonymous hemianopia. Some dynamic overshoot is present. The gain of the first saccade is approximately 0.65. Subsequent saccades are smaller. The target is eventually overshot and refixated with a backwards corrective saccade.](image)

Multiple hypometric saccades made into the blind hemifield have been traditionally interpreted as a compensatory strategy to provide a slow but certain means of locating objects in this field (eg Zangemeister et al., 1982; Meenberg et al., 1981). By making many small saccades into the blind field, the target will eventually be located wherever it lies. If this target is parafoveal it will be reached quickly (see Fig 3.3D), whereas if the target is peripheral, many small saccades may be required before it is reached (Figure 3.3B). The target may also be overshot by the final small saccade and require a backwards corrective saccade for final fixation as shown schematically in both Figures 3.3 B and D, and in the eye movement trace of patient in Figure 3.2. This multiple step eye movement pattern is time consuming for reaching a target in the periphery of the visual field. In contrast, if large saccades were made into the blind hemifield this would rapidly bring the target into the intact visual hemifield by overshooting the target,
allowing subsequent precise visually-guided fixation (Figure 3.3A). This strategy would enable peripheral target foveation to occur more quickly than with the staircase strategy.

For parafoveal targets this hypermetric strategy would cause gross overshoot of the target by the initial saccade, requiring another large reverse saccade in order to foveate it (Figure 3.3C). Such a hypermetric strategy has been reported previously (Meienberg et al., 1981; Zangemeister et al., 1982; Zangemeister et al., 1995). Assuming that rapid target foveation is a requirement of the primate visual system, we would expect the saccadic system to favour a strategy that enabled target fixation in the minimum amount of time. This choice of strategy may be determined by the drive to minimise saccadic flight-time (see Harris, 1995) or the total time taken to reach the target (i.e. including the intersaccadic intervals).

**Peripheral targets**

![Diagram A and B]

**Parafoveal targets**

![Diagram C and D]

*Figure 3.3.* The figure shows representations of two alternative saccadic strategies. The target movement from the centre to an eccentric position is represented by the dashed line. In the hypermetric strategy (A&C) a large saccade is made into the periphery and the target subsequently fixated by making a visually-guided saccade into the seeing hemifield. In the multiple hypometric strategy (B&D) many small saccades are made until the target is reached.

### 3.1.2 Pilot study

In order to investigate the characteristics of saccades into the blind hemifield in children with hemianopia a pilot study was initially performed (Mezey et al., 1998). This study involved a retrospective analysis of the electro-oculographic (EOG) records of target-directed saccades made by hemianopic children seen in the eye movement laboratory at Great Ormond Street Hospital as part of their routine clinical assessment in
the eye clinic. In this paper we reported that multiple hypometria was the preferred strategy in children with homonymous hemianopia, in spite of the theoretical benefits of the hypermetric strategy.

The characteristics of saccades in children with hemianopia had not been documented previously and our results were not entirely consistent with previous reports for hemianopic adults. Meienberg et al. (1981) investigated adaptive oculomotor strategies employed by hemianopic adult patients to search for objects in their blind hemifield. They reported the presence of hypermetria to predictable (in both time and space) visual targets in the blind hemifield. Saccades to targets in the seeing hemifield were not hypermetric. Furthermore, they reported one adult who, on a follow-up recording, 7.5 months post-lesion, made spontaneous hypermetric saccades to both random and predictable targets in the blind hemifield. Although some of the patients in the pilot study showed a greater than normal percentage of hypermetric saccades, this was not a consistent feature in any subject; hypometria was still predominant.

It was proposed that the use of different eye movement strategies may depend on the predictability of the target position within the blind field (Mezey et al., 1998). It might be predicted that if the hemianopic subject expected the target to appear at a known eccentricity, then it would pay to slightly overshoot this eccentricity, rapidly bringing the target into the seeing hemifield, so that only a small return saccade would be needed to fixate the target. On the other hand, if the hemianopic patients had no idea where in the blind field a visual target was going to appear then it would be safer to make many small saccades to ensure finding it eventually. Thus greater target predictability would induce more hypermetric saccades. In our pilot study the targets were predictable in amplitude, though not in direction nor time. This may account in part for the lack of observed hypermetria in our pilot study. Had the visual targets been more predictable, a greater number of hypermetric saccades may have been made, giving a pattern of results more like those reported by Meienberg et al. (1981) in hemianopic adults.
In follow-up to our pilot study, we set out to investigate further the effect of target predictability on the saccadic eye movements of children with homonymous hemianopia. This study was done using the more accurate infra-red reflection technique. Although this technique is more difficult to use in children, it has a much higher resolution than EOG and thus enabled the detection of much smaller saccades. This is particularly important when detecting saccadic hypermetria as backwards corrective saccades to overshooting primary saccades are generally much smaller than onwards correctives after undershooting primary saccades (Weber and Daroff, 1972). The low resolution of EOG may prevent the detection of small amounts of hypermetria and so mask the true proportion of hypermetric saccades.

Our aims in this experiment were: firstly, to characterise the gain of saccades made by hemianopic children in a more quantitative manner, using more controlled experimental conditions and a recording technique with higher resolution to compliment our previous report (Mezey et al., 1998); second, to determine the effect of target predictability on saccadic gain. Given the desire to minimise the amount of time taken to acquire the target (be that saccadic flight-time or total time including inter-saccadic intervals) we would predict that higher gain saccades and more hypermetria would be seen with the increasing predictability of the target movement.

An additional interesting issue that was mentioned but not addressed in the pilot study was whether any hypermetria observed represents the upper end of the primary saccadic distribution, or is in fact a separate distribution representing the use of a distinct saccadic strategy. If hypermetria does represent a distinct strategy of the saccadic system, then we would expect to see some evidence of bimodality in the distribution of primary saccadic gains, with peaks both below and above 1.0, representing a hypometric and hypermetric strategy respectively. Thus, our third aim was to determine whether hypermetria represents the upper end of a unimodal primary saccadic distribution, or a separate distribution representing a distinct strategy.
3.2 Methodology

3.2.1 Subjects

Ten children between the ages of 6 and 18 (average age 11) at the time of eye movement recording were studied. Informed consent was obtained from the parents and the children who took part in this study. One child was rejected from the analysis due to very slow saccades and very poor attention as a result of anti-epileptic medication. All children were seen at the Department of Ophthalmology at Great Ormond Hospital as part of their routine clinical assessment. Dense homonymous hemianopia was diagnosed using visual field testing (Goldmann perimetry) and in some instances pattern evoked potentials (Blumhardt et al., 1992). The field results are shown for each subject in Figure 3.4 (overleaf). Neuroimaging findings were available to confirm these findings in all subjects. Patient details are listed in Tables 3.1 and 3.2.

Homonymous hemianopia had a variety of causes and was probably congenital in one patient, had an early onset in one other, and was acquired in the rest. Testing was performed a minimum of 2 years after the approximate date of onset of hemianopia.

No patients were previously noted to have visual neglect in addition to hemianopia. However, testing for neglect was performed to confirm this. Testing was carried out using two tasks: a line cancellation task and a copying task (four simple pictures). None of the patients showed any deficits on either of these tasks. See Figure 3.5.

Figure 3.5. An example of the two neglect tasks completed by one of the hemianopic children in this study. On the left is a figure copying task; the original figures are on top, the patient’s copy below. On the right is a line cancellation task.
Figure 3.4. The Goldmann visual fields for the 7 patients whose data is used in the analysis. The field for the left eye is on the left hand side and vice versa. The patient ID is shown. Continued overleaf.
Figure 3.4. cont. The Goldmann visual fields for the 7 subjects whose data is used in the analysis. The field for the left eye is on the left hand side and vice versa. The patient ID is shown.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age /Sex</th>
<th>Age at onset</th>
<th>Cause</th>
<th>Imaging?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6/M</td>
<td>perinatal</td>
<td>L temporoparietal cyst</td>
<td>MRI</td>
</tr>
<tr>
<td>2</td>
<td>8/M</td>
<td>3y 11m</td>
<td>stroke, R medial occiput</td>
<td>MRI</td>
</tr>
<tr>
<td>3</td>
<td>8/M</td>
<td>~6y</td>
<td>pilocytic astrocytoma</td>
<td>MRI</td>
</tr>
<tr>
<td>4</td>
<td>9/M</td>
<td>~6y</td>
<td>L temporal astrocytoma</td>
<td>MRI</td>
</tr>
<tr>
<td>5</td>
<td>11/F</td>
<td>~8y</td>
<td>L functional hemispherectomy</td>
<td>MRI</td>
</tr>
<tr>
<td>6</td>
<td>14/F</td>
<td>2 months</td>
<td>R temporal lobe damage</td>
<td>CT</td>
</tr>
<tr>
<td>7</td>
<td>15/F</td>
<td>~11y</td>
<td>L focal motor epilepsy</td>
<td>MRI</td>
</tr>
<tr>
<td>8</td>
<td>16/F</td>
<td>~11y</td>
<td>parietal astrocytoma</td>
<td>MRI</td>
</tr>
<tr>
<td>9</td>
<td>18/F</td>
<td>~16y</td>
<td>craniopharyngioma</td>
<td>MRI</td>
</tr>
</tbody>
</table>

Table 3.1. Patient details. MRI - magnetic resonance imaging. CT - computed tomography

<table>
<thead>
<tr>
<th>Patient</th>
<th>Blind field</th>
<th>Vision</th>
<th>Fields</th>
<th>Macular sparing?</th>
<th>Visual Neglect?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R</td>
<td>R 6/7.5 L6/6</td>
<td>Goldmann</td>
<td>slight (L and R)</td>
<td>no</td>
</tr>
<tr>
<td>2</td>
<td>R</td>
<td>R 6/5 L6/5</td>
<td>Goldmann</td>
<td>yes (L)</td>
<td>no</td>
</tr>
<tr>
<td>3</td>
<td>L</td>
<td>R 6/5 L 6/5</td>
<td>Goldmann</td>
<td>slight (R)</td>
<td>no</td>
</tr>
<tr>
<td>4</td>
<td>R</td>
<td>R 6/9 L 6/6</td>
<td>Goldmann</td>
<td>slight (R)</td>
<td>no</td>
</tr>
<tr>
<td>5</td>
<td>R</td>
<td>R 6/9 L 6/6</td>
<td>Goldmann</td>
<td>slight (R)</td>
<td>no</td>
</tr>
<tr>
<td>6</td>
<td>L</td>
<td>R 6/7.5-2 L6/5</td>
<td>Goldmann</td>
<td>yes(L) slight (R)</td>
<td>no</td>
</tr>
<tr>
<td>7</td>
<td>L</td>
<td>R 6/12 L 6/12</td>
<td>Goldmann</td>
<td>yes (L and R)</td>
<td>no</td>
</tr>
<tr>
<td>8</td>
<td>L</td>
<td>R 6/6 L 6/6</td>
<td>Goldmann</td>
<td>none</td>
<td>no</td>
</tr>
<tr>
<td>9</td>
<td>L</td>
<td>R 6/6 L 6/5</td>
<td>Goldmann</td>
<td>yes (R and L)</td>
<td>no</td>
</tr>
</tbody>
</table>

Table 3.2. Patient details continued. The amount of macular sparing was determined from Goldmann field assessment on the day of eye movement recording. Visual neglect was assessed by the tasks described.

The seeing hemifield is often used as a convenient control for the blind hemifield in psychophysical experiments in hemianopic patients (Morland et al., 1999). However, it has been reported that saccades into the seeing field also show some oculomotor adaptation (Meienberg et al., 1986). Thus we recruited age-matched control subjects to determine the standard saccadic response in our experimental paradigm and enable comparison of the saccadic response into both the blind and seeing hemifields.

3.2.2 Experimental set-up

Horizontal eye movements were recorded using an infra-red eye tracker (Skalar IRIS eye tracker). Dimmed lighting levels (luminance 2cd/m²) were used. Patients were seated on a height-adjustable comfortable chair 89cm in front of a blank white screen onto
which a red laser spot was projected. The height of the chair was adjusted until the patients reported that they were comfortable and level with the target spot. Head stabilisation was provided by an adjustable chin rest. See methodology for full details.

3.2.3 Experimental paradigm

The first two patients tested (numbers 5 and 9) were run on two separate paradigms: a ‘semi-predictable’ paradigm and a ‘random’ paradigm. The semi-predictable paradigm consisted of a total of 100 trials: 50 trials that were predictable in eccentricity (5°) but not in direction (left or right), followed by another 50 trials with a target eccentricity of 15°, again to the left or right. The random paradigm consisted of 100 trials in which the target was randomised both in eccentricity (5° or 15°) and direction (left or right). These two paradigms together took over 20 minutes including the calibration procedure before each paradigm. This was found to be too long, particularly for young and tired subjects (patients were generally tested after numerous out-patient appointments in the eye clinic). Thus, the seven subsequent patients were tested on a modified paradigm (125 trials) in one continuous session. This kept the experiment as short as possible without the need for repeating time-consuming and tiring calibration procedures. All patients and control subjects completed the experimental paradigm although substantial encouragement was sometimes required and some subjects became restless towards the end of the session.

All saccades were elicited to only one of two different target eccentricities, 5° and 15°. The peripheral target was chosen as 15° to ensure that even hypermetric saccades to this eccentricity would be within the linear range of the equipment. There were four phases to the experimental protocol:
1) Phase 1. **Random phase.** This phase consisted of 50 trials with target eccentricities of ±5° and ±15° pseudo-randomly presented. This phase of the protocol provided stimuli randomised in both direction and eccentricity.

2) Phase 2. **Semi-predictable phase (15°).** This phase consisted of 25 trials with ±15° targets pseudo-randomly presented. This phase provided stimuli randomised in direction but predictable in eccentricity, thus increasing the level of predictability relative to the first phase of the protocol.

3) Phase 3. **Semi-predictable phase (5°).** This phase was the same as phase 2 except for the use of 5° target eccentricities instead of 15°.

4) Phase 4. **Predictable phase.** The final phase consisted of targets presented at an eccentricity of 15° only within the blind field of the patient. In control subjects the side was nominated at random. These targets were thus fully predictable in both direction and eccentricity.

All of the target presentations were randomised in time in order to prevent the generation of predictive saccades. Predictive saccades have been shown to have decreased gains and an altered main sequence in comparison to reflexive saccades (Bronstein and Kennard, 1987; Smit and van Gisbergen, 1989).

Each trial started with the target spot in the centre. After a random time delay (1100-2500msec) the spot moved instantaneously to a peripheral position. The target light was always present on the screen thus movement of the target into the blind hemifield was indicated by the offset of the central fixation target. The spot remained at the peripheral position for 1500msec before returning to the centre for the start of the next trial. Subjects were simply asked to keep their eye on the target at all times and follow it as quickly and accurately as possible when it moved. They were also reminded not to move their heads.
3.3 Results

3.3.1 Control subjects

No differences were found between the mean gains of saccades to the left or right in each phase of the experiment within the control group. This was valid for both 5° and 15° target eccentricities.

In the random phase the average gain of saccades to 5° target eccentricities was greater than to 15° target eccentricities. See Table 3.3 and Figure 3.6. This difference has been called the ‘range effect’ (Kapoula, 1985). The same pattern was surprisingly also seen in the semi-predictable phase, even though the 5° and 15° target eccentricities were presented separately in this phase.

There were no significant differences between the average gains in any of the phases of the experiment for either 5° or 15° target eccentricities. We can conclude that the predictability of the target eccentricity made no difference to the gain of saccades in control subjects in our experiment.

<table>
<thead>
<tr>
<th>Phase</th>
<th>5° target eccentricity</th>
<th>15° target eccentricity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gain</td>
<td>SD</td>
</tr>
<tr>
<td>Random</td>
<td>1.010</td>
<td>0.049</td>
</tr>
<tr>
<td>Semi-Pred</td>
<td>1.001</td>
<td>0.070</td>
</tr>
<tr>
<td>Predict</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3.3. To show the mean gain and standard deviation (SD) of saccadic gain for each target eccentricity in each phase of the experiment in control subjects.

Figure 3.6. Control subjects. The mean gains (and 95% confidence interval) (CI) for saccades to each target eccentricity, in each phase of the experiment.

— 5 degree targets

--- 15 degree targets
3.3.2 Hemianopic patients

The results for the first two patients who were tested with longer paradigms were found to be qualitatively the same as the results from the remainder of the patients who were tested on the shortened paradigm. Thus the results from only the patients tested on the shorter paradigm will be discussed in detail as representative of the whole group. Examples of typical saccade profiles will be shown first, followed by quantitative analysis of the data.

Saccades into the blind hemifield

All patients made both multiple hypometric and hypermetric saccades, as well as saccades that were normometric into their blind hemifield. Multiple hypometric saccades were common in all patients. They were more often made to 15° target eccentricities but were occasionally observed to 5° target eccentricities. See Figure 3.7A and B.

Figure 3.7A. Eye movement traces of multiple hypometric saccades to 15° targets in the blind field of the hemianopic patient. The top two patients have left hemianopia, and the bottom two patients have right hemianopia. Patients 4 and 6 both show dynamic overshoot.
Variability was a distinctive feature of the saccades made into the blind field by the hemianopic children in this study. The primary saccade of a multiple hypometric sequence varied greatly in size. See for example Figure 3.7A. The final saccade in a hypometric sequence either overshot the target, eliciting a backwards corrective saccade (Figure 3.8B, left hand graph), or appeared to land directly on-target, not requiring any further correctives (Figure 3.8B, right hand graph).
Hypermetric saccades generally had a small amount of overshoot followed by a small backwards corrective saccade (Figure 3.9A). Occasionally a large amount of overshoot was seen, this was more often to 5° target eccentricities (Figure 3.9B).

**Figure 3.9A.** Hypermetric saccades to 15° target eccentricities. The amount of overshoot was usually quite small.

**Figure 3.9B.** A large amount of overshoot was more often observed to 5° target eccentricities.

Saccades into the seeing hemifield

Saccades made by hemianopic patients into their seeing hemifield appeared to be normal. They generally showed a small amount of hypometria, as expected, especially for saccades to 15° target eccentricities. The similarity between the gain of saccades made by hemianopic patients into their seeing hemifield, and control subjects into the nominated hemifield can be seen in Table 3.4 and Figure 3.10, see over.
3. Hemianopia

Figure 3.10. Two examples of saccades into the seeing hemifield made by patient 8.

Variability and Predictability

As mentioned, a common feature of the saccadic responses of the hemianopic patients in this study was the large amount of variation in the gain of their saccades particularly into the blind field. The standard deviation about the mean was generally at least double as much for the blind hemifield as the seeing hemifield in the patients. See Table 3.4 and Figure 3.11.

<table>
<thead>
<tr>
<th></th>
<th>5° target eccentricities</th>
<th>15° target eccentricities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blind field</td>
<td>Seeing field</td>
</tr>
<tr>
<td>Phase</td>
<td>Gain</td>
<td>SD</td>
</tr>
<tr>
<td>Random</td>
<td>0.928</td>
<td>0.28</td>
</tr>
<tr>
<td>Semi-P</td>
<td>0.960</td>
<td>0.36</td>
</tr>
<tr>
<td>Pred.</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3.4. To show the mean and standard deviations for saccades to 5 and 15° target eccentricities in the blind and seeing hemifields in each phase of the experiment. Data is also shown for the control subjects.

Figure 3.11. The mean gain and 95% CI for primary saccades made by control subjects (diamonds and dotted lines) and patients into their blind (squares and solid lines) and seeing (circles and long dashes) hemifields during each phase of the experiment. Each target eccentricity is plotted separately.
No obvious effects of target predictability were observed in the data. There was a slight trend for the gain of saccades into the blind hemifield to increase as the target eccentricity became more predictable. This may suggest that there is a small effect of target predictability for the gain of saccades into the blind hemifield, however predictability clearly did not induce the use of a hypermetric strategy and the mean gain of saccades into the blind field remained low, especially for 15° target eccentricities, even when the target was fully predictable.

The low gain of saccades into the blind hemifield was particularly prominent for the 15° target eccentricities in the random and semi-predictable phases. The large standard deviation was prominent for saccades to both target eccentricities in the blind hemifield. See Figure 3.12. 5° target eccentricities were not tested in the predictable phase.

Figure 3.12. The mean gain and standard errors for saccades made into the blind, seeing and control fields, for each target eccentricity. Each phase of the experiment is shown separately. Continued overleaf.
This low mean gain was also associated with a very large standard deviation for all saccades into the blind hemifield. The large standard deviation prevents a statistical difference of the mean gain between the blind and seeing or control fields being obtained in parametric statistical analyses. In fact, parametric analyses are not strictly valid for data groups with such dissimilar standard deviations.

**Modality of the gain distribution**

The third aim of this experiment was to determine whether saccadic hypermetria represents a distinct strategy or simply the upper end of the primary gain distribution. This may be determined from the modality of the frequency distribution of the primary saccade gains. The frequency histograms of the gain of saccades for each phase of the experiment, and for each target eccentricity are presented in Figures 3.13A, B and C. The data from all subjects are presented together. Due to our method of determining gain, there is an artificial peak at 1.0 in all distributions. All histograms for the seeing and control fields show a narrow distribution of gain with a peak just under 1.0. This reflects the well-known phenomenon of the undershoot bias. The influence of the range effect can be seen in the gain distributions for the saccades of hemianopic patients in to their seeing fields, and for control subjects. That is, there is a leftward skew for 15° target
eccentricities and a rightward skew for 5° target eccentricities in both the random and semi-predictable phases. The figures also all clearly show the large distribution of gains for saccades into the blind field in contrast to the seeing and control fields. In spite of this large distribution of the gains, there is still a general bias to undershoot the target in the blind field.

**Random Phase**

**5° target eccentricities**

**15° target eccentricities**

![Graphs showing saccadic gain distributions for 5 and 15° target eccentricities in the random phase.](image)

**Figure 3.13A.** The primary saccadic gain distributions for saccades to 5 and 15° target eccentricities in the random phase.

For the blind field, in the random phase (Figure 3.13A), there is evidence of bimodality for both 5° and 15° target eccentricities. The peaks above and below 1.0 are not prominent and given the relatively low numbers involved, and the wide distribution of
the data, a firm conclusion as to whether these peaks represent distinct strategies is hard to make.

Semi-predictable Phase

**5° target eccentricities**

<table>
<thead>
<tr>
<th>Blind</th>
<th>Seeing</th>
<th>Control</th>
</tr>
</thead>
</table>

**15° target eccentricities**

<table>
<thead>
<tr>
<th>Blind</th>
<th>Seeing</th>
<th>Control</th>
</tr>
</thead>
</table>

*Figure 3.13B. The gain distributions for saccades in the semi-predictable phase.*

In the semi-predictable phase (Figure 3.13B) the same pattern is seen for the distribution of gains in the seeing and control fields. The evidence for bimodality in the blind field is less convincing.
In the predictable phase there is certainly no evidence of bimodality. This phase show the clearest leftward skew of the distribution, i.e. a bias to undershoot the target in spite of the large spread of the data. This again confirms that for the subjects in our study, increasing the predictability of the target eccentricity does not induce more hypermetric saccades to be made.

3.4 Discussion

The hemianopic children in this study were all found to make low gain saccades to targets in their blind hemifield in the majority of trials. No children showed consistent hypermetria. This result is in agreement with the previous findings from our pilot study (Mezey et al., 1998).
3.4.1 Effect of predictability

There was no significant effect of predictability found to 5° or 15° target eccentricities in either our control subjects or hemianopic patients. The differences observed between the gain of saccades to 5° and 15° target eccentricities in both the random and semi-predictable phases were most probably due to the range effect (Kapoula, 1985). Although the 5° and 15° target eccentricities were presented in separate groups, not intermingled, in the semi-predictable phase, it is possible that the range effect established during the random phase was still influencing the gain of saccades in the semi-predictable phase. This may explain why the same differences in gain were seen in both the random and semi-predictable phases.

Temporal predictability in saccadic tasks in known to induce short-latency saccades (predictive or anticipatory saccades) with low gains (Bronstein and Kennard, 1987). We did not want temporal predictability to influence the gain of saccades in this experiment thus we randomised target presentation temporally to discourage such short latency, low gain saccades. Trials in which predictive saccades (with a latency of <80msec) were made were removed from the analysis. Although spatial predictability was found to have no significant effect on gain in our control subjects, this may have been due to the relatively limited number of trials in each phase of our experimental paradigm. This may have prevented the build up of ‘expectation’ in our subjects as to where the target would appear next. Furthermore, we did not inform our subjects as to the predictability of each phase of the experiment. We have not found reports that specifically address the issue of saccadic gain with respect to the predictability of target eccentricity. Voluntary saccades are reported to be more accurate than reflexive saccades (Lemij and Collewijn, 1989). This difference may be partly as a result of the obvious target spatial predictability as well as other factors regarding the pathways involved in generation of voluntary saccades and issues of attention.
Meienberg et al. (1981) reported two situations in which adults with homonymous hemianopia produced hypermetric saccades. Firstly, when the target was predictable in both eccentricity and time, the initial few attempts to find the target resulted in a staircase pattern of saccades; however, once the target position has been learned subsequent attempts consisted of a single overshooting saccade, followed by a backwards saccade or glissadic movement. Meienberg et al. (1981) did not report how many attempts it took before the hypermetric strategy emerged. This paradigm was similar to our predictable paradigm in that the target eccentricity was fully predictable although in our paradigm the temporal properties were not predictable. It is unlikely that the temporal predictability of Meienberg's paradigm was solely responsible for the emergence of the hypermetric strategy amongst the hemianopic adults. No association between temporal predictability and saccadic hypermetria has been reported previously either in a normal or patient population.

The second situation in which Meienberg et al. (1981) reported saccadic hypermetria was in one patient in a follow-up recording made 7.5 months after an acute occipital lesion. Initial recordings made at 4 months post-lesion revealed the pattern of saccadic behaviour mentioned above, i.e. staircase saccades to begin with and then the development of hypermetria. However, at 7.5 months this patient overshot targets into the blind hemifield, even on the first trials and even when eccentricities were large. Backward glissades were also found to be larger and faster. All of our patients were recorded a minimum of about 2 years after the onset of hemianopia. Thus they had relatively more time for compensatory strategies to develop than the adult patient reported. We were unable to replicate the hypermetria reported by Meienberg et al. (1981) either with predictable targets, or with long post-lesion periods to allow for the development of compensatory strategies.

Our prediction that more hypermetria would be seen with increased target predictability in order to minimise the time taken to fixate the target was not supported.
Our data suggest that the predictability of the target eccentricity does not significantly affect the gain of saccades to this eccentricity.

3.4.2 Effect of target eccentricity

We found that our hemianopic patients in general undershot both 5° and 15° target eccentricities in all phases of the experimental paradigm. It was not possible to make true statistical comparisons between the gain of saccades to 5° or 15° target eccentricities into the blind, seeing and control fields due to dissimilar standard deviations. However, it can be seen that the amount of undershoot was not substantially different for 5° target eccentricities in the blind field in comparison to the seeing field or control subjects while the amount of undershoot was much greater for the 15° target eccentricities (Figure 3.11). These differences are a likely result of using the staircase strategy for acquiring the target in the blind hemifield. In making the initial saccade into the blind hemifield relatively small, this may still produce a relatively high gain primary saccade for small target eccentricities, while this will result in a much lower gain saccades to larger target eccentricities.

It is puzzling however that the average gain of primary saccades to 15° target eccentricities (0.64 in the random paradigm) reflects a saccade of an amplitude (9.66°) that would grossly overshoot a 5° target eccentricity. Three alternative explanations for this finding are possible. Firstly, there is the possibility that some of the patients in this study had a degree of macular sparing, or perhaps even islands of spared vision, that enabled them to see the 5° target. From the Goldmann field records it is evident that this was a possibility in three of the seven subjects. These three subjects all had apparent sparing along the horizontal meridian of 5° or more in one eye. Second, a gradual head turn towards the blind hemifield may have brought the 5° target eccentricity within an area of macular sparing. While no clear head turn was noted during the experiment in any
of our subjects, a subtle change may have gone unnoticed. However, no systematic shift in the absolute initial eye position into the blind field of each patient over the course of the experiment was noted. Thirdly, this finding may suggest that there was some knowledge of the target location in the blind field in these hemianopic patients. This could be subserved by the well-documented subcortical retino-collicular pathways (Cowey and Stoerig, 1991) that might well be preserved in our patients who all had cortical damage causing their hemianopia and no reported subcortical damage. The retino-collicular pathway is popularly believed to be used primarily for visuo-motor control and spatial attention and subserves the controversial phenomenon of ‘blindsight’ (Weiskrantz et al., 1974). The retino-occipital pathway, on the other hand, is traditionally believed to underlie pattern analysis and recognition, and hence, conscious perception. If there was indeed some knowledge of target location within the blind field in hemianopic subjects which could be employed when making saccades to 5° target eccentricities, why should this information not be available to the saccadic system when making saccades to 15° target eccentricities? Holtzman (1984) reported that collicular ‘vision’ is of limited spatial resolution. This is also consistent with the collicular physiology of the monkey: the receptive fields of collicular neurons tend to be much larger than those in the visual cortex (Goldberg and Robinson, 1978). There may merely be subcortical ‘knowledge’ that the target is somewhere in the periphery, rather than close to the fovea as with the 5° target eccentricity, without the resolution to enable a more accurate saccade to be confidently programmed.

3.4.3 Adaptive effects in the seeing hemifield

There were no significant differences observed between the gain of saccades made by hemianopic patients into their seeing hemifield relative to control subjects for either 5° or 15° target eccentricities. In fact, in the random paradigm the average gain of saccades made by hemianopic subjects were almost identical to the gain of saccades made by
control subjects for both 5° and 15° target eccentricities. It might be predicted that subjects would aim to undershoot targets in their seeing hemifield by slightly more than usual in order to prevent the risk of losing the target into the blind hemifield by overshooting it. Such an adaptation was reported in hemianopic adults by Meienberg et al. (1981). They reported that along with the appearance of the hypermetric strategy to targets in the blind hemifield of hemianopic adults, an increasing degree of saccadic hypometria towards targets in the seeing field developed. This adaptation reported by Meienberg may have been directly related to the development of hypermetria into the blind hemifield, especially since it developed with the same time course. Given that we did not observe any development of a hypermetric strategy into the blind field, this may also be the reason why we did not observe any adaptation of saccadic gain into the seeing hemifield in our patients.

3.4.4 Variability

Variability was a distinctive feature of saccades to both 5° and 15° target eccentricities in the blind field of our hemianopic patients. They did not show increased variability into their seeing hemifield, except to 5° target eccentricities in the random phase, see Figure 3.11. However, the variance of saccades to targets in the blind field was consistently at least five times greater than that of control subjects.

This variability is most probably a result of target location uncertainty within the blind field of the hemianopic subject, rather than a physiological consequence of damage to the saccade generating pathways. The association of this high variability with low gain is a phenomenon that has been predicted by the saccadic flight-time minimisation hypothesis (Harris, 1995). Using this hypothesis, computer simulations have indicated that the greater the standard deviation of target-directed saccades, the lower the gain of saccades to this target. This is in order to minimise saccadic flight-time which has the
effect of preventing excessive numbers of overshooting saccades and explains the undershoot bias. High variability and low gain saccades are also seen in infants (Harris et al., 1993), in predictive saccades (Bronstein and Kennard, 1987) and saccades to remembered targets (Bracewell et al., 1990, White et al., 1994).

Low gain saccades may have other causes. Cerebellar lesions in particular have been reported to cause saccadic dysmetria (Leigh and Zee, 1991) with lesions to the vermis causing hypometria. Basal ganglia diseases are also associated with saccadic hypometria of voluntary saccades (Leigh and Zee, 1991). None of our patients were reported to have cerebellar or basal ganglia damage, nor showed any of symptoms of such deficits. There is also no evidence that making low gain saccades is a conscious strategy adopted by hemianopic subjects to assist with target fixation.

The high variability of saccades into the blind field indicates that the saccadic system is not simply producing a saccade of a standard amplitude to any target within the blind hemifield. This has been demonstrated previously (Mezey et al., 1998).

3.4.5 Saccadic strategies

Hypermetria was not a consistent strategy employed by any of the hemianopic children in this study. The third question to be answered in this study was whether the saccadic hypermetria observed represents a distinct saccadic strategy or whether it simply represents the upper end of the saccadic gain distributions. The number of saccades made by patients to each target eccentricity in each phase was too low to make assessments on an individual basis. There was some evidence of bimodality when all patients were assessed together.

This bimodal appearance may be due to our method of assessing gain which may create artificial dips below and/or above the peak at 1.0. A dip around the peak at 1.0 may develop when high gain saccades (though not hypermetric) to a 15° target eccentricity are made, and the system does not follow-up with a corrective saccade, despite the fact that
the target has not yet been fully foveated. These saccades would thus by default have a gain of 1.0. This ‘laziness’ of the saccadic system may be due to the lack of any information-processing demands in our experiment that would require precise target foveation. Kapoula and Robinson (1986) have suggested that possibility of such a lazy strategy. We could have encouraged target foveation by using a discrimination task., however, this was beyond the limitations of our equipment. An additional explanation could be due to macular sparing in our patients. Most patients had some degree of macular sparing. It is possible that these patients were not making further saccades if the initial saccade was large enough that it took the target to anywhere within the region of sparing in the blind hemifield. The lack of corrective saccades after saccades which do not foveate the target, and should therefore, in reality, have slightly lower gains, would create the lack of gains around a gain of 1.0 and thus increase the number of saccades with a gain of 1.0. These dips above or below the peak at 1.0 may give an incorrect impression of bimodality.

This inability to judge whether the target was indeed being consistently precisely foveated was one of the drawbacks of our method of individual calibration of trials. This method of calibration was nevertheless the most effective to use given the inevitable small amount of head movement in our young patients. This method enables the gain of the primary saccade in each trial be related to the internal goal of the saccadic system in that trial, rather than independently to the target eccentricity. The saccadic system may alter its behaviour towards the target over the course of the experiment.

The hypermetric strategy has been discussed as being ‘more efficient’ than the staircase type saccades for locating objects in the blind hemifield (Meienberg et al., 1981). We proposed that this may indeed be the case for predictable and/or peripheral targets (Mezey et al., 1998). This efficiency can be interpreted from the flight-time characteristics of sequences of saccades. Undershooting saccades have been shown to minimise saccadic flight-time relative to overshooting saccades, given the same
magnitude of error (Harris, 1995), see Section 1.5.3. However, when gain is very low, more corrective saccades are required and the undershooting strategy becomes less efficient, due to the cost of making each corrective saccade. The time saved using a hypermetric strategy in such a situation may be found not only in terms of total saccadic flight-time, but also in the total time taken to acquire the target, including intrasaccadic intervals.

If it was known that the target would appear in the periphery, it would be more efficient to employ a hypermetric strategy, both in saccadic flight-time and the total time taken to fixate the target. Although there was a suggestion of this in the hemianopic adults reported by Meienberg et al. (1981) there was no consistent use of this strategy in our hemianopic children. This may have been because this strategy was yet to develop in this young patient population, or because the experimental paradigm was not suitable to elicit the strategy, or because the staircase strategy is in fact optimal, for an unknown parameter, for fixating a target in the blind hemifield. The staircase strategy has been proposed to indicate the use of local, bottom-up control processes in the context of scanning eye movements (Zangemeister et al., 1995). This is in contrast to the top-down cognitive control that is believed to guide scanning saccades in the seeing field.

The development of saccadic strategies may be dependent upon the age at which the visual input was lost to the saccadic system. Most of our patients became hemianopic after the maturation of the visual and saccadic systems were completed, in terms of the measurable visual acuity levels and saccadic characteristics at least. The oculomotor system develops rapidly in the first few months of life (Harris et al., 1993). Adult-like characteristics of saccades are thought to be obtained at around the age of 12 months. In this sense one would expect them to behave similarly to adults. In patients with congenital or very early onset hemianopia however, the immaturity of the visual and saccadic systems at the point of visual loss may have implications for the development of saccadic strategies.
It has been proposed by Paysee and Coats (1997) that children with early-onset homonymous hemianopia adopt an anomalous head turn in order to enlarge their functional visual field, allowing larger saccades to be made into their blind field. The presence of such a head turn is open to a number of interpretations including those involving visual scanning and improving the optic flow field (see Mezey et al., 1999). Coats and Paysee (1999) further proposed that only children with the most immature visual systems at the time of visual loss are likely to develop and utilise these adaptive mechanisms. There is some support for their proposal from the work of Zangemeister et al., (1982) who reported that patients with congenital hemianopia were more likely to use single, large, overshooting saccades with contraversive drifts in order to locate a target in their blind field. One of our patients (Patient 7) was remarked by her parents to have a head-turn, though this was not noted during her eye examination. This patient did not make a greater percentage of overshooting saccades into the blind field than any of the other patients.

There may be distinctions between the adaptive strategies that occur when the eyes move alone without movement of the head or body, or with co-ordinated eye and head movements. The frame of reference would be retinal in the former case and head-, or even body-, centred in the latter. The functional processing of co-ordinated gaze is reported to be more flexible than eye movements alone (Zangemeister and Stark, 1982a). On the other hand co-ordinated gaze is less efficient in terms of time than saccades alone (Zangemeister and Stark, 1982b). It has been reported however that patients with homonymous hemianopia often reduce or omit the head-movement component of a gaze-shift (Zangemeister et al., 1982). This is especially pronounced in patients with congenital hemianopia.
3.5 Conclusion

Children with homonymous hemianopia make low gain saccades into their blind hemifield. Saccadic hypermetria is not found to be a common strategy in these patients. Neither is there an indication of adaptations occurring to saccades made into the seeing hemifield. The low gain of saccades into the blind hemifield is believed to be a consequence of the high variability of the error, as proposed by the saccadic flight-time minimisation hypothesis (Harris, 1995).

Target predictability was found to have no effect on the use of the hypermetric strategy in our experimental paradigm.

There is also no clear indication that hypermetric saccades represent a distinct saccadic strategy, as is the suggestion of previous investigators (Meienberg et al., 1981; Zangemeister et al., 1982). The saccadic hypermetria reported separately by Meienberg and Zangemeister came from the same group of patients and thus constitute only one instance of such a clear use of hypermetria. This may have been a strategy unique to the patients in their study, or characteristic of their experimental protocol.

We conclude that the relatively good compensation seen in the patients in our study was not due to a hypermetric saccadic strategy, even those with many years post-lesion visual experience. Individual differences in the location of the lesion and the ability to adapt would predict that each patient in our study would be employing strategies based on individual experience. However, the fact that hypometria was found to be the most consistent saccadic strategy suggest that a generic interpretation may be possible.

It is possible the sub-cortical retino-collicular pathway plays a role in the guidance of saccadic movements into the blind hemifield.
Chapter 4. Antisaccades

4.1 Introduction

Antisaccades were introduced as a novel oculomotor task by Hallett (1978). The antisaccade task requires the subject to inhibit a reflexive saccade towards a suddenly appearing peripheral target and instead generate a voluntary saccade equal in amplitude but opposite direction to the target stimulus. This process is thought to fundamentally involve areas of the frontal lobes and basal ganglia (O’Driscol et al., 1995; Müri et al., 1994) and the significance of deficits in the task was soon noted in patients with lesions in these areas. More recently the task has been investigated in the context of various psychiatric and neurological conditions that are believed to involve the frontal lobes and/or basal ganglia, for example schizophrenia, Tourette’s syndrome, obsessive-compulsive disorder, Parkinson’s disease and Huntington’s disease. Patients with these disorders have all been variously reported to show characteristic deficits on the antisaccade task relative to a normal prosaccadic task (see Everling and Fischer, 1998).

The antisaccade task has also been very popular in non-clinical populations for investigating theories regarding saccadic programming and the latency characteristics of saccades (Hallett and Adams, 1980, Fischer and Weber, 1992, 1996, 1997; Reuter-Lorenz et al., 1995; Weber, 1995). The parameters of interest in antisaccadic tasks are the same as those for normal saccadic tasks, with the particular addition of assessing the percentage of erratic prosaccades and subsequent corrective antisaccades made. Primary saccades in the direction of the target will be called prosaccades in this chapter to distinguish them from antisaccades which are correctly made in the opposite direction to the target.
Deficits in the antisaccade task can be manifest in two distinct ways. The subject may be unable to inhibit the reflexive saccade towards the visual target but then subsequently correct this initial error with an antisaccade (an erratic prosaccade followed by an antisaccade). Alternatively, the subject may never initiate the antisaccade and only generate the prosaccade (Guitton et al., 1985). These problems involve the inhibition of reflexive behaviours and the generation of voluntary behaviours respectively. The latter is generally only relevant to clinical populations (Guitton et al., 1985) and in children (Fischer et al., 1997) while the errors in the inhibition of reflexive behaviours is common to ‘normal’ populations as well. Comprehension of the task in the first place may also be an issue, particularly in children or patients with learning deficits or short term memory problems.

Hallett (1978) reported that the error rate (erratic prosaccades) settled to a level of 5-7% in normal adults but was as high as 30-80% initially (in the first 100 trials). The introduction of a gap between the offset of the central fixation point and the onset of the peripheral stimulus has a systematic effect on both the error rate and latency of antisaccades, dependent on the size of the gap (Fischer and Weber, 1997).

Antisaccades have increased latencies relative to prosaccades (Hallett, 1978). This was originally suggested to represent the long conduction time, in unmyelinated visual fibres across the corpus callosum of the information regarding the generation of a saccade into the opposite hemifield (Hallett, 1978). This has been refuted (Fischer and Weber, 1992) and more recently the latency difference has been attributed to the extra time taken to program a saccade to a position where no visual stimulus occurs (Fischer and Weber, 1992). Hallett and Adams (1980) have shown that antisaccade latency characteristics in normal subjects are directly related to their performance in prosaccadic tasks.

The metrics and dynamics of antisaccades are also found to be altered relative to prosaccades, in addition to their latency characteristics. The amplitude of antisaccades is
reported to show larger errors and a greater spread than reflexive saccades (Hallett, 1978; Hallett and Adams, 1980). Variations were found both between and within subjects, although the mean amplitude within a session remained roughly constant (Hallett, 1978). Although the average gain is reported to be low, Hallett and Adams (1980) remarked a greater number of overshooting saccades in antisaccade experiments. It has also been found that primary saccades are regularly not followed by secondary saccades, unless the end point error of the primary saccade was particularly large. The peak velocity of antisaccades is decreased by approximately 30% (Smit and van Gisbergen, 1987; van Gelder et al., 1997).

The interest in the antisaccade task with respect to this thesis lies not so much with the error rate, which is particularly relevant to clinical populations, or the latency characteristics that have been the focus of the majority of reports concerning antisaccades, but primarily in the metrics of antisaccades. In the previous chapter we reported that a characteristic of saccades made by hemianopic patients into their blind hemifield was the large variation in the saccadic accuracy. In spite of this variation there was still a strong bias to undershoot the target; the mean gain of saccades was low. We proposed that this provided support for the theory that in the face of a large standard deviation of the saccadic error, the optimal gain of saccades is lowered in order to prevent overshooting saccades and so minimise saccadic flight-time (Harris, 1995). The previous reports of antisaccades discussed above indicate that antisaccades may show similar characteristics in their metrics to saccades made by hemianopic patients into their blind hemifield. We set out to record antisaccades in normal adults in order to relate our findings to predictions of the saccadic flight-time minimisation (SFM) hypothesis.
4.2 Subjects and Methods

Antisaccades were recorded from 5 subjects between ages of 25 and 32. Each subject was recorded in their usual refractive state. No subjects had any known neurological or oculomotor problems.

The experimental set-up has been described previously in the methodology chapter. Horizontal eye movements were recorded with an infra-red eye tracker (Skalar IRIS eye tracker).

Each subject was explained the antisaccade task and given the instruction to make a saccade ‘opposite in direction but equal in size’ to the visual target. A few practice trials were made to ensure the comprehension of the task.

After calibration, each experiment began with the subject making 25 prosaccadic trials, and then after a short pause and a reminder of the antisaccade instructions, the antisaccade task began. Subjects performed 200 antisaccadic trials. The experiment took just over 15 minutes in total. The initial prosaccades provided not only baseline parameters for each individual, for comparison to antisaccade parameters, but also hopefully served to settle subjects and induce similar mind-sets in advance of the antisaccadic trials beginning. Some investigations into antisaccades have interleaved normal reflexive trials with antisaccade trials to obtain the baseline parameters, and to provide some degree of visual feedback regarding the desired eye position in the antisaccade task. However, such interleaving has not been found to aid performance. Hallett (1978) reported that angular error and secondary latencies were the same whether antisaccade were performed alone, or in combination with reflexive saccades. Thus, we used a solid block of antisaccade trials, with no interleaving, to enable the maximum amount of antisaccade data to be gathered within a reasonable period of time.
Each trial began with the target at the central fixation spot. After a randomised time delay of 1500-3000 msec the target jumped 10° to either the left or the right hand side, along the horizontal meridian. The side to which the target jumped was randomised. In the prosaccadic task (trials 1-25) the subject was simply required to follow the spot with their eyes wherever it moved, while in the antisaccade task (trials 26-225) they had to look in the opposite direction. There were no differences in the stimulus parameters, only the requirements of the subject in relation to the stimulus.

Saccadic data was analysed using our standard computer program which produced the metric, dynamic and latency characteristics of each saccade made in each trial. The data from error trials were not included in the analysis of the metrics and latency characteristics of antisaccade trials, unless specified in the text.
4.3 Results

The gain and error parameters for all subjects are shown in Table 4.1.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Prosaccades</th>
<th>Antisaccades</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gain</td>
<td>SD</td>
</tr>
<tr>
<td>1</td>
<td>0.868</td>
<td>0.066</td>
</tr>
<tr>
<td>2</td>
<td>0.957</td>
<td>0.055</td>
</tr>
<tr>
<td>3</td>
<td>0.954</td>
<td>0.091</td>
</tr>
<tr>
<td>4</td>
<td>0.959</td>
<td>0.039</td>
</tr>
<tr>
<td>5</td>
<td>0.917</td>
<td>0.075</td>
</tr>
<tr>
<td>Average</td>
<td>0.931</td>
<td>0.039</td>
</tr>
</tbody>
</table>

Table 4.1. Parameters of prosaccades and antisaccades made by each of the subjects in this experiment are shown. Gain - mean gain; SD - standard deviation; n - total number of antisaccade trials completed out of the 200 presented (i.e. trials not lost to blinks or other artefacts); % error - percentage of trials, from the total n, in which an erratic prosaccade preceded the antisaccade.

4.3.1 Prosaccades - metrics

Four subjects had similar gains and standard deviations, around the usual gain obtained in our experience and reported in the literature (Becker, 1989) for the reflexive prosaccades in the initial phase of the experiment. See Figure 4.1.

![Figure 4.1](image.png)

Figure 4.1. A reflexive prosaccade to the right. A small amount of undershoot is standard. Primary latency is approximately 200msec.

Subject 1 had a mean gain that was on the low side (mean = 0.868, SD = 0.06). We do not know the reason for this low gain. There were no significant differences between the gain
of saccades made to the left or right, thus the results were merged for the two directions. The overall mean was 0.931 (SD = 0.039). This average gain is typical of the undershoot bias. The distribution of gains for all 5 subjects together is shown in Figure 4.2.

The average percentage of hypometric prosaccades made in the initial phase was 80.4%, of hypermetric saccades 11.5% and of saccade with no correctives 8.1%.

![Figure 4.2. Histogram to show the distribution of gains of normal reflexive prosaccades in the first phase of the experiment. The data shown is for all subjects together.](image)

### 4.3.2 Antisaccades - error rate

The five subjects in this study varied greatly in their ability to perform the antisaccade task. Concentration was believed to be good for all subjects as relatively few trials were lost to blinks or a lack of saccadic movement in response to target movement. The average number of trials lost due to blinks or not attending the central fixation target at beginning of the trial was 11.2 out of 200 (range 4-19). An error was defined by a primary saccade that had the same direction as the target, i.e. an erratic prosaccade. The error rate ranged from 3.1-39.2% with no significant differences between errors made in the first and second 100 antisaccade trials. All erratic prosaccades were corrected by an antisaccade. This confirms that the high percentage of errors made by three subjects was not due to a lack of understanding of the task; the subject was aware that they had made an error. Erratic prosaccades were corrected with an antisaccade (a 'corrective' antisaccade) after an
intersaccadic interval of mean 112.3 msec. See below, Figure 4.3A. Some corrective antisaccades occurred with very low latencies (Figure 4.3B), and even with no latency at all, appearing as ‘back-to-back’ saccades (Figure 4.3C). These distinctive saccades have been previously reported not only in antisaccade paradigms (Hallett, 1978; Hallett and Adams, 1980) but also in other experiments (Becker and Jürgens, 1979; Zee et al., 1976) and when subjects are fatigued or inattentive (Becker, 1989). Such saccades were confirmed as true back-to-back saccades, and not an unusually symmetric blink artefact of the two eye movement traces, by video-recording one eye during the experiment and going back to observe the behaviour of the eye during the appropriate trials.

![Figure 4.3](image)

**Figure 4.3.** Eye movement traces of typical error trials. Corrective antisaccades are made after erratic prosaccades. A - The target moves to the left and the eye is required to move to the right. The eye first makes an erratic prosaccade towards the target to the left and then corrects itself, after an intersaccadic interval of approximately 140msecs, making an antisaccade to the right. B - The target moves to the right. An erratic prosaccade is made to the right followed after a short intersaccadic interval of <100msec, by the corrective antisaccade. C - the erratic prosaccade to the right is corrected by the antisaccade with virtually no intersaccadic interval.

### 4.3.3 Antisaccades - metrics

Primary saccades were mostly hypometric with respect to the final eye position (Figure 4.4A and B). Some primary saccades were not followed by any corrective saccades (we have called these single saccades) (Figure 4.4C), or they overshot the target by a small amount (Figure 4.4D). Large overshoots were rare.
The average gain of correct antisaccades was 0.825 with a standard deviation of 0.093. This level of gain is much lower than that of reflexive prosaccades (0.913, SD = 0.039), while the standard deviation is much greater. Statistical testing for a significant difference between these mean gains was not appropriate due to the greatly different standard deviations and number of data points in the prosaccade and antisaccade data sets. It can be seen nevertheless in Figure 4.5 that although the mean gain of antisaccades is much lower than the mean gain of prosaccades, this difference would not be significant due to the large standard deviation of the antisaccades.
The average gain and standard deviation values cannot reveal the details of the distribution of gains that are particular to this experiment. Single saccades (saccades not followed by any corrective saccades) are reported to be numerous in antisaccade experiments (Hallett, 1978; Hallett and Adams, 1980). They have been interpreted as representing trials in which the corrective saccades have been ‘lost’ due to either the lack of post-saccadic visual error signals, or due to the excessive delay of the corrective so that they are lost from the data collection period. A greater than average percentage of single saccades was found in four out of the five subjects in this experiment. These saccades have a gain of 1.0 (G = 1.0) by default due to our method of calculating gain. Caution must be taken not to assume that a gain of 1.0 necessarily indicates that a saccade is exactly on target.

<table>
<thead>
<tr>
<th>Subject</th>
<th>%Hypo G&lt;1</th>
<th>%Hyper G&gt;1</th>
<th>%Single G=1</th>
<th>%Hypo G&lt;1</th>
<th>%Hyper G&gt;1</th>
<th>%Single G=1</th>
<th>Amp(°) G=1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>95.8</td>
<td>4.2</td>
<td>-</td>
<td>64.9</td>
<td>4.7</td>
<td>30.4</td>
<td>8.03</td>
</tr>
<tr>
<td>2</td>
<td>72.0</td>
<td>16.0</td>
<td>12.0</td>
<td>33.1</td>
<td>26.7</td>
<td>40.1</td>
<td>8.27</td>
</tr>
<tr>
<td>3</td>
<td>66.7</td>
<td>16.7</td>
<td>16.7</td>
<td>75.5</td>
<td>4.6</td>
<td>19.9</td>
<td>4.64</td>
</tr>
<tr>
<td>4</td>
<td>80.0</td>
<td>8.0</td>
<td>12.0</td>
<td>56.8</td>
<td>6.3</td>
<td>36.8</td>
<td>11.45</td>
</tr>
<tr>
<td>5</td>
<td>87.5</td>
<td>12.5</td>
<td>-</td>
<td>73.0</td>
<td>20.0</td>
<td>7.0</td>
<td>9.00</td>
</tr>
<tr>
<td>Average</td>
<td>80.4</td>
<td>11.5</td>
<td>8.2</td>
<td>60.7</td>
<td>12.5</td>
<td>26.8</td>
<td>8.28</td>
</tr>
</tbody>
</table>

Table 4.2. The percentage of hypometric (Hypo), hypermetric (Hyper) and single saccades made, comparing prosaccades and antisaccades. The numbers cannot be statistically compared due to the different number of trials made in each phase but can be used to make qualitative comparisons between the relative amounts of each type of saccade made. The average amplitude (Amp) of a single saccade in an antisaccade trial is shown. G = gain.
All subjects except Subject 2 made a majority of hypometric saccades in the antisaccade trials (see Table 4.2). Subjects 2 and 5 were notable in that they made a large number (26.7 and 20.0% respectively) of hypermetric antisaccades. In Subject 5 these hypermetric saccades appear to represent the tailing off of the top end of the gain distribution, while in Subject 2 they form a peak which appears to be distinct from the lower distribution of gains. See Figure 4.6 (overleaf).

Not only did antisaccades have low gain with respect to the final eye position (internal visual goal), but the external visual goal (10° to the left or right in the context of this experiment) was also generally underestimated by the final eye position. The average amplitude of saccades not followed by any correctives was 8.28°. The underestimation of the visual goal was particularly pronounced in Subject 3. This was noted during the original recording session. Primary saccades not followed by any corrective in this subject had an average amplitude of only 4.64°. This is in contrast to primary saccades not followed by any correctives in the initial prosaccadic phase of the experiment which had a mean amplitude of 9.65°. The low mean amplitude value in Subject 3 was similar for antisaccades both to the left and right (left 4.53°, right 4.71°). This suggests that movement of the head with respect to the central target, or the sensors with respect to the eyes, is not to blame for this low amplitude. Subject 4 was the only subject to overestimate on average the final eye position with primary saccades that were not followed by any correctives (11.45°). The poor estimation of the visual goal even after any corrective saccades can also be observed in the eye movement traces in Figures 4.3 and 4.4. Secondary saccades are believed to be corrective, in the sense of making up for some estimation of post-primary saccade error, because primary saccades followed by a backwards corrective had a greater mean amplitude (9.508°) than the mean of single saccade trials (8.28°) and those followed by an onwards corrective (6.57°) i.e. less than the mean of single saccade trials.
Figure 4.6. Gain distribution histograms for all subjects separately, and all subjects together (bottom right hand graph). Gain is represented along the x-axis, and the number of saccades on the y-axis.
4.3.4 Latency characteristics

The mean latencies of primary and secondary prosaccades were both within the normal ranges that have been reported for reflexive saccades and their correctives to visual targets (180-220msec for primary saccades and 120-160msec for secondary, Becker, 1989).

See Table 4.3.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Prosaccades 1°</th>
<th>2°</th>
<th>Correct Antisaccades 1°</th>
<th>2°</th>
<th>Erratic Prosaccades 1°</th>
<th>2°</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>171.04</td>
<td>93.38</td>
<td>249.84</td>
<td>122.12</td>
<td>199.05</td>
<td>108.48</td>
</tr>
<tr>
<td>2</td>
<td>175.36</td>
<td>167.41</td>
<td>228.22</td>
<td>216.77</td>
<td>204.11</td>
<td>118.73</td>
</tr>
<tr>
<td>3</td>
<td>198.08</td>
<td>157.00</td>
<td>341.07</td>
<td>221.87</td>
<td>206.18</td>
<td>134.61</td>
</tr>
<tr>
<td>4</td>
<td>195.84</td>
<td>185.68</td>
<td>256.73</td>
<td>193.39</td>
<td>236.00</td>
<td>107.50</td>
</tr>
<tr>
<td>5</td>
<td>165.54</td>
<td>139.96</td>
<td>273.30</td>
<td>119.37</td>
<td>187.58</td>
<td>92.16</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>181.37</strong></td>
<td><strong>148.69</strong></td>
<td><strong>269.83</strong></td>
<td><strong>174.70</strong></td>
<td><strong>206.58</strong></td>
<td><strong>112.3</strong></td>
</tr>
</tbody>
</table>

Table 4.3. The latencies (msec) of primary (1°) and secondary (2°) prosaccades and antisaccades are shown. For antisaccades the primary and secondary latencies are shown for both trials in which the antisaccade was performed correctly (1° and 2° correct), and trials in which an erratic prosaccade was made first (1 and 2° incorrect); in this case the secondary saccade is a corrective prosaccade.

The primary latency of correct antisaccades was much longer than for prosaccades, as is expected from previous reports. This has been attributed to the extra time taken to program a saccade to a position where no visual stimulus occurs (Fischer and Weber, 1992). It may also originate from the time taken to cancel the prepared reflexive saccade and generate a new voluntary saccade instead. The primary latency of erratic prosaccades (206.58msec) is less than of correct antisaccades (269.83msec), and within Becker’s (1989) range for normal reflexive saccades (180-220msec), though not as low as average for the normal prosaccades amongst these subjects (181.37msec). It is interesting that the secondary saccades of correct antisaccades have a longer intersaccadic interval (ISI) than the secondary saccades of normal prosaccades. At 174.70 msec they are within the primary reflexive latency range. According
to the proposals of Becker and Jürgens (1979) and Becker and Fuchs (1969) this long latency
ISI suggests that this secondary saccade is not pre-programmed with the primary saccade.
The secondary saccade after an erratic prosaccade, i.e. a corrective antisaccade, has a low ISI,
slightly lower than the range quoted for normal ISI. These low ISI saccades are believed to
reflect the parallel generation of a corrective antisaccade with the erratic prosaccade (Becker
and Fuchs, 1969).

4.4 Discussion

Antisaccades in this study are found to have mainly low gain primary saccades with a
large standard deviation of the mean. This finding is interpreted to be an adaptive strategy in
the context of the SFM hypothesis (Harris, 1995). In contrast to the overall mean low gain,
some subjects were also found to show large numbers of high gain (hypermetric) saccades,
and all subjects showed significant amounts of primary saccades with no correctives which
nominally have a gain of 1.0 in our data. Such saccades have been interpreted previously in
the context of the generation and triggering of corrective saccades according to the theories
of Becker and Fuchs (1969) and Becker and Jürgens (1979). The increased number of
hypermetric saccades cannot be readily explained.

4.4.1 Error Rate

The error rate of antisaccades showed great variation between subjects, with a range
of 3.1-39.2% over the 200 trials in our study. Large error rates (30-80%) have been reported
at the beginning of a recording session (within the first 100 trials), with a reduction to 5-7%
later in the session (Hallett, 1978). The error rates for our subjects remained approximately
the same in the second 100 trials as in the first 100 trials. Only Subject 1 showed a large
difference, and this was not an improvement in performance as reported by Hallett (1978).
This subject made 12.6% errors in the first 100 trials and 30.1% in the second 100 trials. Thus it appears that this group of five subjects contained three subjects who were relatively poor at performing the antisaccade task relative to the three subjects reported in Hallett (1978) paper. It has been reported that subjects who make a large number of short latency ‘express saccades’ are unable to perform the antisaccade task well (Biscaldi et al., 1996). This explanation applied to none of the three subjects who made a high percentage of errors in our antisaccade paradigm. An interesting point that has recently been revealed by Mokler and Fischer (1999) is that approximately 50% of the time, the subject is unaware that they made an erratic prosaccade in advance of the corrective antisaccade. This can even occur in spite of temporary fixation of the target at the end of the erratic prosaccade before the corrective antisaccade is made. The larger the erratic prosaccade is and the later it is corrected, the more likely the subject is to recognise its occurrence.

4.4.2 Why low gain?

Low gain saccades were prominent in the data of all subjects. The standard deviation of the mean saccadic gain was large. Such a low gain and high spread has been reported previously (Hallett, 1978; Hallett and Adams, 1980). In the data of Hallett (1978), the error at the end of the primary saccade from Subject H (Figure 4, p1283) can be seen to be approximately 3° short of the real goal, while the final eye position after corrective saccades is still 2° short of the goal. It is difficult however to quantify these figures into a measure of gain as the angular errors presented by Hallett are made in relation to different target eccentricities, and thus total eye movements of different sizes. It is again relevant to note that in spite of the large standard deviation of the gain, there is relatively little overshoot overall and a strong bias to undershoot. To clarify this point Figure 4.7 shows the gain distribution for prosaccades and antisaccades again, side by side, on the same gain scale, for comparison.
The large peak at 1.0 in the gain distribution of antisaccades has been discussed previously and should be ignored for the sake of the point being made. Note the similarity of these figures to the hypothetical gain distributions shown in Figure 1.4 on page 32.

![Prosaccades and Antisaccades Gain Distribution](image)

**Figure 4.7.** To show the gain distributions of prosaccades and antisaccades. Note the low gains for the antisaccades. Despite the large standard deviation of antisaccade gain there are still relatively few hypermetric saccades. The broken lines represents the gain of 1.0

Few explanations of the source of the primary saccade inaccuracy have been proposed in relation to antisaccades. Hallett (1978) suggested that it may reflect the characteristics of the fast peripheral retinal acuity channels. The inaccuracy is explained due to a coarse approximation of the goal due to large receptive fields, combined with errors of translation of the neural image into the contralateral retinotopic hemifield. It is not clear however why a normal prosaccadic task should not also be subject to increased visual errors when the peripheral retinal channels are required. There is no such substantial increase in error as the target moves towards the periphery of the visual field. No explanation has been offered either for why the translation of the neural image from one hemisphere to the other should cause the systematic underestimate of the target location.

Fatigue may be predicted to affect gain over long periods of saccadic trials. However, we noticed no systematic changes in gain in any subject over the course of this experiment and we have shown that there is no significant change in gain over the course of 300 prosaccadic trials to one target eccentricity (See Section 6.3.1). Furthermore, Hallett (1978)
reported that even after 1000 antisaccade trials with rich feedback there is no reduction in the angular errors of antisaccades. The only noticeable effect of training was a decrease in the number of error trials.

Another explanation for the low gain may lie in the similarity of this antisaccade task to making a saccade to a remembered target. Saccades to remembered targets have been shown to have decreased gains in monkeys (White et al., 1994) and humans (Bracewell et al., 1990). The target eccentricity in this experiment was consistent, enabling the subject to potentially build up a memory of the target position in each field, thus there may have been an element of interaction between the antisaccade task and making a saccade to a remembered target in our paradigm. However, the degree of undershoot in this antisaccade task was still far greater than that reported for remembered saccades.

The SFM hypothesis (Harris, 1995) predicts that when the standard deviation of the error is large, the optimal gain decreases. The finding of a low mean antisaccade gain in association with a large standard deviation in these antisaccade trials supports this hypothesis. The interpretation is the same as that presented in the context of low gain saccades in hemianopic children in the previous chapter. If there were an increased standard deviation with no concurrent reduction in gain, this would lead to a greater number of overshooting saccades. Given the same amplitude of error, overshooting saccades result in an increase in flight-time relative to undershooting saccades, over the sequence of saccades produced to reach the visual goal. This increase in flight-time represents time of lost, or at least, degraded, vision and is interpreted as an increase in ‘cost’ by the SFM hypothesis. In order to reduce the cost of saccadic sequences, the mean gain is predicted to be reduced in order to lower the number of overshooting saccades. Overshooting saccades are not predicted to be totally eliminated though according to the SFM hypothesis. This would require the mean gain to be greatly reduced and would cause the cost of a saccadic sequence to rise again.
due to the high number of saccades that would be required to fixate the target. As explained in the introduction (Section 1.5.3) the generation of each saccade in a sequence has a constant ($\alpha$) cost associated with it that originates from the intercept value of the main sequence for duration.

It is important to note that in this investigation the gain of saccades was quantified with respect to the total saccadic eye movement component within each trial (component gain, see Section 1.4.2). In the antisaccade task, this visual goal is an internally generated concept, and the final eye position is assumed to coincide with this visual goal. The gain of saccades with respect to the external visual goal described by a position equal and opposite to the visual stimulus (i.e. always 10° from the centre) was not systematically analysed, although there is clear evidence that the subjective visual goal did not coincide with the actual visual goal. The final eye position was noted in many subjects not to be at exactly 10°. There were some very large amplitude saccades, such as that shown in Figure 4.4A, in which the actual goal was grossly overshot, although the primary saccade was low gain with respect to the final eye position. On the other hand, the actual visual goal was often undershot too, see for example Figures 4.4C and D. One subject in particular made very low amplitude antisaccades throughout the experiment as discussed in Section 4.3.3 (page 121).

4.4.3 Hypermetric antisaccades

The mean percentage of saccades that were hypermetric (with respect to the internal visual goal) remained approximately constant from the prosaccadic phase (11.48%) to the antisaccadic phase (12.5%). This suggests that overshotting on approximately 12% of trials in this experiment may be optimal in order to minimise saccadic flight-time. This figure would be expected to change depending on the magnitude of the overshoot.
Subjects 2 and 5 showed relatively large percentages of hypermetric saccades in the antisaccade task (see Table 4.2). This pattern was absent in the other three subjects. In Subject 5 these hypermetric saccades appear to represent the upper end of a widely spread gain distribution (see Figure 4.5). In Subject 2 however, who made the greatest percentage, these hypermetric saccades may represent a separate peak. Hypermetria is uncommon in both reflexive and voluntary prosaccades (Becker, 1989). It can be induced to small target eccentricities in the context of the range effect (Kapoula, 1985), and is more common for centripetal saccades (Becker, 1989) but otherwise hypermetria is generally associated with disorders of the cerebellum (Selhorst et al., 1976; Leigh and Zee, 1991). Given that none of our subjects had known or manifest cerebellar deficits, the reason for the increased amount of antisaccadic overshoot, combined with the overall decrease in mean gain due to a large amount of low gain antisaccades, is unknown. The presence of these hypermetric saccades cannot be explained by the SFM hypothesis. Neither subject reported being conscious of using this as an adaptive strategy. Subject 2 was the only subject who was experienced in eye movement research, though he was only aware that the error rate was being assessed, not the metrics of his saccades. The hypermetric saccades did not seem to predominate at any stage of the experiment although they were noted to occur often in consecutive trials or soon after one another, interspersed by long gaps, rather than being randomly intermingled with the other types of saccades. This increase in hypermetric saccades can be seen in the data of previous studies (Hallett, 1978) and has been remarked upon (Hallett and Adams, 1980) but no explanation has been offered.

4.4.5 Corrective saccades

Another unusual feature of the antisaccadic task was that most subjects made a high percentage of saccades which were not followed by a corrective saccade. Subject 2 made the
highest percentage of such saccades (40.1%). Subject 5 made relatively few (7%). Both the low gain antisaccades, and such saccades without any corrective can be interpreted according to the hypotheses of Becker and Fuchs (1969), and Becker and Jürgens (1979). They proposed that corrective saccades may be generated under three modes: 1) a retinal mode if the predicted error is small in which the extra-retinal error signal is ignored and the corrective saccade is generated in response to post-saccadic retinal feedback and thus has a relatively long ISI, in the range of a normal reaction time (180-220msec); 2) a mixed mode in which the corrective saccade is prepared awaiting post-saccadic retinal confirmation and has a regular ISI (120-160msec); 3) an extra-retinal mode in which large correctives are produced in response to primary saccades with a large predicted error without waiting for post-saccadic retinal confirmation. These correctives have a relatively short ISI (10-100msec). Although Becker and Jürgens (1979) expressed these predictions based on the absolute magnitude of the error, the same predictions may hold with respect to the magnitude of gain. It would seem unlikely, if the ISI is dependent on predicted error, that the size of the predicted error involved in each mode of corrective generation would remain constant even if the size of the target eccentricity varied substantially. For example, a 5° error is large relative to a 10° target eccentricity, though may be normal in the context of a 40° target. A larger amount of error is generally predicted for larger target eccentricities (Becker, 1989).

If the saccadic system produced the low gain saccades to the antisaccade visual goal by mistake, rather than by design as we predict, then one might expect the system to recognise that an excessively low gain saccade had been elicited and generate a corrective saccade to follow with a short ISI (in the extra-retinal mode of Becker and Jürgens (1979)). This did not appear to be the case. Although all of the subjects in this study did produce secondary saccades with latencies as low as approximately 20msec (suggesting generation in the extra-retinal mode of Becker and Jürgens, 1979), the average ISI of a secondary saccade
in our antisaccade paradigm was 174.70 msec. This is relatively long for an ISI, and is very close to the normal reaction time of a prosaccade. This further points to the proposal that the low gain of antisaccades is an adaptive strategy, not simply a targeting error.

The relatively long ISIs of secondary saccades indicates that these corrective saccades are generated with dependence on retinal feedback. However, in the antisaccade paradigm of course, there is no retinal feedback in the traditional sense. Retinal feedback is available from the target which now lies in the periphery of the contralateral visual hemifield. Data from target blanking experiments suggest that if there is no retinal feedback available, the two proposed modes of corrective saccade triggering that depend on retinal feedback are substantially affected (Becker and Fuchs, 1969); corrective saccades generated in the retinal mode (that depends absolutely on post-saccadic retinal feedback for the generation of a corrective) are lost while saccades generated in the mixed mode (in which the corrective is pre-programmed awaiting post-saccadic retinal confirmation) are greatly delayed.

This loss of corrective saccades from the retinal mode has been proposed to explain the relatively large number of saccades in the antisaccade paradigm that do not have any corrective saccades (Hallett, 1978). The retinal feedback in this mode may be rejected because it conveys no useful positional information.

4.5 Conclusion

The antisaccade task produces low gain saccades with a large standard deviation. We propose that this low gain represents an adaptive strategy of the saccadic system in the face of a large standard deviation of the error. This finding supports the predictions of the SFM hypothesis that when the standard deviation of the error is large, the optimal gain decreases.

A similar association was reported in the previous chapter in the context of low gain saccades made by hemianopic children into their blind hemifield. The antisaccade task
presents the oculomotor system with a similar problem to that encountered in hemianopia. In both situations there is a lack of direct visual input to guide the eye to the precise location within the hemifield in which the saccade is to be made. In both situations this leads to an increase in the standard deviation of the error.

Subjects were found to show substantial individual variation in their antisaccade errors rates and the relative amounts of hypermetric, hypometric and single saccades made. The large amount of hypermetric saccades made by one subject cannot be interpreted according to the SFM hypothesis.
Chapter 5. Saccadic Gain and the Main Sequence

5.1 Introduction

The saccadic flight-time minimisation hypothesis (Harris, 1995) proposes that the gain of saccades depends on both the standard deviation of the error, and the main sequence for duration of saccades made by an individual. In the previous two chapters evidence was presented from both normal and abnormal subjects to support the first of these two predictions. In this chapter, the second prediction regarding the influence of the main sequence for duration is investigated. Additionally, an alternative theory to explain the undershoot bias is considered. This theory is known as the hemispheric facilitation hypothesis and was originally proposed by Robinson (1973). The undershoot bias and the theories that have been proposed to account for it have been discussed in the Introduction but will be reviewed here due to their direct relevance to the experiment in this chapter.

5.1.1. The Undershoot Bias

Reflexive saccades to single peripheral targets are generally found to fall slightly short of the target, requiring a small secondary corrective saccade to make up for this undershoot and foveate the target. This phenomenon is known as the undershoot bias and has long been remarked as a feature of saccades (Becker, 1972; Henson, 1978). The bias is generally reported to be in the order of 10%. The undershoot bias is known to be a deliberate strategy of the saccadic system. Evidence comes from the finding that if the primary saccade is artificially induced to land on target by shifting the saccadic target back slightly intrasaccadically, the saccadic system adapts to lower the amplitude (gain) of the primary saccade to re-establish undershoot over the course of some tens of trials (Henson, 1978). This suggests that the minimisation of retinal error is not the aim of the primary saccade.
5. Main Sequence Correlations

5.1.2 Robinson’s hemispheric facilitation theory

One of the first theories to account for the undershoot bias was made by Robinson (1973). This was proposed in relation to the findings of Young et al. (1968) that the latency of an onwards (in the same direction as the primary saccade) corrective saccade was half as much as the latency of a backwards (in the opposite direction to the primary saccade) corrective saccade. Robinson (1973) suggested the possibility of a time penalty associated with switching saccade control between hemispheres, as would be required when an overshooting primary saccade is followed by a corrective in the opposite direction. When a visual target crosses the midline, its representation in the visual cortex crosses from one hemisphere to the other. If there were a time penalty associated with the hemispheric transfer of the image and generation of the appropriate eye movement then by keeping the representation of the visual target in the same hemisphere during refixational eye movements this penalty could be avoided.

Robinson’s (1973) spatial-temporal model of the saccadic system attributed latency differences incurred by switching hemisphere to the facilitation and disfacilitation of both cortical visual-processing and non-visual-processing areas of their counterparts in the opposite hemisphere. Connections between functionally congruent areas of the two hemispheres lends support to this possibility. The concepts of facilitation and disfacilitation are not unique to saccade generation but are also now thought to be important in many of the processes surrounding control of attention and goal directed motor activity (Hughes and Zimba, 1985).

Experimental data has variously both supported and rejected the hemispheric facilitation theory. Significant latency differences between onwards and backwards corrective saccades have been reported by Henson (1978) and Deubel et al. (1982); though not by Weber and Daroff (1972), Becker (1972) or Kapoula and Robinson (1986). In both experiments in which differences were found, the gain of saccades was artificially manipulated in order to induce more overshoots. This was done by altering visual
feedback through a contact-lens-spectacle combination (Henson, 1978), or by double target steps (Deubel et al., 1982). It may be that using such artificial techniques produces abnormal latency responses from the saccadic system so that the differences reported do not reflect the natural behaviour of the system. A further potential explanation for the latency differences reported is associated with two well-known characteristics of saccades: firstly, that the amplitude of undershooting errors is generally greater than that of overshooting errors (Weber and Daroff, 1972; Kapoula and Robinson, 1986) and second, that the smaller the magnitude of the corrective error, the greater the intersaccadic interval (Becker, 1972; Henson, 1978; Kapoula and Robinson, 1986). Henson (1978) could not rule out amplitude differences as determining the significant differences found between the latencies. Deubel et al. (1982) however did take the amplitude of the corrective saccade into account, though not on an individually-matched basis, and still reported a significant difference between the latencies of onwards and backwards corrective saccades. He thus concluded that his data were consistent with Robinson’s theory.

The consideration of the amplitude of the corrective saccade is clearly an important issue for the reliable analysis of latency differences. Of the researchers who reported no significant differences between onwards and backward corrective latencies, neither Weber and Daroff (1972) nor Becker (1972) state whether amplitude was taken into account in their calculations. Kapoula and Robinson (1986) did take amplitude into account, but only by limiting the size of the saccades that could be included in the calculation in order to eliminate the variability that is seen for saccades <0.4°, not by individually matching saccades.

We propose that it is necessary to match onwards and backwards saccades on an individual basis, within-subjects and within-sessions in order to make a truly valid comparison of the relative latencies. We present the results of such a comparison in Section 5.4.1 of this chapter.
5.1.3 Pre-programming theories

Robinson’s (1973) theory was based on the principal that only one saccade can be prepared and executed at a time, in series, because all goal directed-saccades are generated in direct relation to the target’s retinal eccentricity. Thus the time delay between each saccade would be equal to at least one reaction time with the system having a ‘refractory period’ during which no saccade could be generated. However, Becker and Fuchs (1969) had previously put forward an alternative hypothesis for the latency differences reported by Young et al. (1968), based on the idea of eye movement responses being pre-packaged as two saccades. Their model still predicted differences in corrective saccade latencies, but dependent on whether the error was correctly predicted or not rather than simply the direction of the error. They proposed that if the error at the end of the primary saccade was correctly predicted then the secondary saccade, which had been partly pre-programmed with the original primary saccade, could be executed, after a brief visual-sampling period of 70msec to confirm the error, with a latency shorter than the standard reaction time. Predicted error was estimated to be an undershoot of approximately 10% on the basis of previous reports. If however error was not correctly predicted, the pre-programmed corrective saccade would be cancelled and a new saccade generated under visual guidance. This would result in a much longer latency for this backwards corrective saccade. Such a long latency response would also be predicted for an onward saccade if it was not correctly predicted, eg the undershoot was larger than 10%.

Becker and Jürgens (1979) elaborated on this earlier theory proposing that the post-saccadic predicted error is estimated on a trial-by-trial basis by comparing the memorised target position to a copy of the saccadic motor command, rather than assuming a standard error. The existence of such an extra-retinal feedback pathway has been suggested by the work of Becker (1972), Barnes and Gresty (1973) and Shebilske (1976). The comparison of these signals would enable the preparation in parallel of the
appropriate corrective, only requiring confirmation via the post-saccadic retinal signal before being executed. The direction of this corrective saccade would be predetermined due to this decision process being localised to two competing lateralised channels. The preparation and execution of the corrective would however be ultimately dependent on the magnitude of the predicted error, giving rise to 3 modes of error correction: a retinal mode, generating the correction via post-saccadic retinal feedback if the predicted error is very small (<2-3°); a mixed mode in which the corrective saccade is prepared, awaiting post-saccadic retinal confirmation, if the predicted error is in an intermediate range (3-10°); an extra-retinal mode where a corrective saccade is triggered straight after the primary saccade, not waiting for post-saccadic retinal confirmation, if the predicted error is relatively large (>10-15°). This trimodal theory, dependent on the size of the predicted corrective saccade, rather than its direction, provides an explanation for the substantial increase in latency as the corrective saccade amplitude becomes very small (see Figure 5.2D).

The pre-programmed nature of corrective saccades (secondary saccades at least) is supported by further evidence. The foveola subtends less than 1° at the central retina of the human (Cohen, 1992). Thus one would expect that an eye movement that placed the target within this foveal area would be deemed ‘on target’. However, Lemij and Collewijn (1989) reported that even if the primary saccade lands within 0.1° of the target, a corrective saccade will still occur 50% of the time. Furthermore, corrective saccades still occur after the primary saccade even if the target stimulus is extinguished before the primary saccade has finished, and if saccades are made in the dark (Becker and Fuchs, 1969). Both of these lines of evidence suggest that secondary saccades are not dependent purely on retinal error for their generation.

The theories of Becker and Fuchs (1969) and Becker and Jürgens (1979) do not explicitly provide explanations for the undershoot bias, but their theories can be
understood to interpret the systematic undershoot as a means of providing the saccadic system with a level of predictability in the face of inevitable systemic random variation. This could then enable the total time to foveate the target to be minimised by pre-programming the corrective saccade.

5.1.4 The flight-time minimisation hypothesis

In contrast to the previous theories outlined above in which the undershoot bias of the saccadic system functions to optimise saccadic performance by minimising the total time taken to foveate the target, the saccadic flight-time minimisation (SFM) hypothesis (Harris, 1995) proposes that undershooting is an economical strategy for maximising the time of clear vision by minimising saccadic flight-time.

There is little effective vision during saccades, due to a combination of the speed with which the visual scene is passing across the retina, greatly reducing contrast, and a phenomenon described as ‘saccadic omission’ (Matin, 1974; Campbell and Wurtz, 1978) in which perception during saccadic eye movements, albeit of reduced contrast, is masked by the effect of a clear image before and after the saccade. Since vision is interrupted hundreds of times each minute by saccades with durations of up to 100msec, it would logically seem desirable that this time of lost vision be kept to a minimum.

Harris (1995) showed in computer simulations that the undershoot bias is intimately tied in with saccadic error, ie the amount of spread in the end points for saccadic movements, for targets of a particular eccentricity if flight-time is minimised. Using the saccadic data of Collewijn et al. (1988) it was shown that when the standard deviation of saccadic error is about 10% of target eccentricity, the optimal gain of primary saccades is about 0.93 for centrifugal saccades, ie there is a bias to undershoot. If the standard deviation of the error is much greater than 10%, as for example in the case of infants (Harris et al., 1993), the optimal gain was found to be 0.6 which also fits with
observations that infants produce multiple hypometric saccades (i.e., low gain saccades) to visual targets (Aslin and Salapatek, 1975; Harris et al., 1993).

The magnitude of the undershoot bias is not only dependent on the standard deviation of the error but also the main sequence for duration. The main sequence for duration is a stereotypical relationship that is observed between the amplitude and duration of saccades. It can be quantified by the slope ($\beta$) and intercept ($\alpha$) of the linear regression (see Section 1.5.3, Figure 1.2). As discussed in Section 1.5.3, the value $\alpha$ represents the cost of making each saccade, irrelevant of the size of this saccade. The main sequence for duration varies, not only between subjects, but also within subjects depending on the particular experimental protocol and type of saccade being elicited. For example, Collewijn et al. (1988) have shown that the main sequence varies between centrifugal and centripetal saccades. Harris (1995) reported a simulated optimal gain value of 0.97 for centripetal saccades again using Collewijn’s data (in contrast to a gain of 0.93 for centrifugal saccades). This agrees with reports from Becker (1989) and with the findings of Kapoula and Robinson (1986) that centripetal saccades to stationary targets show less undershoot than centrifugal saccades.

The most important prediction of the SFM hypothesis with respect to this chapter is that the more costly it is to make a corrective saccade (i.e., the greater the value of $\alpha$) the more restricted the range of saccadic gains is expected to be (i.e., less divergence from a gain of 1.0). This is because the more the gain diverges from unity, the more corrective saccades will be made, (assuming that no correctives are made when gain = 1.0).

Thus, in order to minimise saccadic flight time the optimal gain of primary saccades appears to be closely linked not only to the standard deviation of the error, but also to the amplitude-duration relationship of the saccades.
5.1.5 Aims

In this experiment we set out to investigate both Robinson’s hemispheric facilitation theory and the saccadic flight-time minimisation theory. We propose to use robust comparison techniques to determine any latency differences between onwards and backwards corrective saccades in order to address Robinson’s theory.

If saccadic undershoot functions to prevent the extra time associated with generating a backward corrective saccade after an overshooting primary, we would expect the latency of onward corrective saccades to be consistently less than the latency of backwards correctives within subjects. If saccadic undershoot were functioning to minimise saccadic flight-time we would expect to find correlations in predictable directions between the main sequence for duration and the gain of saccades, as predicted by the SFM hypothesis.

One hundred centrifugal reflexive saccades to a range of target eccentricities were collected from each of 20 subjects. The data collected enabled both the between and within subject relationships to be investigated. The presentation of a range of target eccentricities not only enables the main sequence for duration for each subject to be determined, but also induces a phenomenon known as the ‘range effect’ (see Section 1.4.4) and naturally elicits a substantial number of overshooting saccades to the smaller targets which elicit backwards corrective saccades. The general parameters of the saccadic data collected are analysed first, in order to check the reliability of the data against previously reported data.
5.2 Methodology

5.2.1 Subjects

Twenty normal, healthy subjects were recorded (7 females, 13 males). Their ages ranged between 16 and 45 (mean = 29.05 years). None had a history of squint or of visual problems, though some had refractive errors. These subjects were recorded in their usual refractive state (i.e., wearing glasses or contact lenses) to avoid any oculomotor adaptations taking place during the course of the experiment. Two out of the 20 subjects were experienced in oculomotor research.

5.2.2 Experimental Set-up

Binocular horizontal eye movements were recorded with an infra-red eye tracker (Skalar). Subjects sat in a room with low lighting levels (luminance 2cd/m²) in front of a large blank white screen at a distance of 89cms onto which the red target laser spot was projected. Subjects rested their chin on a chin rest and had their head stabilised with ‘ear muffs’ to minimise head movements.

A one hundred trial paradigm was used consisting of 10 peripheral positions along the horizontal meridian (5 different eccentricities to the left and right of the central target location) presented in a pseudo-random order. The eccentricities presented were (+/-) 2.5, 5, 10, 15, 20 degrees. Each trial started with the target spot in the centre and after a random time delay (1100-2500msec) moved instantaneously to a peripheral position. The target spot remained in this position for 1500msec before returning to the centre for the start of the next trial.

Only centrifugal saccades were recorded and analysed. Centripetal and centrifugal saccades show marked asymmetries in terms of velocity (Collewijn et al., 1988) and accuracy (Kapoula and Robinson, 1986). These asymmetries are believed to result from not only neural and mechanical inhomogeneities but also higher level processes resulting
from prior knowledge of the end position of the centripetally directed saccades in such experiments. Thus, in order to reduce the levels of analysis and collect as many saccades of a specified type as possible, only centrifugal saccades were recorded.

Before the experiment began each subject performed a calibration procedure. Ten target eccentricities were presented in positional order along the horizontal meridian. Each trial was examined on-line by the experimenter for a 500msec period of stable fixation and then either accepted, or rejected and repeated. A linear regression was produced on-line and again either accepted or, if necessary, the apparatus was re-adjusted and the calibration procedure repeated until an acceptable linear relationship between eye position and target position was obtained.

Subjects were instructed to keep their eye on the red target spot all the time and follow it with their eyes only when it moved. Subject’s heads were restrained by earmuffs, but the importance of keeping their head still was stressed nevertheless.

The data were scored and analysed as described in the methods section.

5.2.3 Characterising the Range Effect

No investigations have previously attempted to quantify the range effect. The range effect was quantified in this experiment by applying a linear regression over the relationship of the mean gain to each of the 5 different target eccentricities. This gave a simple two number summary (the slope and intercept of the linear regression) of the strength and level of the range effect for each subject, rather than having to consider each eccentricity separately.

The range effect represented by mean gain plotted against each target eccentricity would be predicted to have a negative slope and an intercept value of greater than 1. This is due to the overshot of the smallest target eccentricities, and the undershoot of the larger eccentricities, as has been reported previously (Kapoula, 1985).
However, as will be discussed in Section 5.3, many of our subjects had one, or more, points which diverged from the expected pattern of the range effect. The divergent points were generally either to target eccentricities of $2.5^\circ$, $20^\circ$ or both. Thus linearity, or at least a consistent trend, was not necessarily present for all subjects across all 5 eccentricities, but more likely to be present across the 3 central eccentricities ($5^\circ$, $10^\circ$ and $15^\circ$). This pattern was also observed in the data of Kapoula and Robinson (1986). As such, an alternative measure of the range effect was also calculated by linear regression across the mean gains at each of these three eccentricities alone in order to avoid the influence of the unpredicted results at the extreme eccentricities. This alternative will be called the ‘limited range effect’ in contrast to the ‘full range effect’ to distinguish the two means of quantifying the range effect.

5.2.4 Characterising the Main Sequence

The main sequence can be quantified by calculating the slope and intercept of a linear regression fitted over a restricted range of the duration-amplitude relationship (see Figure 1.2 page 31). Two alternative means of defining the range over which the linear regression was fitted were used. One range was defined by amplitude, the other by duration. A range defined by amplitude has traditionally been used by other researchers (see Becker, 1989). The threshold is usually taken at $5^\circ$, however, we estimated that linearity began lower than this. The slope and intercept values in our subjects were almost identical whether using a $4^\circ$ or $5^\circ$ threshold. Thus we used a threshold of $4^\circ$ for the linear regression calculations in order that a greater number of saccades would be included in this calculation. Remarkably slow saccades, with durations off the main sequence, were a feature of some subjects (for example, see the main sequence for duration plots for subject CH on page 74 of the methodology chapter). Such saccades could artificially increase the slope and lower the intercept of the linear regression of the main sequence. Thus, an
alternative a range defined by saccadic duration was used. The duration range for applying the linear regression was taken as those saccades that had durations of between 40 and 75 msec. This removed most saccades with abnormally long durations. As the same range had to be applied to all subjects, the lower threshold was chosen to represent the approximately point at which the subject with the slowest saccades entered the linear part of their main sequence. This threshold of 40 msec approximately corresponded to a saccade of amplitude 4°, and so this lower threshold was similar for both methods.

A further parameter for characterising the main sequence, mentioned in Section 1.5.3, is gamma (γ). This represents the trade-off between the effects of the slope and intercept and is obtained from the ratio of the slope and intercept of the regression function. This was calculated for both types of linear regression.

The results and discussion will be presented in three sections. The first section (Section 5.3) presents the general parameters of the data and the characteristics of the main sequence for duration and range effect in the context of previously reported data. The second section (Section 5.4) interprets the data in the context of Robinson's hemispheric facilitation theory. The final section (Section 5.5) deals with the flight time minimisation hypothesis.

5.3 General Parameters

5.3.1 Results

Latency

The mean latency of primary saccades for all our subjects was 177.03 msec. The data showed a positive skew (sk=0.833) and no evidence of bimodality. See Figure 5.1A. One subject showed remarkably low reaction times with a mean primary latency of 138.16 msec.
The mean intersaccadic interval (ISI) of all corrective saccades was 173.1 msec, with a strong rightward skew (sk=1.702). See Figure 5.1B. This skew is partly due to the fact that very small saccades have relatively long latencies, but also that some non-foveating saccades or random micro-saccades may occur very late in the data collection period. The ISI of secondary and tertiary saccades was 158.37 msec (See Figure 5.1C) and 212.88 msec respectively. There was a clear trend for the intersaccadic interval to increase with the saccade amplitude (See Figure 5.1D).

![Figure 5.1](image)

**Figure 5.1.** Figures A, B & C show the latency characteristics of primary saccades, all corrective saccades, and secondary saccades alone, respectively. Figure D shows the relationship between the amplitude of corrective saccades, and their latency. The data shown is for all subjects together.

There was a trend for saccadic latency to increase with increasing target eccentricity. The latency increased gradually at the lower target eccentricities (2.5°, 5°, 10°) and then more markedly between 10° and 15° (See Figure 5.2). This same general trend was observed in each subject individually, except for two subjects (Subjects 14 and 28) who both showed the opposite trend.
The Main Sequence for Duration

The main sequence for duration for all saccades collected in this experiment is shown below. Fitting a linear regression to all saccades with an amplitude of greater than 4° produces a slope value of 2.57 and an intercept value of 27.83.

Some subjects occasionally produced conspicuously long saccades, especially to the largest target eccentricities. The longest duration of saccade made by any subject was 131 msec for a saccade of amplitude 17.45°. This is almost double the 72.13msec that would be predicted from the linear regression function of the main sequence data. These long saccades showed a glissadic profile with a prolonged drift towards the final eye position. These did not necessarily occur towards the end of the recording session.

Some subjects showed a dissociation between abducting and adducting saccades in the same eye. Four subjects showed slightly faster adducting saccades, while 3 subjects
showed slightly slower adducting saccades. The other 13 subjects showed no clear differences.

**Peak Velocity Measures**

The main sequence for peak velocity for all saccades from all subjects showed the stereotypical relationship. See Figure 5.4A. Substantial between and within subject variability was noted, particularly at the higher eccentricities. The lowest maximum recorded in any subject was 411.75 °/sec and the highest 697 °/sec. This latter subject had markedly fast saccades with peak velocities of over 500°/sec for saccades of greater than 10°.

There was some dissociation between adducting and abducting saccades in the same eye, however, again this was not consistent between subjects. The ratio of peak velocity to mean velocity was 1.67. Figure 5.4B.

![Figure 5.4](image.png)

**Figure 5.4.** Scatterplots to show the main sequence for peak velocity (A) and the relationship between peak velocity and mean velocity (B).

**Gain and the Range Effect**

The overall gain to each of the 5 target eccentricities, for the three different ways of calculating gain outlined in the introduction are shown below in Figure 6. This ‘range effect’ is seen for each of the different types of gain, although it is displaced to lower values for the traditional gain relative to the component and net gains. The gain for 15°
saccades is lower than would be predicted for all types of gain, being less than the gain for 20° target eccentricities in two cases.

**Figure 5.5.** Mean gain at each target eccentricity for the three different ways of determining gain.

The range effect can be also be confirmed by observing the relative number of overshooting and undershooting saccades to each of the different target eccentricities. This is plotted below for each of the 3 types of gain. A greater number of overshooting saccades are seen to the smaller target eccentricities. The component gain has a significant number of saccades with no correctives (which therefore have a gain of 1.0).

**Figure 5.6.** To show the relative amounts of undershooting, overshooting and orthometric saccades.

The range effect, although clearly present for all types of gain when all subjects were considered together, was highly idiosyncratic. In 7 of our subjects the range effect was clear, while ambiguous or discontinuous in another 7, and apparently absent or even
inverted in the 6 remaining subjects. The three different means of determining the gain did not necessarily produce corresponding results. Traditional gain produced a much greater spread of values than either the component or net gain. The slope and intercept of the range effect for traditional gain did not correlate to the slope and intercept respectively of either the component gain or net gain measurements. However, there was a strong correlation of the range effect slopes ($r = 0.837$, $p < 0.001$) and intercepts ($r = 0.752$, $p < 0.001$) between component gain and net gain.

5.3.2 Discussion

The general parameters outlined below of the saccades made by the subjects in this experiment concur with previously reported ranges by other investigators. Thus we can be certain that we have a representative set of data with which to examine the two theories that propose to explain the undershoot bias.

Latency

The primary saccade latency we report (177.03msec) is relatively short compared to other unpredictable reflexive paradigms. It lies within the ‘fast regular saccade’ range of 140-180 msec as defined by Fischer et al. (1993). One of our subjects had an unusually short mean primary latency of 138.16msec which lies only just above the latency range that is normally attributed to ‘express saccades’ which are believed to be generated via a direct collicular pathway from the retina (see Cowey and Stoerig, 1991), rather than the cortical pathway known to be involved in the generation of normal reflexive saccades. Even if this subject was removed from the data set, the mean latency was still relatively low at 181.93 msec ($sd=41.01$, $n=1724$). Although there was a positive correlation between primary saccade latencies and secondary saccade latencies within subjects, this was not significant ($r=0.332$, $p = 0.153$).
Our finding that reaction times increase with target eccentricity agrees with the findings of White et al. (1962), Kapoula (1985) and Becker (1989). This finding has been attributed to both motor (Wyman and Steinman, 1973) and sensory (Doma and Hallett, 1988) processes.

**The Main Sequence for Duration**

The slope and intercept values for the main sequence for duration obtained from the data of all our 20 subjects together matches very closely that reported by Becker (1989) for a group of 26 subjects. We find a slope of 2.57msec/deg, and an intercept value of 27.83msec, while Becker (1989) reported a slope of 2.5msec/deg and an intercept ranging between 20 and 30msec. Collewijn et al. (1988) who differentiated between centripetal and centrifugal saccades, reported similar values for *centripetal* saccades to those we obtained for *centrifugal* saccades. Centrifugal saccades in their study had a steeper slope and lower intercept. These differences are possibly due to the fact that Collewijn et al. (1988) recorded voluntary saccades, self-paced to an auditory input, (from only 4 subjects). Voluntary saccades are known to be generated by at least partially different neural mechanisms (Erkelens and Hulleman, 1993) and thus may be expected to have different metrics, as has been reported for other types of non-reflexive saccades such as predictive saccades (Bronstein and Kennard, 1987).

The presence of conspicuously slow saccades is not unusual. Slow saccades have been reported when subjects become very fatigued (Bahill and Stark, 1975) especially if the saccades are large. They are not believed to result from extra-ocular muscle fatigue as the extra-ocular muscles are reported to be fatigue-resistant (Fuchs and Binder, 1983). They are more likely to result from mental fatigue (Schmidt et al., 1979). As our experiment only lasted approximately 7 minutes, and an effort was made to carry out the experiment in the morning so that subject would be relatively alert, is was unlikely that these conspicuously slow saccades resulted from physical fatigue. Furthermore, they did
not necessarily occur towards the end of the recording session, they came as isolated incidents. Each slow saccade came after and was followed by saccades of normal parameters, there was no gradual increase in duration. Thus it is more likely that they resulted from inattention or mental fatigue. This saccadic task was repetitive and boring and as such subjects may have easily have become inattentive. Bahill et al. (1981) reported that such slow saccades can be eliminated with constant encouragement to keep up the alertness of the subject. Our subjects were encouraged at regular intervals during the course of the experiment but nevertheless still produced some slow saccades.

The differences between the duration of abducting and adducting saccades in the left eye were not correlated to handedness, and for the fact that none of our subjects reported a squint or had had any surgery to their eye there is no obvious explanation apart from random differences, either of neural or muscular origin.

**Peak Velocity**

The variation in peak velocity observed is quite typical of the main sequence relationship between peak velocity and saccade amplitude, and has been reported previously (Schmidt et al., 1979; Jürgens et al., 1981). Variations between studies may be due in part to different recording and analysis techniques, although these differences do not appear to be systematic. The ‘normative database’ of Bahill et al. (1981) recorded using infra-red reflection technique reported much higher peak velocities than previously reported by others with the same technique (Schmidt et al., 1979; Boghen et al., 1974) or with other techniques: EOG, Becker (1989), Baloh et al. (1975); search coil, Collewijn et al. (1988).

One of our subjects had notably high saccadic velocities, even higher than those reported by Bahill et al. (1981). This is unlikely to be due to our recording equipment or analysis program since these were identical for all the other subjects with lower velocities, but rather an individual trait. Once again, in quantifying our data, we found very similar
results to those previously published. We found a ratio of peak velocity to mean velocity of 1.67. This is very close to the value, 1.64, reported by Becker (1989).

A dissociation between the peak velocity of adducting and abducting saccades has been previously reported, with abduction being faster than adduction (Collewijn et al., 1988). Similar distinctions were not characteristic of our subjects. There were clear differences in only 2 subjects and suggested differences in some others. These differences were however, not all in the same direction.

**Gain and the Range Effect**

Our finding of the high degree of inter-subject variation in the presence, size and level of the range effect has also been shown in the data of Kapoula and Robinson (1986). Although it is not discussed, it can be interpreted from their data that in 3 of their 5 subjects, there was a relatively linear decrease in gain across the 5°, 10° and 15° target eccentricities while the saccades to 20° target eccentricities had higher gains than would have been predicted from the rest of the data. See Figure 5.7. Looking at the mean gain (dashed line) for the 5 subjects in Kapoula and Robinson's (1986) data, the gain for 15° and 20° target eccentricities is almost the same. A similar pattern can be seen in Figure 5.5, the data from the 20 subjects in this experiment. The reason for this divergence from the predicted pattern of the range effect is unknown. It is unlikely to be an artefact of our recording or analysis techniques, as it is clearly not unique to our experiment; indeed Kapoula and Robinson (1986) who reported the same phenomenon used the search-coil technique which is not prone to the effects of non-linearity or drift. One explanation could be that the influence of the range effect begins to induce saccadic gains that are at odds with an acceptable level of undershoot judged on an individual saccade to saccade basis by the saccadic gain controller. This saccadic gain controller may impose a range of
acceptable gain values for each eccentricity and prevent the range effect from imposing a lower than acceptable value for any particular target eccentricity.

These data suggest that a linear regression may not be the most appropriate manner in which to quantify the range effect, at least over the full range of eccentricities presented in this experiment. However, a linear regression would still appear to be suitable over the limited range of eccentricities.

![Graph](image)

Figure 5.7. The gain of saccades with respect to target eccentricity. Adapted from the data of Kapoula and Robinson (1986).

5.4 Robinson’s hemispheric facilitation theory

Although overshooting saccades are generally rare, we were able to elicit a substantial number of backwards corrective saccades in this experiment by the use of the range effect. The amplitude and latency parameters for all of the secondary and tertiary, onwards and backwards corrective saccades are presented in Table 5.1.

5.4.1 Results

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Onwards</th>
<th>Backwards</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>ISI (msec)</td>
<td>amp (degs)</td>
</tr>
<tr>
<td>Secondary</td>
<td>1423</td>
<td>158.47</td>
<td>1.14</td>
</tr>
<tr>
<td>Tertiary</td>
<td>488</td>
<td>212.35</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Table 5.1 to show the mean intersaccadic intervals (ISI) and amplitudes (amp) for onwards and backwards corrective saccades. The data are shown for secondary and tertiary corrective saccades, and both combined (all).
It can be seen in Figure 5.8 that there is a significant difference between the intersaccadic interval of onwards and backwards corrective saccades for both secondary and tertiary saccades. A significant difference is also present for the mean amplitude of onwards and backwards secondary correctives, but not for tertiary correctives.

Robinson’s theory proposes that there would be within-subject differences between the latencies of onwards and backwards corrective saccades. Thus it was necessary to find corrective saccades matched for both amplitude and saccade number (secondary or tertiary) within each subject. This matching had to be done by hand. The matching criteria used were that each pair should have a maximum difference in amplitude of 0.075° and have the same saccade number (i.e. secondary or tertiary). Only secondary and tertiary saccades were matched. 204 matched pairs were identified across all subjects. See Table 5.2.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Amplitude (°)</th>
<th>ISI (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2° onwards</td>
<td>126</td>
<td>0.484</td>
<td>180.87</td>
</tr>
<tr>
<td>2° backwards</td>
<td>126</td>
<td>0.489</td>
<td>178.23</td>
</tr>
<tr>
<td>3° onwards</td>
<td>78</td>
<td>0.466</td>
<td>254.95</td>
</tr>
<tr>
<td>3° backwards</td>
<td>78</td>
<td>0.488</td>
<td>231.44</td>
</tr>
</tbody>
</table>

Table 5.2. To show the mean amplitudes and ISI of amplitude-matched secondary (2°) and tertiary (3°) corrective saccades used in testing the hemispheric facilitation hypothesis.
Due to the varying number of matched pairs provided by each subject (range 2-18) it was necessary to calculate a weighted standard error for all 20 subjects in order to correctly compare the means. No significant differences were found between the latencies of amplitude matched pairs of onward and backward corrective saccades. This finding held whether results from tertiary and secondary saccades were combined ($t=1.651$, $0.2 > p > 0.1$), or whether just secondary saccades were used in the calculations ($t=0.019$, $p > 0.2$).

5.4.2 Discussion

We have found no significant differences between the latencies of amplitude matched pairs of corrective saccades dependent on whether they are onwards or backwards corrective saccades. This finding has been previously reported by Weber and Daroff (1972) and Kapoula and Robinson (1986) although in neither study did they explicitly take into account the systematic variation in the amplitude of onwards and backwards corrective saccades. In the study of Kapoula and Robinson (1986), only saccadic movements greater than $0.4^\circ$ in unmatched data from a small group of subjects were compared. They used the threshold of $0.4^\circ$ due to the large scatter in the data above below this level. However, for the fact that the average amplitude of overshooting secondary saccades among our 20 subjects was $0.489^\circ$, this suggests that many overshooting saccades would have been lost from their comparison. Furthermore, due to the large individual variation in latency characteristics it is important that such calculations are made within subjects, and not averaged between subjects in which case differences may be lost. Kapoula and Robinson (1986) do not specify whether their finding of no significant differences came from within-subject calculations, or from the averages found between subjects. Finally, they did not explicitly match their onwards and backwards correctives saccades for amplitude, despite noting the clear reciprocal
relationship between latency and amplitude for small corrective saccades. Our calculations address all these issues to provide a more robust result regarding latency differences between onwards and backwards corrective saccades.

Harris *et al.* (1993) also reported no significant differences in the latency of overshooting and undershooting saccades. This however was reported from infants of up to 7 months, and has some of the same drawbacks as Kapoula and Robinson’s (1986) paper. We have provided confirmation of this result in adults.

The theory of the significant differences between undershooting and overshooting corrective latencies appears to have gained credence from relatively little empirical evidence. It has been pointed out by Becker (1989) that, apart from the original report of Young *et al.* (1968) of the latency of onwards corrective being half as much as the latency of backwards correctives, such significantly longer latencies have only been observed when an overshoot error was artificially induced in double target step experiments, eg Deubel *et al.* (1982). Becker proposes that this artificially induced error conflicts with the extraretinally prepared onward corrective, as outlined in his theory regarding the pre-programmed nature of corrective saccades (Becker and Fuchs, 1969; Becker and Jürgens, 1979). See Section 1.5.3. Cancelling this prepared saccade and generating a new saccade may account for the increase in latency observed in Deubel’s experiment.

The finding reported above of no significant difference in latency between onwards and backwards corrective saccades indicates that even if there is a physiologically imposed delay in the hemispheric transfer of the spatial representation of the target, this is not reflected in the time taken to generate the corrective movement as represented by the intersaccadic interval. Thus latency differences cannot be the driving force behind the undershoot bias, as these results indicate that the saccadic system would not be able to differentiate between these contrasting types of corrective saccades according to their latency characteristics.
5.5 The flight time minimisation hypothesis

5.5.1 Results

The data from each subject were quantified in many different ways, as discussed in the methods section of this chapter. There were 18 parameters for each subject: the slope, intercept and gamma value for the main sequence, limited either by duration or amplitude; and the slope and intercept of the range effect, either across all target eccentricities or limited to the central 3 target eccentricities, for each of the three different types of gain. These 18 parameters were used in bivariate correlations to investigate the linear relationship between them. The correlation coefficients for all these measures can be seen in Tables 5.2 and 5.3. The Spearman rank correlation was used, rather than the Pearson correlation as the data did not have a normal distribution.

<table>
<thead>
<tr>
<th>Full Range Effect</th>
<th>Main sequence (amplitude limited)</th>
<th>Main sequence (duration limited)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Slope</td>
<td>Intercept</td>
</tr>
<tr>
<td>Traditional gain</td>
<td>S</td>
<td>0.059</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>-0.215</td>
</tr>
<tr>
<td>Component gain</td>
<td>S</td>
<td>-0.183</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>0.017</td>
</tr>
<tr>
<td>Net Gain</td>
<td>S</td>
<td>0.023</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>-0.059</td>
</tr>
</tbody>
</table>

Table 5.3. to show the Spearman rank correlation coefficients of the full range effect measures for each different type of gain correlated to the main sequence parameters. S-slope, I-intercept

<table>
<thead>
<tr>
<th>Limited Range Effect</th>
<th>Main sequence (amplitude limited)</th>
<th>Main sequence (duration limited)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Slope</td>
<td>Intercept</td>
</tr>
<tr>
<td>Traditional gain</td>
<td>S</td>
<td>-0.041</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>-0.153</td>
</tr>
<tr>
<td>Component gain</td>
<td>S</td>
<td>-0.351</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>0.168</td>
</tr>
<tr>
<td>Net Gain</td>
<td>S</td>
<td>-0.079</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>-0.120</td>
</tr>
</tbody>
</table>

Table 5.4. to show the Spearman rank correlation coefficients of the limited range effect measures for each different type of gain correlated to the main sequence parameters. ** correlation significant at the 0.01 level (2 tailed); * significant at the 0.05 level (two tailed). S-slope, I-intercept
There was a consistent positive correlation between the slope of the range effect and the intercept and gamma values of the main sequence. Reciprocally, there was a negative correlation between the intercept of the range effect and intercept of the main sequence. In all cases, these relationships were stronger for the limited range effect. No significant differences were found between the main sequence parameters and the range effect when the range effect was quantified by linear regression across all eccentricities (full range effect). However, when the range effect was quantified across only the central 3 eccentricities (limited range effect) there were highly significant correlations between both the slope and the intercept of the range effect derived from the component gain and the intercept and gamma values of the main sequence. These relationships can be seen in the scatterplots in Figure 5.9.

![Scatterplots](image)

**Figure 5.9.** Scatterplots to show the relationship between the main sequence intercept and the slope (A) and intercept (B) of the range effect.

### 5.5.2 Discussion

Highly significant correlations were found between the main sequence for duration and the range effect in this study of 20 subjects. These correlations were found most strongly between the intercept of the main sequence, and both the slope and intercept of the range effect. This result supports predictions made by the saccadic flight-time minimisation hypothesis (Harris, 1995).
Quantifying the Main Sequence and Range Effect

We used two different methods for quantifying the main sequence for the data in this experiment. The data included in the linear regression calculation was either limited by amplitude or duration. These did not produce significantly different results, the means of the slope and intercept values for all 20 subjects were very similar for both groups. Nevertheless, the correlations were generally stronger when using the main sequence limited by duration. This was probably due to the fact that in limiting by duration, we were ensuring that only typical saccades were being included in the analysis. Outliers at either extreme would be removed from the analysis. Outliers were noted to occur in four of our 20 subjects and, as has been discussed previously, were probably associated with fatigue and inattention.

The range effect has not been quantified in the literature previously. We quantified the range effect in two ways, either across the full range of eccentricities presented, or across a limited central range. Highly significant correlations were found when the limited range effect was used. No significant correlations were found when the full range effect was used in the correlation analyses. The highly idiosyncratic nature of the range effect when taken across all 5 target eccentricities was probably the cause of the loss of significance. As discussed in Section 5.3.2 (gain and the range effect) the range effect may not be best quantified by a linear regression over a wide range of eccentricities due to non-linearity at either end. The gain of saccades to the smallest and largest target eccentricities were often found to diverge from the expected pattern.

Three subjects in particular could be identified as showing atypical range effects. If these three subjects were removed from the correlation analyses a significant correlation emerged between the full range effect (component gain) and the intercept of the main sequence for duration ($r = -0.589$, $p = 0.013$).

The presence of an atypical range effect could be due to a number of internal or external factors. Behavioural inattention, fatigue or perhaps acoustic distractions from
noise outside the experimental room could have affected the characteristics of saccades, although this should not have preferentially affected saccades to the smallest and largest target eccentricities. The experimental area was kept as quiet as possible during the experiment, but external noises could not be otherwise controlled. Fatigue has been shown to cause slow saccades (Bahill and Stark, 1975), though the effects on saccade gain have not been reported. In our experience, some saccades are found to have a notably slow, glissadic end. This causes an increase in the saccade duration, but also, if the slow glissadic component falls below the saccade detection threshold, potentially an attenuation of the apparent amplitude of the saccade. There is also the possibility that head movements were made during the experiment could have affected saccade parameters. Although subjects had their head restrained by ear muffs, these do not provide the same degree of stability that, for example, a bite bar does. However, again, if a head movement were affecting results, it would be unlikely to affect preferentially the saccades to the smallest and largest target eccentricities. Furthermore, there was no evidence in the eye movement traces of a tell-tale vestibularly-induced slow phase that would be elicited if a head movement were combined with the eye movement.

**How the range effect and main sequence are related**

The SFM hypothesis can be used to predict the direction of the correlations that would be expected between the parameters of the main sequence for duration and the range effect.

The minimisation of saccadic flight-time is particularly relevant to larger saccades as these are more likely to be followed by corrective saccades, and thus more prone to the effects of overshooting and undershooting on flight-time. Smaller saccades may often not be followed by any correctives at all and thus the trade-off between overshooting and undershooting saccades is not relevant. The relative number of trials, for each target eccentricity separately, in which no corrective saccades are generated, can be obtained
from the bar chart of component gain in Figure 5.6 (page 147). It is clear that larger saccades are more likely to elicit correctives. Furthermore, Figure 5.10 (below) shows that larger target eccentricities more likely to elicit corrective saccades.

The intercept and slope of the range effect are of course closely related. As the intercept decreases, the slope becomes flatter. The slope of the range effect has a negative sign. Thus, as the slope becomes more positive, the intercept becomes less positive. This correlation is highly significant ($r = -0.799, p < 0.001$). An individual with either a high magnitude slope (more negative) or a high (more positive) intercept value will be expected make more corrective saccades, because their gain values are further from 1.0. Figure 5.11 shows that the number of corrective saccades made does not only vary with the target eccentricity as already discussed, but also with the primary saccade gain to this target eccentricity. The figure shows data for saccades to 20º target eccentricities, the same trend was seen for all target eccentricities.

Corrective saccades each incur a cost ($\alpha$) (see Section 1.5.3), which is obtained from the intercept value of the main sequence for duration for each subject. The more correctives that are made, the lower one would expect $\alpha$ to be, in order to minimise the cost of making these correctives. Thus, the more negative the slope for the range effect (and the more positive the intercept) the lower the main sequence intercept would be
expected to be. These predictions are supported by the experimental data presented here, see Figure 5.9 in particular.

No significant relationship was found between the slope of the main sequence and the parameters of the range effect. Indeed the direction of the correlation was not even consistent between the different variations of the same parameters. The slope of the main sequence represents an amplitude-dependent cost of making a saccade. As corrective saccades are generally very small (generally $< 2^\circ$ for a secondary corrective, and $< 1^\circ$ for further correctives in this experiment) the differences in the flight-time of such small saccades is relatively small, and the flight-time of such small saccades will only be slightly greater than the intercept value $\alpha$. What makes the difference in terms of total flight-time is the actual number of corrective saccades made as this incurs the minimum cost ($\alpha$) in terms of time. Thus, we would expect to see the strong relationship between $\alpha$ (the intercept of the main sequence) rather than the slope ($\beta$) as this has a greater influence of total saccadic flight-time in this context.

A significant relationship between $\gamma$ and the slope and intercept (duration-limited $\gamma$ only) of the range effect was also found. $\gamma$ represents that trade-off between $\alpha$ and $\beta$. The correlation between $\gamma$ and the range effect parameters are consistently in the same direction as the correlations between $\alpha$ (intercept) and the range effect parameters. This confirms the results above and further indicates that the main sequence slope has no systematic affect on the gain in this experiment. If the main sequence slope did have an effect on gain in addition to the affect of the intercept, one would expect a slightly stronger correlation to be seen between $\gamma$ and the range effect parameters.

The reasons for the correlations only being present when the limited range effect was used have been discussed above. However, it is also relevant that correlations were only found with the component gain, and not the other two methods of determining gain. This is probably because the correlations that we sought in this analysis were very subtle.
Any variation in saccadic parameters due to head movements, drift or slow eye movement components would particularly affect traditional and net gain and cause a loss of significance.

### 5.6 Conclusion

In this experiment reflexive centrifugal saccades to a range of target eccentricities were recorded in 20 normal subjects. The latency, duration and velocity parameters were all found to be within previously reported ranges. The range effect was noted to be idiosyncratic, although in general the typical pattern was seen. Robust within-subject analyses of the latencies of onwards and backwards corrective saccades failed to provide any support for Robinson’s hemispheric facilitation theory.

Between-subject analyses revealed predictable correlations between main sequence characteristics and the gain of saccades. These correlations were highly significant between the intercept value of the main sequence and both the slope and intercept values of the range effect. This finding supports the general prediction made by the SFM hypothesis that the gain of saccades is intimately related to the main sequence parameters of each individual. Specifically, as the ‘cost’ of making a saccade decreases, as reflected by a lower main sequence intercept, the less time-consuming it becomes to make more correctives and thus the lower the gain to larger target eccentricities can be.

The gain parameters in an individual are more able to be manipulated to optimise behaviour with respect to the main sequence for duration parameters than vice versa. The main sequence for duration parameters are relatively hard-wired within the oculomotor system. The system for controlling gain on the other hand is known to be under adaptive control mechanisms that enable rapid, subtle and reversible changes to take place. In the following chapter we shall investigate these adaptive control mechanisms and demonstrate the highly flexible nature of the gain of saccades.
Chapter 6. Adaptive Control of Gain

6.1 Introduction

In the previous chapters the gain of saccades has been examined in the context of the saccadic flight-time minimisation (SFM) hypothesis (Harris, 1995). Low gain saccades are interpreted to be generated by an adaptive control system that attempts to minimise total saccadic flight-time over sequences of saccades. In this chapter the active functioning of the adaptive control system will be investigated. This experiment attempts to distinguish between the traditional belief that the adaptive system strives to minimise post-saccadic retinal error, rather than saccadic flight-time as proposed by the SFM hypothesis.

Adaptive control processes have already been discussed in Sections 1.6 and 1.8, and will be briefly reviewed here.

6.1.1 What is adaptive control?

Adaptive control is the process of controlling motor behaviour by monitoring performance and adjusting parameters to refine accuracy and optimise behaviour. It is important in many control systems to enable plasticity and learning, especially in open-loop motor control systems, such as the saccadic system, where the motor behaviour takes place too quickly for on-going feedback to be provided.

Effective vision depends fundamentally on the finely controlled movement of the fovea around the visual environment. Precise knowledge of the relationship between visual input and motor output is necessary in order to make accurate goal-directed saccades and also in a wider sense to build up a reliable representation of the visual environment and the spatial relationships between objects.
The adaptive control system for saccades compensates for both long term and short term changes to the input and output parameters of the visual system. These can be due to changes in oculomotor physiology and anatomy as well as altered visual input. Loss of strength in the extraocular muscles due to natural ageing or disease processes, repeated changes to the magnification of the visual environment due to the use of glasses, or more acute changes to the extraocular muscles due to trauma all require compensatory adaptive control processes to re-establish the optimal behaviour of saccades in response to these altered conditions.

6.1.2 How is adaptive control studied?

Compensatory adaptations of saccades have been studied in both human patients with ocular nerve palsies leading to paretic extraocular muscles (Kommerell et al., 1976; Abel et al., 1978), and in animals which have had similar defects imposed artificially through muscle or nerve resection (Optican and Robinson, 1980).

Adaptive control processes have also been investigated in the laboratory without disrupting ocular anatomy using the intrasaccadic target displacement paradigm. This involves, as the name implies, a secondary small displacement of the target while the primary saccade to the initial target displacement is in progress. This intrasaccadic secondary target step may be either onwards, in the same direction as the primary target step, or backwards in the opposite direction to the original target step. This results in the end position of the primary saccade being further from or nearer to the target than expected. The benefit of this technique for the purpose of studying adaptive control is that the saccadic system behaves as if the resulting dysmetria were due to a malfunction of the oculomotor system, i.e. an internally generated error, rather than an externally generated error due to the movement of the target. As such, the saccadic system attempts to compensate for this perceived error through the process of adaptive control.
The attribution of the induced error to an internal error causes the system to adapt the size of the saccades relative to the target. If the intrasaccadic target step moves the target backwards, the saccadic system finds that it has unexpectedly overshot the target and it will gradually decrease the amplitude of saccades to re-establish a level of undershooting. This is known as a gain decreasing paradigm. If on the other hand, the intrasaccadic target step moves onwards, the saccadic system finds that it has undershot the target by far more than expected and it will gradually increase the size of its saccades to again re-establish a certain level of undershooting. This is called a gain increasing paradigm.

McLaughlin’s (1967) study was the first reported investigation to use this experimental paradigm to make an in depth investigation of the saccadic adaptive control system. He reported that when the target was displaced backwards towards the centre during (voluntary) eye movements this indeed caused the eye to overshoot the final position of the target. However, if this intrasaccadic target displacement was repeated each time the eye moved, the overshoot quickly disappeared so that the eye landed on target once again. They reported that this process took place very quickly, over as little as 8-10 eye movements. McLaughlin labelled this process the ‘parametric adaptive effect’.

This technique of intrasaccadic target displacement has subsequently been the most popular method used to examine adaptive control in both monkeys (Fitzgibbon et al., 1986; Fuchs et al., 1996) and humans (Henson, 1979; Miller et al., 1981; Wolf et al., 1984; Deubel et al., 1986; Semmlow et al., 1989; Erkelens and Hulleman, 1993; Frens and van Opstal, 1994; Deubel, 1994; Straube and Deubel, 1995) and is the technique that we have used in this experiment.

6.1.3 What is the adaptive controller controlling?

A change in saccade amplitude with respect to the target eccentricity is the most obvious change that takes place during adaptive control processes. Whether gain
adaptations also change saccade dynamics has produced conflicting stories. Some investigations have reported that the dynamic characteristics of saccades, the main sequences for both duration and peak velocity, were not affected by the adaptation process in experiments in man (Frens and van Opstal, 1994), in monkey (Optican and Robinson, 1980), or in both (Albano and King, 1989). Other researchers have however reported that saccade dynamics are affected by the adaptation process. Fitzgibbon et al., (1986) reported that adapted saccades in monkey had a lower peak velocity-amplitude relationship than unadapted saccades in a gain decreasing paradigm. Straube and Deubel (1995) reported that saccade dynamics are also affected in man, in differing ways for the gain increasing and gain decreasing paradigms. These were not however the same as those reported by Fitzgibbon et al., (1986) in monkey and were found to be quite idiosyncratic.

Understanding what the adaptive process changes can provide clues to the level and even precise location at which gain adaptation is taking place.

6.1.4 What is the goal of the adaptive controller?

Adaptive control processes have repeatedly been shown to reduce the percentage of overshooting saccades and re-establish a degree of undershooting. This undershoot bias is a robust phenomenon, particularly in humans, in the face what has been shown to be a highly sensitive adaptive control system. Although the prevention of an excessive amount of overshooting saccades can be understood to be the outcome of the adaptive control system, the driving force behind achieving this goal, and the cues used to guide the adaptive control system are little understood.

Wallman and Fuchs (1998) have proposed that the cue used to drive the system is a visual error cue, with the possibility of a non-essential motor cue also being involved. However, knowledge of the cue or the error signal, used by the system does not necessarily help with determining what drives the system towards its goal.
The minimisation of average post-saccadic retinal error via a negative feedback loop is most widely believed to be the goal of the system. By averaging post-saccadic visual error over time the saccadic system employs what would appear to be an economic self-regulatory process. An error would have to be persistent and systematic in order to elicit an adaptive change in gain. This would prevent unnecessary gain adjustments being made when an error was simply a random event caused by anything from passing fatigue to a cognitive strategy. An alternative view however, is that the system is trying to minimise saccadic flight-time (Harris, 1995) in order to prevent the extra ‘cost’ associated with making an overshooting rather than an undershooting saccade. See Section 1.5.3.

In this experiment the effect of post-saccadic retinal error on the adaptive control processes was investigated. In order to investigate whether the minimisation of average retinal error is the driving force behind saccadic adaptation a novel variation on the target displacement paradigm was used in which the average post-saccadic retinal error was reduced to zero.

Subjects were tested on standard gain increasing and gain decreasing paradigms and also on a third paradigm involving randomised backwards and forwards intrasaccadic target steps of the same magnitude. We have called this the ‘random paradigm’. This paradigm was designed to eliminate the average post-saccadic retinal error over time. The intrasaccadic target step was randomised such that 50% stepped onwards and 50% stepped backwards. Thus, over the course of the experiment the average retinal error would be 0.

If retinal error signals are averaged over time we would expect to find no adaptation during the random paradigm. If however the system was being driven to minimise saccadic flight-time we would expect to see a decrease in saccadic gain over the random paradigm, as the system tries to reduce the induced overshooting.
6.2 Methodology

6.2.1 Subjects

Six subjects, ranging in age from 24 to 44 years, participated in this experiment. All subjects were tested in their normal refractive state, to prevent any confounding factors due to optical corrections. Subjects had no known oculomotor deficits. Four of the six subjects were naïve as to the purpose of the study. The two subjects who were not naïve did not however know which of the four experimental paradigms they were being presented with at any time.

6.2.2 Experimental set-up

Experiments were performed under dimmed lighting conditions. The full details of the experimental set-up have been described previously (see Chapter 2, Methodology). In brief, subjects were seated comfortably in a chair with their chin supported by a chin-rest in front of a large white non-reflective screen. The target stimulus was a red laser spot, front-projected on to the screen and controlled by a x-y laser deflection system.

Eye movements were recorded with an infra-red eye tracker (IRIS eye tracker, Skalar Medical, Holland). In order to calibrate the recorded eye movements, subjects were first required to fixate 6 points along the horizontal axis, located at 5°, 10° and 15° eccentricity either side of the central fixation point.

6.2.3 Experimental paradigm

All experiments were performed in the same manner. Each experiment consisted of three different phases: the pre-adaptation phase (50 trials), the adaptation phase (200 trials) and the post-adaptation phase (50 trials). All testing took place to an initial target step of 10° to the right of the central fixation target. The pre and post-adaptation phases
were the same in all paradigms and consisted only of a single target step of 10° to the right of the central fixation point.

The adaptation phase consisted of 4 different variations:

1) a gain increasing paradigm in which the secondary intrasaccadic target step was 2° in the same direction as the original target step (onwards);

2) a gain decreasing paradigm in which the intrasaccadic target step was 2° in the direction opposite to the original target step (backwards);

3) a random paradigm in which 2° target steps were either onwards or backwards, pseudo-randomised so that exactly the same number of each type were presented over the 200 trials;

4) a control paradigm in which there was no intrasaccadic target step, ie all 300 trials in this paradigm were identical.

An intrasaccadic target step of 2°, representing a change in eccentricity of 20%, was selected to ensure that the secondary movement of the target was not detected by the subjects. Bridgeman et al., (1975) has reported that if the intrasaccadic target step is less than about 30% of the initial movement, it is not generally noticed. All the naive subjects reported that they had been completely unaware of the secondary target step when enlightened after all experimental paradigms were completed. One of the non-naive subjects commented that the backwards target step was easier to detect than the onwards target step.

Each phase of the experiments were run in series directly after each other with no break. This was to ensure that no de-adaptation takes place in response to normal visual feedback during the experiment. Each subject performed all 4 different paradigms in a randomised order. Testing sessions for the different paradigms were separated by a minimum of 24 hours.
Testing and induced adaptation was performed in one direction and to one eccentricity only in order to facilitate as much adaptation as possible within the time scale of the experiment. It is known that adaptation is induced separately according to the direction of movement and also that the speed of adaptation is much slower if multiple target eccentricities are used (Miller et al., 1981).

From pilot work it was determined that approximately 300 trials was the maximum number of trials that a subject could reliably perform before the effects of fatigue and the lack of comfort became too great. These 300 trials took approximately 22 minutes to complete; with the additional set-up and calibration time each session took approximately 30 minutes. Subjects were simply asked to watch the target spot and follow it with their eyes at all times as quickly and accurately as possible. Subjects were encouraged to maintain attention throughout the experiment.

In all trials the target spot began at the central fixation point and then after a randomised time delay (500-2500msec) jumped to a peripheral position of 10° to the right of the centre. In the pre and post adaptation phases the target then remained in this position for 1000msec before returning to the centre where it again remained for 1000 msec before the start of the next trial began. In the adaptation phases, eye velocity was monitored on-line by computer and a secondary target step was elicited when an eye velocity threshold of 100°/sec was reached given the saccade was in the same direction as the target movement. The intrasaccadic target step was initiated immediately this velocity threshold was crossed. Only one intrasaccadic target step could be generated in each trial. Subsequent saccades did not elicit any further target movement, even if they did exceed the eye velocity threshold, until the beginning of the next trial.

The velocity threshold of 100°/sec was determined in a pilot study on two subjects to elicit intrasaccadic target steps to all primary saccades but the very smallest. Previous investigators have generally used lower thresholds, ranging from 30°/sec (Deubel, 1995) to 75°/sec (Frens and Van Opstal, 1994). A saccade with a peak velocity of 75°/sec can be
less than 1° in amplitude. As such these thresholds may elicit an intrasaccadic
displacement to even very small amplitude saccades such as small random movements or
very low gain anticipatory saccades made in advance of the target-directed saccade. The
threshold of 100°/sec was found to be advantageous as it triggered an intrasaccadic target
step primarily with target directed primary saccades. The first saccade to cross the
velocity threshold elicited the intrasaccadic target step.

6.2.4 Data analysis

The parameters of the computer program used to detect saccades in off-line
analysis has been discussed in detail previously (see Chapter 2, Methodology). The
program supplied all timing, metric and dynamic aspects of each saccade made within
each trial. A trial consisted of all saccades made within 900 msec of the first movement of
target. Trials which contained saccades closely associated with blinks; with latencies in
the predictive saccade range; or with excessively long durations due to glissadic endings
were excluded from the analyses. Some subjects were much more consistent than others.
The number of trials excluded in any one paradigm ranged from a maximum of 74 to a
minimum of 11 (average 10.4%).
6.3 Results

In order to assess the effects of the adaptive protocol for each paradigm, both between and within subjects, the average gain of saccades in the pre- and post-adaptation phases were compared. The magnitude of the adaptive effect was taken as the change in mean gain during the pre-adaptive and post-adaptive phases. The control condition revealed whether there were any changes in gain due to non-adaptational processes over the course of a long experiment such as this.

The average gain of primary saccades in the pre-adaptation phase (baseline gain) generally lay between 0.9 and 1 which is within the range reported for primary reflexive saccades (Becker, 1989). Subject DS had relatively low baseline gains. This was due to the high number of express saccades made by this subject, as discussed in the results Section 6.3.4.

6.3.1 Control condition

Control paradigms were performed by 5 of the 6 subjects who took part in this experiment. Unfortunately one subject was unable to return to complete this part of the experiment. No subjects showed any significant changes in the gain of their saccades over the course of the 300 trials. See Table 6.1 for details.

6.3.2 Gain increasing and gain decreasing paradigms

Adaptive changes in the gain of primary saccades took place in the expected direction in all subjects over the course of the 200 saccades in each of the gain increasing and gain decreasing adaptive paradigms (approximately 15 minutes). This result confirms that we have been able to elicit a robust adaptive response similar to previous reports in all our subjects given our experimental set-up and paradigm.
The average gain of saccades in the pre- and post-adaptation phases are presented for all 6 subjects in Table 6.1. The change in gain over the course of the adaptive phase was statistically significant for both the gain increasing and gain decreasing paradigms (paired samples t-test, p<0.01).

<table>
<thead>
<tr>
<th>Subject</th>
<th>Control Before</th>
<th>Control After</th>
<th>Gain Decrease Before</th>
<th>Gain Decrease After</th>
<th>Gain Increase Before</th>
<th>Gain Increase After</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS</td>
<td>-</td>
<td>-</td>
<td>0.901</td>
<td>0.814</td>
<td>0.898</td>
<td>0.987</td>
</tr>
<tr>
<td>MH</td>
<td>0.951</td>
<td>0.938</td>
<td>0.955</td>
<td>0.849</td>
<td>0.914</td>
<td>0.985</td>
</tr>
<tr>
<td>SMG</td>
<td>0.964</td>
<td>0.950</td>
<td>0.928</td>
<td>0.824</td>
<td>0.929</td>
<td>0.957</td>
</tr>
<tr>
<td>CH</td>
<td>0.959</td>
<td>0.953</td>
<td>0.959</td>
<td>0.844</td>
<td>0.953</td>
<td>0.997</td>
</tr>
<tr>
<td>PV</td>
<td>0.877</td>
<td>0.906</td>
<td>0.900</td>
<td>0.810</td>
<td>0.939</td>
<td>0.962</td>
</tr>
<tr>
<td>SG</td>
<td>0.973</td>
<td>0.978</td>
<td>0.963</td>
<td>0.849</td>
<td>0.962</td>
<td>1.018</td>
</tr>
<tr>
<td>Average</td>
<td>0.945</td>
<td>0.945</td>
<td>0.934</td>
<td>0.832**</td>
<td>0.934</td>
<td>0.984**</td>
</tr>
</tbody>
</table>

Table 6.1. Average gains to a 10° target eccentricity for the pre- and post-adaptation phases of the gain increasing and gain decreasing paradigms. ** indicates a statistically significant change in gain between pre- and post-adaptation gain levels (paired samples t-test, p<0.01)

These results are presented in graphic form in Figure 6.1 (overleaf) for all six subjects. In the gain decreasing paradigm a significant difference can be seen between the average saccadic gains in the pre- and post-adaptation phases for all subjects individually. In the gain increasing paradigm, 4 out of the 6 subjects show significant differences between their pre- and post-adaptation phase gains. The two subjects who did not show significant differences were Subjects SMG and PV.

To investigate the possibility that the lack of significance between the pre- and post-adaptation gains for Subjects SMG and PV in the gain increasing paradigm could have been due to a certain amount of re-adaptation taking place (in the post adaptation phase) gain changes over the post-adaptation phase were examined. In the post-adaptation phase, when the target no longer makes an intrasaccadic target step, after the induced gain increase of the adaptation phase, the system will again be under pressure to adaptively alter its gain, in this case to reduce its gain. This would counteract the effects of the gain
increasing phase, and if the rate of decrease is rapid, as suggested by previous studies (Wolf et al., 1984; Deubel et al., 1986), may mask significant changes in gain after the adaptive phase of the experiment, when averaging over 50 trials. Subject PV did show readaptation (a decrease in gain) in the post adaptation phase, from a gain of 0.993 in the first 10 post adaptation trials, to a minimum of 0.931, and ending up at 0.944 in the final 10 of the 50 post adaptation trials. This could thus have resulted in the loss of significance. Subject SMG however did not show readaptation in the 50 trial post-adaptation phase.

Figure 6.1. Average gain (with 95% confidence interval (CI) bars) before and after adaptation in the gain increasing and gain decreasing paradigms for all subjects.

---

---
It is notable that four subjects showed remarkable consistency between sessions in the average gain and standard error of their pre-adaptation saccades. Subject DS had a large standard error, especially for saccades in the gain decreasing paradigm.

Figure 6.2 represents the change in gain for each subject over the course of the adaptive phase of the experiment. The graphs show the gain and standard deviations averaged over every 10 trials. The gains are calculated with respect to the final target eccentricity. Thus, in the gain decreasing paradigm, where the target jumps from 10° back to 8° during the primary saccade, the initial saccades of the adaptation phase all overshoot the final target position and thus have a gain of greater than 1.0. On the other hand, in the gain increasing paradigm, the target jumps from 10° to 12° during the primary saccade and the initial saccades of the adaptation phase grossly undershoot the final target position and thus have a low gain.

**Figure 6.2.** Gain plotted against the trial number over the adaptive phase (trials 51-250) of the experiment in 10 trial averages (with 95% CI bars) for the gain decreasing paradigm (solid bars) and gain increasing paradigm (broken bars).
A clear decrease in gain over the 200 trials can be seen in the gain decreasing paradigm for all subjects. This is harder to determine in Subject DS due to the large error bars. In contrast, an increase in gain for the gain increasing paradigm is not as clear. This dissociation between the strengths of adaptation supports previous reports discussed in Section 1.6.4 of the introduction. There was however no correlation between the magnitude of gain increase and gain decrease within each subject. See Figure 6.3. Furthermore, no correlations were found between the pre-adaptation gain levels and the strength of adaptation within subjects.

![Figure 6.3](image.png)

**Figure 6.3.** The relationship between the magnitude of gain change in the gain increasing and gain decreasing paradigms for each subject. The line with slope of 1.0 indicates the line of equality.

An initial rapid phase of adaptation within the first 50 trials was evident in the gain decreasing paradigm in four subjects (MH, SMG, CH, PV). A similar rapid phase of adaptation in the gain increasing paradigm was not evident in any subjects.

### 6.3.3 Random paradigm

When the average retinal error over the course of the experiment was zero, as in the random paradigm, it was found that there was a consistent trend in all subjects for the gain of saccades to decrease. A graphical comparison of the gains before and after adaptation in the random paradigm are presented for all 6 subjects below (Figure 6.4).
Figure 6.4. Randomised paradigm: the mean gain before and after adaptation for each subject (with 95% confidence interval bars).

<table>
<thead>
<tr>
<th></th>
<th>Before adaptation</th>
<th>After adaptation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject</td>
<td>Gain</td>
<td>Gain</td>
</tr>
<tr>
<td>DS</td>
<td>0.894</td>
<td>0.731</td>
</tr>
<tr>
<td>MH</td>
<td>0.973</td>
<td>0.905</td>
</tr>
<tr>
<td>SMG</td>
<td>0.954</td>
<td>0.895</td>
</tr>
<tr>
<td>CH</td>
<td>0.952</td>
<td>0.889</td>
</tr>
<tr>
<td>PV</td>
<td>0.938</td>
<td>0.855</td>
</tr>
<tr>
<td>SG</td>
<td>0.991</td>
<td>0.955</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>0.950</strong></td>
<td><strong>0.872</strong></td>
</tr>
</tbody>
</table>

Table 6.2. Mean gain before and after adaptation for all subjects. ** indicates a statistically significant change in gain between pre- and post-adaptation gain levels (paired samples t-test, p<0.01)

All subjects showed a decrease in average gain from the pre- to the post-adaptation periods in the random paradigm. Overall this difference was statistically significant (paired samples t-test, p<0.01). The difference between the average pre- and post-adaptation gains was significant in all subjects individually except Subject SG. Table 6.3 (over) shows the magnitude of gain change for each subject in each experimental paradigm.
Table 6.3. The magnitude of gain change for each subject in each paradigm.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Increasing paradigm</th>
<th>Decreasing paradigm</th>
<th>Random paradigm</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS</td>
<td>+0.089</td>
<td>-0.087</td>
<td>-0.163</td>
</tr>
<tr>
<td>MH</td>
<td>+0.071</td>
<td>-0.106</td>
<td>-0.068</td>
</tr>
<tr>
<td>SMG</td>
<td>+0.028</td>
<td>-0.104</td>
<td>-0.059</td>
</tr>
<tr>
<td>CH</td>
<td>+0.044</td>
<td>-0.115</td>
<td>-0.063</td>
</tr>
<tr>
<td>PV</td>
<td>+0.023</td>
<td>-0.090</td>
<td>-0.083</td>
</tr>
<tr>
<td>SG</td>
<td>+0.056</td>
<td>-0.114</td>
<td>-0.036</td>
</tr>
<tr>
<td>Average</td>
<td>+0.052</td>
<td>-0.103</td>
<td>-0.079</td>
</tr>
</tbody>
</table>

It can be seen that the magnitude of gain decrease is bigger than the magnitude of gain increase for all subjects except DS. The magnitude of gain change in the random paradigm was not found to be related to either magnitude of gain change in the increasing paradigm or the decreasing paradigm. See Figure 6.5A (below).

Figure 6.5. To show the relationship between the magnitude of the gain change in the random paradigm (x axis on both graphs) and the gain decreasing and increasing paradigms (A), and the difference between the magnitude of gain increase and decrease (B). The diagonal line represents the line of equality for each graph.

If post-saccadic retinal error were the driving force for adaptation on a trial-to-trial basis it could be predicted that the decrease in gain results from the aforementioned differences in the strength of adaptation in the onwards and backwards directions. If this were the case one would predict that the change in gain during the random paradigm would be approximately equal to the difference between the changes in gain of the decreasing and increasing paradigms. No clear relationship was observed between the
change in gain during the random paradigm, and the difference between the magnitudes of change in the gain decreasing and gain increasing paradigms. See Figure 6.5B.

6.3.4 Express saccades in Subject DS

Subject DS was notable in having a relatively large standard deviation of gain, see especially Figure 6.2. In general, Subject DS had a standard deviation that was at least one order of magnitude greater than the other subjects. This was a consistent feature across all three of his experimental paradigms. A possible reason for this substantial difference became clear once the latency distribution of his primary saccades was investigated (see Figure 6.6, below).

Figure 6.6. Latency histogram of the primary saccades for all paradigms combined, for all subjects. Note the bimodal distribution for Subject DS.
Bimodality was clear in the latency histogram of the primary saccades of Subject DS. No clear evidence for bimodality was seen in any of the other subject's data. The two peaks in Subject DS's data were estimated to be at 118 msec and 163 msec, divided by a minimum at approximately 143 msec. The first peak lies within a latency range of 90-130 msec that has been classified as the 'express saccade' range for humans (Fischer and Ramsperger, 1984), while the second peak lies within the 'short latency regular saccade' range for primary saccades (Fischer and Breitmeyer, 1987). Express saccades are visually guided saccades characterised by an extremely short latency. They are typically observed in experiments with a gap (of approximately 200 msec) between the target offset and target onset, in which case this decrease in latency is known as the gap effect (Saslow, 1967). Our experiment did not involve a gap between the target offset and onset and the timing properties were identical in all paradigms across all subjects. However, 'express-saccade makers' who produce large numbers of express saccades independent of the gap effect i.e. in no-gap and overlap paradigms, have been reported in normal subjects, as well as in particular association with dyslexia (Biscaldi et al., 1995). Cavegn and Biscaldi (1996) reported a non-dyslexic express-saccade maker who produced 65-95% express saccades even in an overlap paradigm. Our Subject DS, who was not dyslexic, made an average of 52.3% express saccades (46.4%, 43.8% and 65.3% in the gain decreasing, gain increasing and random paradigms respectively). However, Cavegn and Biscaldi (1996) reported that their express-saccade maker did not show a clear modal peak for the short-latency regular saccades which were instead scattered widely. Subject DS showed two clear peaks in his bimodal distribution.

A similar bimodal pattern was seen in each of Subject DS's three paradigms (see Figure 6.7 below). The maxima and minima were consistent between paradigms while the relative amounts of early and late saccades varied from one paradigm to another. The high number of express saccades made by Subject DS may have been due in part to the
predictability of the target direction and approximate eccentricity, although these factors did not induce express saccades in any other subjects.

Express saccades have been reported to show a low gain and almost never overshoot the target (Fischer et al., 1993). An increased scatter in the amplitude of the primary express saccades could also be observed in the data of Fischer et al., (1993). Express saccades are believed to be generated via the superior colliculus as collicular lesions (in monkey) abolish the ability to make express saccades (Schiller et al., 1987).

In order to investigate the effect of these distinct populations of saccades, the data from Subject DS were divided into 'express saccades' and 'non-express saccades' by imposing an artificial division at 143 msec (the estimated minima between the two peaks). It was found that the mean gain of the express saccades (0.846) was substantially lower than the mean gain for the non-express type saccades (0.949), while the standard deviation for express saccades was much higher (0.129 for express saccades in contrast to 0.052 for non-express type saccades). See Figure 6.8 (below).
It has been not reported whether express saccades can be independently adaptively controlled. While it has been shown that adaptation of normal reflexive saccades may be substantially transferred to express saccades in monkey (Fuchs et al., 1996), similar investigations have not been done in humans. Thus, we investigated how the high amount of express saccades, especially in the random paradigm, may have affected any gain changes seen in Subject DS. Figure 6.9 shows the pre- and post-adaptation gains for express and non-express type saccades for Subject DS in each of the three adaptation paradigms.

![Graphs showing gain changes before and after adaptation for express and non-express saccades over three paradigms.](image)

**Figure 6.9.** The average gains before and after adaptation for express (solid lines) and non-express type (dashed lines) saccades for Subject DS in each paradigm.

The express type saccades showed a lesser magnitude of adaptive change relative to the non-express type saccades in the gain increasing and gain decreasing paradigms but a larger magnitude of change in the random paradigm. This greater magnitude of change in the random paradigm may have been due to the larger percentage of express-type saccades made in this paradigm. These results suggest that express saccades can be adapted independently.

### 6.4 Discussion

The aim of randomising the direction of the intrasaccadic target step in the random paradigm was to eliminate *average* post-saccadic retinal error over the course of the experiment. If the minimisation of average post-saccadic retinal error was a goal of the
saccadic system we would not expect any adaptive change to the gain of saccades in the random paradigm. On the other hand, if the system were trying to minimise saccadic flight-time we would expect a decrease in gain as the system attempts to compensate for the increase in standard deviation of the apparent error.

The gain increasing and gain decreasing paradigms not only confirmed that each subject was capable of adaptively manipulating gain in both directions, but also enabled a quantitative comparison of the magnitude of the adaptive change in the random paradigm to be made with the increasing and decreasing paradigms.

Our result that the random paradigm showed significant gain decreases is not compatible with the theory that the adaptive controller is attempting to minimise average post-saccadic retinal error, and provides support for the SFM hypothesis.

The magnitude of gain changes varied both between subjects and between paradigms. It was greater in the gain decreasing paradigm than the gain increasing paradigm except in Subject DS. This supports previous findings regarding the differences in the magnitude and rate of adaptation (Miller et al., 1981, Deubel et al., 1986). The reason for the unique results of Subject DS are discussed in Section 6.4.6.

6.4.1 Support for the saccadic flight-time minimisation hypothesis

Our findings are compatible with the predictions made by the SFM hypothesis (Harris, 1995). This hypothesis predicts that when the standard deviation of the saccadic error is large, the optimal gain decreases in order to prevent overshooting saccades and minimise saccadic flight-time. In the random paradigm the saccadic system is induced to make far more overshooting saccades, and relatively larger undershooting saccades, than normally expected. This is due to the random onwards and backwards intrasaccadic displacement of the target. Thus, the standard deviation of the error is large. Being unaware of the intrasaccadic target displacement, this error is attributed to internal rather than external causes. The SFM hypothesis predicts that this large standard deviation will
induce the adaptive system to lower the gain of the primary saccade. This will bring the amount of overshooting saccades back down to an acceptable level in order to minimise saccadic flight-time to this apparent 10° target eccentricity. For the reasons discussed previously related to the main sequence for duration of saccades, overshooting saccades are not required to be completely eliminated in order to minimise saccadic flight-time (see Section 1.5.3).

6.4.2 Previous studies

Although the mixing of gain increasing and gain decreasing adaptive trials for saccades to the same target eccentricity, as in our random paradigm, has not been investigated previously, two studies have reported results when gain increases and gain decreases were induced to separate target eccentricities, though both in the same direction (Miller et al., 1981; Semmlow et al., 1989). Miller et al., (1981) induced gain increases to a small target eccentricity (3°) and gain decreases to a large target eccentricity (12°) in three subjects. Two subjects showed a simultaneous decrease in gain to the large saccade with an increase in gain to the small saccade, while the third showed a decreased gain to both. The simultaneous decrease to one eccentricity and increase to another eccentricity seen in two subjects contradicts the ‘parametric’ nature of the adaptive gain control and supports the more recent view regarding ‘restricted adaptation fields’ (Frens and van Opstal, 1994); that the effects of adaptation are restricted and do not necessarily transfer to saccades of other amplitudes, or directions (see Section 1.6.4. Is adaptive control really parametric?). However, the results of Miller et al., (1981) may have been confounded by the range effect. The range effect causes small target eccentricities to be overshot and large target eccentricities to be undershot when presented in the same paradigm (Kapoula, 1985). The pattern of results seen in the two subjects discussed above would be predicted by the range effect, and may not be wholly as a result of adaptive control processes.
Semmlow *et al.* (1989) avoided the possible confounding influence of the range effect, in a ‘dual adaptive training’ paradigm, by inducing gain changes in the opposite direction to those changes that may be caused by the range effect. Semmlow induced gain increases to an +8° target eccentricity and gain decreases to a +5° target eccentricity. The size of the intrasaccadic target step was also different for each of these eccentricities. When the intrasaccadic target steps were relatively small (+4° (ie 50%) for the +8° target eccentricity; -1° (ie 20%) for the +5° target eccentricity) gain increases were seen for the +8° target eccentricity and gain decreases for the +5° target eccentricity. This result demonstrated that separate adaptive processes could indeed take place to separate saccade amplitudes. Semmlow *et al.* (1989) described the range of saccade amplitudes that are affected by adaptation to a single saccade amplitude as ‘activity regions’. This supports the results of Miller *et al.* (1981) and the idea of restricted adaptation fields introduced later by Frens and van Opstal (1994). However, if the intrasaccadic target steps were much larger (+8° (ie 100%) for the +8° target; -2° (ie 40%) for the +5° target), gain reductions were seen to both 5° and 8° target eccentricities. Semmlow *et al.* (1989) interpreted this result as suggesting that the training stimulus to the 5° target was more effective and that the overall decrease represents a superimposition of the individual influences of the two activity regions. An alternative explanation is however possible. A subject would certainly be aware of an intrasaccadic target step of +100%. Bridgeman *et al.* (1975) determined that intrasaccadic targets steps are undetectable if they are less than about 30% of the original eccentricity. This 100% target displacement is so large that the subject may treat the target position before and after the intrasaccadic step as two separate and unrelated events, and not due to an internally generated targeting error. In this case, there would be no adaptive influence to increase the gain to the 8° target eccentricity. As such, the only influence on the 8° target eccentricity would be the gain decreasing influence from the 5° target eccentricity, given that the adaptation field of the 5° target
eccentricity had some overlap with the adaptation field of the 8° target eccentricity. An interesting aspect to the findings of Semmlow et al. (1989) was that gain reductions were approximately equal to the sum of induced changes produced by each of these adaptive paradigms when administered alone. These findings suggest that activity regions are subject to first order relationships between gain increasing and gain decreasing modifications when these are induced to overlapping activity regions.

In the random paradigm in this experiment opposing adaptive gain changes were induced on an identical activity region. If there were a first order relationship between the gain modification processes, we would expect to see this reflected in our results, i.e. the difference in magnitude between the gain increasing and decreasing paradigms should approximately equal the change in magnitude in the random paradigm. Evidence from the six subjects in this experiment was not conclusive. The relationship can be seen in Figure 6.5B (page 179). No subject had an identical match between the magnitude of gain change in the random paradigm and the difference between the increasing and decreasing paradigms. Subject DS had particularly divergent results.

Apart from the lack of data points to make a reliable judgement about the presence of a linear relationship between gain increasing and decreasing elements, there are two other factors that may confound this result. Firstly, natural day-to-day variations within subjects may affect their adaptive capabilities. Variation in baseline saccade metrics on different days (i.e. in the separate adaptive paradigms) in the same subject was seen in our data. While some subjects varied by as little as 0.006 units of gain in their pre-adaptive baseline over the four sessions, others varied by as much as 0.059 units of gain. Given this variation in behaviour, we would not expect to see a robust linear relationship, unless perhaps the three paradigms could all be recorded within the same experimental session. Second, the number of adaptive trials being compared are not matched. The gain increasing and gain decreasing paradigms both involve 200 adaptive trials in each direction, while the random paradigm only involves 100 trials in each direction. On the
other hand, the majority of adaptation occurs within the early part of an adaptive experiment (Deubel et al., 1986). If the lower number of adaptive trials each direction in the random paradigm did have an effect, we would expect to see consistently less adaptation in the random paradigm. This was not the case.

6.4.3 Separate adaptive elements?

The finding of the separate strengths of the gain increasing and gain decreasing adaptive processes, and the first-order relationship between them proposed by Semmlow et al. (1989) that is not clear in our results, suggests that the time-constants of the adaptive elements are separate; which begs the question as to what mechanism sets these time constants? There would have to be a supervisory mechanism to determine the appropriate time-constants in order to maintain the optimal gain.

It is possible that the different time constants could be an artefact of intrasaccadic target displacement paradigms in which error is induced to the primary saccade only. If the activity regions of the primary and corrective saccades overlap at all then the adaptive influence of these regions would be combined. In the gain increasing paradigm the corrective saccade is in the same direction as the primary saccade, yet error is only induced to the primary saccade. As such, the brain may receive conflicting signals regarding saccadic error. The lack of error after the corrective saccade contradicts the presence of error after the primary saccade. This may attenuate the rate of gain change in the gain increasing paradigm. In the gain decreasing paradigm in contrast, the corrective saccade is made in the opposite direction to the primary saccade. Therefore the activity regions of the primary and corrective saccade will not overlap, due to the known directional specificity of adaptation, and they will have no influence on each other.

Empirical support for this idea comes from the adaptive control experiments of Albano and King (1989). They induced intrasaccadic target steps to all saccades made in a sequence. Each time a saccade was made, the target was moved by an amount relative to
the size of the saccade. They found that in this case the rate of adaptation in the gain increasing and the gain decreasing paradigms were the same.

6.4.4 Alternative explanations for our results

Our results indicate that average retinal error is not minimised over the course of the experiment. There is however an alternative explanation that could account for our results given the separate adaptive processes. Minimisation of retinal error could still be the goal of the system if adaptive changes were imposed, not on the basis of average retinal error over time, but on a trial-to-trial basis. Error control on a trial-to-trial basis can be seen to hold advantages in the immediacy of the compensatory response, and also because there is no need for any sophisticated averaging of error over time, or memory demands for previous errors. Given the differing strengths of the gain increasing and gain decreasing elements, if each trial were to independently invoke an adaptive change, this could also explain the overall decrease in gain in the random paradigm. It is of course possible that there is not just one goal driving adaptive control processes. Two, or more, processes may work in combination. The drive to minimise saccadic flight-time may be a long-term process which oversees a short-term (trial-to-trial) adaptive process driven by retinal error. In this scenario, the gain increasing and gain decreasing elements would have their time constants set by the system in order to facilitate the minimisation of saccadic flight-time

6.4.5 The error signal

The error signal used by the saccadic system to drive adaptive control has generally been assumed to be a post-saccadic visual error signal (Deubel et al., 1986) and this has been used in models of the adaptive control system (Optican, 1982). Recently, Wallman and Fuchs (1998) investigated the distinctions between visual error and motor error in driving the adaptive processes and determined that a motor error input is not
essential to the adaptive control system while a visual error input is required to drive adaptation. They used a novel paradigm, the so-called Deubel paradigm, a variant of the traditional adaptive control experiments. In this paradigm, the intrasaccadic target step was only briefly displaced (backwards) before returning to the original step position before any corrective saccades. See Figure 6.10.

Figure 6.10. To demonstrate the behaviour of the target in the Deubel adaptation paradigm in the paper of Wallman and Fuchs (1998). The eye movement trace (solid line) is offset slightly from the target movement (dashed line) to make the figure clearer.

Thus at the end of the primary saccade the target was in its backwards displaced position, as it would be in a normal adaptation paradigm, however, before the corrective saccade was made, the target moved back to the original position. The remarkable finding using this Deubel paradigm was that in spite of the induced hypermetria (of the primary saccade) there were very few (average 1.2%) backward correctives elicited. This must mean that the movement of the target from its intrasaccadically displaced position back to the original displaced eccentricity was still available to the visual system in enough time to cancel the corrective saccade that would have been planned on the basis of the retinal error after the first saccade. This cancellation and reprogramming of the corrective saccades was reflected in the long intrasaccadic interval for correctives in this Deubel paradigm which can be ascertained from Figure 1 in the paper of Wallman and Fuchs (1998). Furthermore, despite the lack of backward correctives, the saccadic gain was adaptively decreased over the course of the experiment. This finding provides convincing evidence that the driving signal for adaptive gain decreases, in this paradigm at least, does not originate from the (backwards) corrective motor behaviour. On the other hand, it cannot be ruled out that it is the efference copy signal from the planned corrective motor behaviour, on the basis of post-saccadic retinal error rather than the actual motor
behaviour, that is being used. Qualitative differences between this Deubel paradigm and conventional adaptive control such as the relatively constant rate of adaptive change without the usual initial rapid rate of gain decrease may also suggest that the adaptive processes are different in some way. Nevertheless, the interpretation of Wallman and Fuchs (1998) was that motor error input is not essential to the adaptive control system, but that it is the visual error signal that drives saccadic adaptation. Furthermore, this visual error signal is only required briefly in order to elicit adaptation.

The minimisation of saccadic flight-time does not necessarily need to depend on a flight-time error signal. It could also be accomplished indirectly by adjusting another parameter such as visual or motor error to obtain the optimal gain level. For example, adjusting gain to maintain a fixed proportion of overshoots which would in turn minimise flight-time. This process could be enabled using either a visual error signal or a motor error signal. This form of indirect flight-time minimisation supports the existence of gain increasing and gain decreasing elements with different time constants in order to maintain the gain at an optimal undershooting level. However, ultimately there would have to be an overall supervising mechanism to maintain the time constants of these separate increasing and decreasing elements.

6.4.6 Express saccades

There have been no reports of adaptation experiments that have specifically independently adapted express saccades. This would require a target control system which could elicit intrasaccadic target steps dependent on the latency of the primary saccadic response. Most subjects do not make many express saccades in normal (no-gap) paradigms with appropriate time randomisation. In our assessment of 20 subjects in Chapter 5 there were only two subjects who showed possible bimodality, with peaks at 110 and 120 msec. However, unlike Subject DS, these peaks were small relative to the later peak. Subject DS did not participate in the experiment in Chapter 5.
Saccades of different types are known to be generated by different pathways (Tusa et al., 1986, Pierrot-Deseilligny et al., 1995). There is convincing evidence that saccades of different types can be separately adapted in humans (Erkelens and Hulleman, 1994; Deubel, 1995) (see Section 1.6.4) which suggests that the adaptive control mechanisms for these different types of saccades may be independent. Both of these studies examined the transfer of adaptation between voluntary saccades (to stationary targets or in a scanning paradigm) and reflexive saccades (to jumping targets). These types of saccades are thought to differ primarily in their cortical origins, while express saccades are believed to be generated subcortically by a direct retino-collicular pathway (Schiller et al., 1987). Fuchs et al. (1996) are the only group to have investigated the transfer of adaptive changes between reflexive saccades and express saccades. They found that adaptive changes to reflexive saccades transferred by 91% to express saccades in monkeys.

Although this suggests that adaptive changes to reflexive saccades can be transferred to express saccades, this result must be treated with caution when extrapolating to humans as their other results regarding gain transfer to other types of saccade do not agree with the studies in humans already mentioned. In contrast to Erkelens and Hulleman (1994) and Deubel (1995) who found little transfer of adaptation between voluntary and reflexive saccades in humans; Fuchs et al. (1993) found that there was a significant level of transfer between different types of saccades in monkeys.

Our results suggest that express saccades can be independently adapted. This can be deduced by comparing the percentage of express saccades made with the amount of adaptive change in each of the three paradigms that subject DS completed. In the gain increasing and gain decreasing paradigms the minority of saccades made were of the express type and the amount of gain change in the express type saccades was less than that of the non-express type saccades. Thus the adaptive change in the express type saccades may be attributed to adaptive transfer from the non-express type saccades, or could have been independently adapted. However, in the random paradigm, the majority
of the saccades are of the express type, and the magnitude of change in the express type saccades is greater than in the non-express type saccades. It seems unlikely from previous evidence that the adaptive change induced to the non-express type saccades could transfer by more than 100% to express type saccades. Thus the evidence suggests that express saccades can be independently adapted and this adaptation must take place at a low level due to the direct retino-tectal-brainstem pathway attributed to express saccades.

Fitzgibbon et al. (1986) have reported that adaptation does not take place at the level of the superior colliculus. Low level input from the cerebellum is of course a possibility, given its known involvement in the adaptive control of other types of saccades.

The independent adaptation of express saccades does not necessarily indicate that there are also independent mechanisms of adaptation. The same adaptive controller could be influencing express and non-express types of saccades simultaneously. An interesting experiment that could be done to clarify whether there are separate adaptive mechanisms at work would be to induce opposing adaptive gain changes to express and non-express type saccades. Such an experiment would depend on having an express saccade maker, such as Subject DS. With software modification, an intrasaccadic target step onwards could be elicited for saccades with latencies in the express saccade range, and a backwards target step for saccades in the normal latency range. Divergent adaptation of these two types of saccades would confirm that they must be under independent adaptive controlling mechanisms.

6.5 Conclusion

In this chapter the adaptive capabilities of the saccadic system have been demonstrated. Gain increases and gain decreases were induced, as predicted by previous studies, with distinct time constants. The random paradigm induced an adaptive decrease
in the gain of saccades. This result indicates that the drive of the adaptive control system is not to minimise average post-saccadic retinal error. This result supports the SFM hypothesis. This hypothesis predicts that the gain of the saccades is decreased in order to minimise saccadic flight-time and due to the increase in the standard deviation primary saccade gain over the course of the adaptive phase of the experiment.

An express saccade maker was serendipitously recruited as one of the subjects in this experiment. The high standard deviation of the gain and the reciprocally low baseline gain in this subject also supports predictions of the SFM hypothesis. Results from this subject additionally indicated that express saccades can be independently adapted from normal reflexive saccades.

In the following chapter this method of inducing adaptive gain changes using the intrasaccadic target displacement paradigm is applied in a clinical context to children and young adults with Dancing Eye Syndrome (opsoclonus myoclonus).
Chapter 7. Adaptive Control in Patients with Dancing Eye Syndrome

7.1 Introduction

In the previous chapter, an adaptive control paradigm was used to investigate the plasticity of the saccadic system in normal adults. The aim of the experiment described in this chapter was to apply this technique in a clinical context to patients who are suspected of having defective adaptive control capabilities by virtue of their dysmetric eye movements. To our knowledge, the use of an intrasaccadic target displacement paradigm has only been used once before to investigate adaptive control in adult patients with Wallenberg’s lateral medullary syndrome (Waespe and Baumgartner, 1992). An additional challenge of this experiment was to apply this technique to children and young adults.

The adaptive control system is continuously active, monitoring the performance of the saccadic system in order to maintain the optimal accuracy of saccades with respect to their target. As such it compensates for changes in the metrics of saccades, whether they are caused by natural processes such as growth and ageing, or disease processes or trauma. If the adaptive control system is functioning properly a lesion elsewhere in the oculomotor system causing saccadic dysmetria may be masked through the adaptive compensatory processes. A lesion in the adaptive control system itself may also result in persistent dysmetria.

The adaptive control system for saccades has been experimentally localised to the vermis of the cerebellum and fastigial nucleus in monkeys (Optican and Robinson, 1980). There is evidence for a homologous localisation in humans (Selhorst et al., 1976, Vahedi et al., 1995, Waespe and Muller-Meisser, 1996). The adaptive control system has been intensely investigated in normal adults (eg McLaughlin, 1967; Miller et al., 1981; Wolf et al., 1984; Deubel et al., 1986; Erkelens and Hulleman, 1993; Frens and van Opstal,
1994). However, the adaptive behaviour of the oculomotor system has rarely been explicitly investigated before in clinical populations. Waespe and Baumgartner (1992) are the only team to have used an intrasaccadic target perturbation paradigm. Other studies have all employed optical devices, either prisms or magnifying lenses to induce oculomotor adaptation (Gauthier et al., 1979; Weiner et al., 1983; Sanes et al., 1990).

The technique described in the previous chapter enables the dynamic behaviour of the adaptive control system to be directly investigated. By examining adaptive control directly we are able to measure the active functioning of the adaptive control system, rather than the passive affects of its failure, in terms of saccade dysmetria.

7.1.1 Saccadic dysmetria in clinical populations

We have reported previously that children with homonymous hemianopia generally undershoot visual targets in their blind hemifield (Mezey et al., 1998 and see Chapter 3). Some patients with homonymous hemianopia are also reported to show some saccadic hypermetria (Meienberg et al., 1981; Mezey et al., 1998). This form of saccadic inaccuracy is believed to be a deliberate compensatory saccadic strategy employed in order to achieve fixation of the target in the most appropriate manner in the face of the missing visual information from one hemifield. They are not presumed to be the result of defective adaptive control. In fact, we proposed in Chapter 3 that these strategies are a direct result of adaptive control processes. These results further demonstrate that the state of the adaptive control system cannot be understood simply by the examination of the saccadic accuracy. It is important to remember that the accuracy of saccades depends on the context in which they are elicited. For example, predictive saccades are found to have low gains (Bronstein and Kennard, 1987).

In general, saccadic dysmetria is often associated with lesions of the vermis of the cerebellum and/or the deep cerebellar nuclei (Selhorst et al., 1976; Bötzel et al., 1993; Vahedi et al., 1995; Waespe and Muller-Meisser, 1996). Evidence from numerous clinical
and experimental studies have demonstrated that saccadic hypometria and hypermetria are caused by distinct lesions in these areas (see Buttner and Straube, 1995).

One clinical population in which saccadic dysmetria has been reported is in patients with Dancing Eye Syndrome (DES). Patients with DES are reported to have overt saccadic hypermetria (Shawkat et al., 1993). It is unknown however whether there are persistent oculomotor abnormalities after resolution of the acute symptoms of DES. If there is persistent dysmetria, this suggests that the adaptive control system of these patients has been permanently damaged by their disease.

7.1.2 Dancing Eye Syndrome

Dancing Eye Syndrome is a rare neurological condition characterised by opsinclonus and myoclonus. Opsinclonus is spontaneous, chaotic, involuntary bursts of back-to-back saccades in all directions. These oscillations are usually short in duration, in the order of a few 100msec, and are often precipitated by refixation saccades or blinking. Myoclonus is the occurrence of similarly jerky involuntary movements, though of the limbs. These symptoms can vary greatly in severity and the degree of incapacity they cause to the patient. Onset is usually in childhood, generally under 3 years of age, and although there can be good recovery from the acute and obvious symptoms of opsinclonus and myoclonus, there are often found to be long-term neurological sequelae (Hammer et al., 1995; Papero et al., 1995; Pohl et al., 1996; Russo et al., 1997) These include learning difficulties, speech problems and motor abnormalities such as persisting residual fine motor co-ordination and ataxia. The aetiology of DES is as yet unknown. It can be a paraneoplastic sign or may be preceded by an infectious illness. The acute symptoms of the disease are initially treated with steroids (prednisolone) or corticotrophin. The duration of opsinclonus or myoclonus has been found to vary from 3 months to 15 years (with symptoms still on-going) (Pohl et al., 1996). In many patients the symptoms of DES may worsen on withdrawal from steroids, or with episodes of illness.
The site of the neuro-anatomical pathology is still unknown. While the presence of a saccadic disorder suggests a lesion somewhere within the saccadic pathway there has been no consistent direct evidence from either imaging or EEG studies as to the exact site of the lesion. There have been two reports of cerebellar abnormalities on computerised tomography (CT) (Tuchman et al., 1989) and SPECT (single photon emission-CT) (Oguro et al., 1997). Indirect evidence for the involvement of the cerebellum is also provided by eye movement studies. In addition to the obvious opscoclonus, saccadic eye movements have been reported to be grossly dysmetric (Shawkat et al., 1993). This further points to the involvement of the cerebellum. The dysmetria reported by Shawkat et al. (1993) was found in five patients with DES who were still experiencing frequent episodes of opscoclonus.

It is not known whether long-term neurological sequelae are manifest in the saccadic system after recovery from the acute symptoms of DES. One of the 5 patients studied by Shawkat et al. (1993) was reviewed after the opscoclonus (and ataxia) had subsided and was shown to have persistent saccadic hypermetria. There are many reports of long-term cognitive deficits in children with DES. This suggests that there are neurological effects that persist after the resolution of the acute symptoms of opscoclonus and myoclonus.

We set out to investigate a group of children and young adults with apparently resolved DES to assess whether there are persistent deficits in adaptive control. The adaptive control capabilities of these patients were tested by using the gain decreasing paradigm as described in the previous chapter.
7.2 Methodology

7.2.1 Subjects

Seven patients with Dancing Eye Syndrome were recruited through the Dancing Eye Syndrome Support Group. Informed consent was obtained from both the children and parents who took part in this study. There were 4 boys and 3 girls with an age range of 10 to 19 years old (average 15.4 years). All patients were tested in their normal refractive state, to prevent confounding factors due to optical corrections. None had a squint.

All patients had been diagnosed with Dancing Eye Syndrome. The average age of onset was 21.7 months. All had initially been treated with steroids. All patients were drug-free at the time of recording (for a minimum of 7 years). No episodes of opsoclonus were noted during recording, nor reported by the parents of the patient. Long-term neurological deficits were reported in 5 of the 7 patients.

Control subjects with an age range of 8-27 years (average 19.1 years) were recruited. None had any known neurological disorder.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at recording</th>
<th>Age at presentation</th>
<th>Treatment</th>
<th>Drug-free years</th>
<th>Opsoclonus now?</th>
<th>Learning Difficulties?</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR</td>
<td>15 years</td>
<td>20 months</td>
<td>Pred</td>
<td>8</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>CC</td>
<td>14 years</td>
<td>21 months</td>
<td>Pred</td>
<td>10</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>JG</td>
<td>19 years</td>
<td>27 months</td>
<td>ACTH</td>
<td>12</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>ND</td>
<td>10 years</td>
<td>~24 months</td>
<td>ACTH</td>
<td>~8</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>SD</td>
<td>18 years</td>
<td>22 months</td>
<td>unknown</td>
<td>13</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>DR</td>
<td>15 years</td>
<td>18 months</td>
<td>ACTH</td>
<td>7</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>JA</td>
<td>17 years</td>
<td>20 months</td>
<td>ACTH</td>
<td>10</td>
<td>no</td>
<td>yes</td>
</tr>
</tbody>
</table>

Table 7.1 Summary of patient details. Pred- prednisolone, ACTH - adrenocorticotropic hormone

7.2.2 Experimental set-up

Experiments were performed under dimmed lighting conditions. The full details of the experimental set-up have been described previously (Chapter 2, Methodology). In brief, the patients were seated comfortably in a chair with their head supported by a chin-
rest in front of a large white screen. The target stimulus was a red laser spot, front-projected on to the screen and controlled by an x-y laser deflection system.

Eye movements were recorded with an infra-red eye tracker (IRIS eye tracker, Skalar Medical). In order to calibrate the recorded eye movements, subjects were first required to fixate 6 points along the horizontal axis, located at 5, 10 and 15 degrees eccentricity either side of the central fixation point.

7.2.3 Experimental paradigm

In this experiment we wished to determine both the metrics of saccades in DES patients and their adaptive capabilities. The experimental paradigm used in this experiment was similar to that described in the previous chapter. This paradigm allowed both of these parameters to be determined in each patient. The pre-adaptive phase was used to determine the baseline gain for each patient. This baseline was determined for centrifugal 10° rightward saccades.

Only the gain decreasing adaptive control paradigm was used. This is because gain decreasing paradigms are known to elicit the fastest and largest adaptive changes in saccadic gain and thus are most suitable to investigate the adaptive control system in as short a time as possible. The baseline gain was used to determine the amount of adaptation that had taken place over the course of the experiment by comparing it to the average gain of saccades after the adaptive phase.

In order to reduce the overall length of the experiment for children while preserving the number of trials within the adaptive phase, the pre-adaptive phase and the post-adaptive phase were reduced to 25 trials each. Although the experiment still lasted almost 20 minutes, it was hoped that this reduction in the length of the experiment would make it more likely that these younger patients would be able to complete the experiment. Completion is important to allow comparison of the pre- and post-adaptive trials in order
to assess the presence and magnitude of adaptation. All patients successfully completed
the full experiment with encouragement.

The experiment consisted of three different phases presented in series with no
breaks between each phase: the pre-adaptive phase (25 trials), the adaptive phase (200
trials) and the post-adaptive phase (25 trials). Although breaks may have facilitated
comfort and concentration during the experiment, they could not be allowed as it is
fundamental that the subject received the appropriate visual feedback at all times.

All testing took place to an initial target step of 10° to the right of the central
fixation target. During the adaptive phase of the experiment the target made an
intrasaccadic target step of 2° backwards so that the final position of the target was 8°
right. In all trials the target spot began at the central fixation point and then after a
randomised time delay (1500-3500msec) jumped to a peripheral position of 10° to the
right of the centre. In the pre- and post-adaptive phases the spot then remained at this
position for 1000msec before returning to the centre where it again remained for
1000msec before the start of the next trial. In the adaptation phase eye velocity was
monitored on-line by computer and a secondary target step was elicited when an eye
velocity threshold of 100°/sec was reached. The target remained in this new position for
1000msec before returning to the centre.

Only centrifugal saccades were recorded and analysed.

7.2.4 Data analysis

All eye movement records were inspected off-line by the experimenter. Trials
which contained saccades closely associated with blinks; with latencies in the predictive
saccade range; or with excessively long durations due to glissadic endings were excluded
from the analyses. A trial consisted of all saccades made within 900 msec of the first
movement of target. Our standard computer paradigm supplied all timing, metric and
dynamic aspects of each saccade made within each trial in off-line analysis. The
parameters of the computer program used to detect saccades has been discussed in detail previously (see Chapter 2, Methodology).

Some subjects were much more consistent than others. The number of trials excluded in each patient varied greatly. In general, the younger the patient or control subject, the more trials had to be excluded. The number of trials excluded from the total of 250 made by all DES patients ranged from 2% in the oldest (19 years old) patient, to 32% in the youngest (10 years old).

The saccadic response from each trial was individually calibrated. Baseline saccade metrics were assessed in the pre-adaptive phase of the experiment. The amount of dysmetria was assessed by analysing both the average primary saccadic gain and the percentage of overshooting saccades over this pre-adaptive phase. It is useful to examine both the gain and the average number of overshooting saccades as a significant amount of hypermetria may be disguised when the gains of overshooting saccades are averaged together with undershooting saccades. Adaptive capabilities were assessed by investigating the change in average gain between the pre-and post-adaptation phases.
7.3 Results

All the DES patients that volunteered to take part in this study were able to complete the experiment successfully. No episodes of opsinclonus were noted during the recording sessions.

7.3.1 Saccade metrics

The results from this group of DES patients produced a mixed picture. See Table 7.2 for a summary of the saccade metrics.

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>DES patients</th>
<th>Control subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gain</td>
<td>SD</td>
</tr>
<tr>
<td>ND</td>
<td>1.04</td>
<td>0.05</td>
</tr>
<tr>
<td>CC</td>
<td>0.94</td>
<td>0.03</td>
</tr>
<tr>
<td>AR</td>
<td>0.96</td>
<td>0.04</td>
</tr>
<tr>
<td>DR</td>
<td>0.63</td>
<td>0.09</td>
</tr>
<tr>
<td>JA</td>
<td>0.90</td>
<td>0.05</td>
</tr>
<tr>
<td>SD</td>
<td>0.80</td>
<td>0.07</td>
</tr>
<tr>
<td>JG</td>
<td>1.00</td>
<td>0.05</td>
</tr>
<tr>
<td>Average</td>
<td>0.90</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Table 7.2 Average primary saccade gains and percentage of overshooting primary saccades of DES patients and controls. The results are presented in order of age, youngest at the top.

The average saccadic gain in our control subjects was 0.94. The range of values was 0.90-0.99. On average, control subjects made few overshooting saccades (9.3%). The two youngest patients both made a relatively large amount of overshooting saccades. This may have been an age-related factor, although an increased percentage of hypermetric saccades has not been reported in younger children before.
Three patients (CC, JA, AR) had saccade metrics within the ranges determined from our group of age-matched control subjects and made less overshooting saccades than the average for the control group.

Two patients showed clear saccadic hypermetria. See Figure 7.1 (below). These patients had average primary saccadic gains of 1.000 (JG) and 1.042 (ND) and percentages of overshooting saccades of 60.3% and 86.4% respectively. Both patients were also noted to have some variable dynamic overshoot.

![Patient JG](image1)

![Patient JG](image2)

![Patient ND](image3)

![Patient ND](image4)

Figure 7.1 Representative eye movement traces from the two subjects who had hypermetric saccades.

Two patients showed saccadic hypometria (SD and DR). See Figure 7.2. These patients had saccadic gains of 0.80 (SD) and 0.63 (DR) and neither made any overshooting saccades. In the previous chapter it was found that the low gain saccades in one subject resulted from a bimodal latency distribution in which the low gain saccades
were ‘express saccades’ with a primary latency in the order of 118msec. Normal primary saccade latency are generally within the range 150-220msec (Becker, 1989). There was no bimodality in the latency distributions for either of the subjects with low gains in this experiment. Their minimum reaction times, over the course of the whole experiment, were 156msec (SD) and 178msec (DR).

![Graphs of eye movements](image)

**Figure 7.2** Representative eye movement traces from the two subjects who had hypometric saccades.

### 7.3.2 Adaptive capabilities

All control subjects showed a significant decrease in gain over the course of the adaptive phase of the experiment. The magnitude of the gain decrease in control subjects ranged from -0.072 to -0.126 (average -0.098). Although two of the younger control subjects had the lowest magnitude of gain change, there was no clear affect of age on adaptive capabilities. See Table 7.3.
### Control Subjects for adaptation

<table>
<thead>
<tr>
<th>Control</th>
<th>Age</th>
<th>Magnitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>-0.072</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>-0.075</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>-0.094</td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>-0.095</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
<td>-0.139</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>-0.084</td>
</tr>
<tr>
<td>7</td>
<td>27</td>
<td>-0.126</td>
</tr>
<tr>
<td>Average</td>
<td>19.1</td>
<td>-0.098</td>
</tr>
</tbody>
</table>

Table 7.3. The age and magnitude of adaptive gain change during the gain decreasing paradigm in the 7 control subjects for adaptive capabilities.

Six out of the seven DES patients showed a significant decrease between the pre-adaptation baseline gain and the post-adaptation gain. See Figure 7.3. The average magnitude of gain change in these 6 subjects was -0.111. This is similar in magnitude to the average gain decrease of our control subjects (-0.098, range -0.072 to -0.126). Both of the patients with initially hypermetric saccades (JG and ND) showed a significant decrease in gain. This suggests that the presence of hypermetria does not necessarily indicate that the adaptive control capabilities have been compromised. Patient SD with hypometric saccades in the pre-adaptive phase also showed a significant decrease in gain. Patient DR, however, with the grossly hypometric saccades in the pre-adaptive phase, did not show a significant change in gain over the adaptive phase of the experiment. In fact, he showed a small, though not statistically significant, increase in gain (+0.042). Table 7.4 on page 207 lists the gain values and percentage of overshooting saccades for each patient in the pre- and post-adaptive phases as well as the magnitude of the gain change.
7. Dancing Eye Syndrome

Figure 7.3 The mean primary saccadic gain (and 95% confidence interval bars) before and after adaptation for each individual patient. The shaded area represents the 95% CI range for the mean gain of control subjects (0.90-0.97)
Table 7.4. The average primary saccadic gain (gain) and percentage of overshooting saccades (% o/s) before and after adaptation, and the magnitude of the change in gain are presented for each DES patient separately. A negative value of gain difference indicates a decrease in gain. ** indicates significance to level p<0.01 (repeated measures ANOVA with post-hoc testing).

Adaptive control is thought to be driven primarily by a visual error signal, and possibly a non-essential motor error signal (Wallman and Fuchs, 1998). The aim of the adaptive control paradigm is to induce such errors using the intrasaccadic target step. For a gain decreasing paradigm the presence of saccadic overshoot can provide the appropriate signal. In order to determine whether the appropriate overshoot error was being induced in each of our patients and control subjects, the presence of saccadic overshooting in the first 50 trials of the adaptive phase of the experiment was investigated. Only the first 50 trials from the adaptive phase of each subject were assessed in order to get an impression of the percentage of overshooting trials before adaptive processes had begun to take affect. Inter-subject differences in the rate of adaptation would soon begin to affect the relative amount of overshoot in each subject.

The control subjects all overshot the target an average of 82% (range 54-100%) of the time in the first 50 trials. In contrast, the two patients (SD and DR) with hypometric saccades in the pre-adaptive phase made relatively few overshooting saccades in this initial adaptive phase. Patient SD overshot the target only 17.4% of the time, while patient DR only overshot the target 2.9% of the time. The other five patients made between 73%
and 98% overshooting saccades in this initial adaptive phase (average 84%). This lack of overshooting saccades in patients SD and DR is due to the fact that, with such low gain primary saccades in these two patients, the initial saccade was still undershooting even the final position of the target, after the intrasaccadic step back. Thus backwards corrective saccades were rarely elicited. Nevertheless, in patient SD, there was no apparent attenuation of adaptive capabilities relative to controls in spite of this relatively low percentage of overshooting primary saccades. On the other hand, patient DR did not show any adaptation over the course of the experiment. The lack of adaptation by subject DR may have been as a result of how rarely he overshot the target.

7.4 Discussion

The aim of this experiment was to determine whether there are persistent oculomotor deficits in children and young adults with DES.

DES is known to have, in many cases, long-term cognitive and motor neurological sequelae (Hammer et al., 1995; Papero et al., 1995; Pohl et al., 1996; Russo et al., 1997). Residual deficits specific to the oculomotor system have been reported only once previously (Shawkat et al., 1993).

It was found that the adaptive control capabilities in a group of 7 patients with DES were generally preserved within normal ranges, even though there may be persistent dysmetria in some patients. The pattern of dysmetria was varied, and not related to the adaptive capabilities of these patients.

7.4.1 Saccade metrics in patients with DES

Of the seven patients in this study, three had no saccade dysmetria (normometria). two had saccadic hypermetria and two had saccadic hypometria. This finding is in contrast to the previous report of Shawkat et al. (1993) who found that all 5 patients with
DES in their study showed persistent saccadic hypermetria. Our results suggest that there may be a more diverse pattern to the symptoms and development of DES than indicated by this previous study.

Saccadic hypometria is known to be a deliberate strategy of the saccadic system in certain situations. This has been demonstrated in the context of saccades made into the blind hemifield by hemianopic children (Mezey et al., 1998, also see Chapter 3) and for antisaccades (see Chapter 4). In these situations the low gain is associated with a high standard deviation of the gain. Patient SD and Patient DR in particular both had low gains in association with a slightly increased standard deviation (see Table 7.2). The increase in standard deviation was not as marked however as the examples reported in the previous chapters. This finding nevertheless supports the saccadic flight-time minimisation hypothesis (Harris, 1995).

The consistent clinical findings of Shawkat et al. (1993) in contrast to the mixed findings of our study may have been due to a number of reasons. Firstly, the patients in Shawkat’s study were much younger in general (age range 18 months - 11 years) than the patients in our study (age range 10 years -19 years). As such, the time since the onset of the symptoms of DES was much greater in our study. A stereotypical pattern of the development oculomotor symptoms over time might be predicted in DES. For example, the hypermetria seen in the young patients is Shawkat’s study may develop over time into hypometria and/or normometria. Our findings do not lend support, however, to such a consistent developmental pattern of the eye movement symptoms in DES patients. No relationship was found between age and presence of hypermetria, hypometria and normometria. Consistent hypermetria was found in both the youngest (10 years) and oldest (19 years) patients in this study.

Secondly, and perhaps more significantly, all 5 patients in Shawkat’s study still had opsoclonus at the time of the eye movement recording. The presence of opsoclonus suggests active neurological problems. In contrast, in our study, none of the patients were
observed to show episodes of opsoclonus during the recording session, and reports from parents did not indicate the presence of opsoclonus in general. It could be that hypermetria is consistently associated with the acute stages of DES (specifically with ongoing episodes of opsoclonus) and that afterwards the eye movements may take a varied course of development depending on the disease process in each individual. This heterogeneous course of development is reflected not only in the oculomotor findings in this study, but also by the diversity in the type and severity of cognitive sequelae reported in DES patients (Pohl et al., 1996).

It is unlikely that further explanations for the differences in findings may be related to the experimental conditions or recording techniques. Hypermetric saccades are occasionally made in normal individuals, especially to small target eccentricities in the context of the range effect (Kapoula and Robinson, 1986), or to centripetal targets (Becker, 1989) but the consistent hypermetria reported by Shawkat et al. (1993), and in two patients in this study, could not be considered normal in the context of the reported experimental conditions.

This investigation involved only a single recording session. In the absence of prior records of the eye movements of the patients in this study it is not possible to report with certainty whether these dysmetric eye movements are indeed residual problems originating during the acute phase of the disease, or whether they are more recently developed. Furthermore, we do not know whether the 3 patients who had normal eye movements had indeed fully recovered from prior saccadic dysmetria, or whether they never developed saccadic dysmetria, even in the acute stage of the disease. This nevertheless seems unlikely given the previous report of Shawkat et al. (1993). It would seem probable that the eye movement symptoms reported are a direct result of the DES and originated around the time of onset of the syndrome.
7.4.2 Is adaptive control affected in DES patients?

Saccade metrics and adaptive control are intimately related. Patients with saccadic dysmetria were expected to have defective adaptive control capabilities. This was not necessarily found to be the case.

The three patients with saccadic metrics within normal ranges also had adaptive control capabilities within normal ranges. However, surprisingly, 3 of the 4 patients with dysmetric saccades were also found to have adaptive control within normal ranges. Given the ability to manipulate gain, one would expect the adaptive control system to be able to maintain the saccadic gain within normal ranges, this was evidently not the case in these three patients. This implies that the maintenance of the normal baseline gain, and the ability to manipulate this gain are not as directly linked as might be expected. A similar dissociation of the expected relationship between baseline gain and adaptive abilities has previously been reported in patients with Wallenberg’s lateral medullary syndrome (Waespe and Baumgartner, 1992). This dissociation supports the suggestion put forward in the previous chapter that the gain level is set by a mechanism that is independent to adaptive elements themselves. This is consistent with the saccadic flight time minimisation hypothesis (Harris, 1995) discussed previously. This requires the existence of an overall gain controller in order to set the time constants of the gain increasing and gain decreasing adaptive control elements. The anatomical location of this supervisory controller may be distinct or diffuse, cortical or subcortical. If this overall gain controller were lesioned or compromised in some manner so that the time constant of the adaptive gain control elements were no longer appropriate, this would not in itself affect the adaptive control processes, only the baseline level of gain. In this context, saccadic dysmetria can be understood to be a deficit in this supervisory mechanism and not necessarily with the adaptive gain controlling apparatus.

Only one of our 7 patients (DR) did not show a significant decrease in gain during the adaptive experiment. This may suggest that this patient had lost the capacity to
adaptively manipulate the gain of his saccades. This patient also had grossly hypometric saccades. In the context of this patient's apparent lack of adaptive capabilities this dysmetria could have been caused either as a direct result of the lack of adaptive capabilities, or due to deficits in the gain level set by the overall adaptive controller, as suggested in the cases above. If the dysmetria in this patient were caused by defective adaptive control processes, it would suggest that this degree of hypometria is a default level of gain that is programmed within with rest of the saccadic circuitry. In this case, the adaptive system functions to augment and fine tune the gain level set by the rest of the saccadic system in order to produce an optimal level of gain. The cerebellum is already known to provide such a supplementary role to the brainstem in the neural integration process of the saccadic command (Zee et al., 1980), augmenting the performance of the brainstem neural integrator.

The supervisory gain mechanism may in fact not be solely linked to gain control via the adaptive control elements of the cerebellum but also determine the activity levels in all parts of the saccadic circuitry, of which the adaptive gain controllers are just one element. As such gain control could be understood as a distributed process combining the inputs of many different parts of the saccadic system, some of which are more plastic than others.

There is an alternative explanation for the lack of adaptive gain decrease in Patient DR. Given the consistent gross undershoot of the target, even after the intrasaccadic step backwards, the lack of induced overshooting during the adaptive phase may have meant that a driving force to decrease gain was absent and the gain was already at a minimum level. If the adaptive control system were working, and the low level of gain was actually at a level imposed by the supervisory gain mechanism, albeit a level that is apparently less than optimal, then it is unclear why the system was unable to maintain this abnormal level of gain through adaptive processes. This is consistent with the idea that the presence of overshooting saccades is fundamental to the adaptive control process. It cannot indicate
however specifically what type of error that is required by the system to drive adaptive changes in gain.

Further investigations of this patient would be interesting to perform to see if adaptive control could be elicited under different circumstances. For example, using a larger intrasaccadic target step backwards, in order to elicit more overshooting saccades during the adaptive phase, or using a gain increasing paradigm with an intrasaccadic target step onwards to see if either of these situations could induce an adaptive modification of gain. It would also be interesting to examine his adaptive control capabilities in the opposite direction to see if his adaptive control deficits represent a lateralised disorder of the cerebellum.

Patient SD was able to adaptively decrease the gain of her saccades despite having relatively few induced overshoots during the adaptive phase of the experiment. If overshooting saccades are indeed required to induce a decrease in gain, this finding suggests that only a few overshooting saccades are required to induce an adaptive decrease in gain. In this case, the time constant of the decreasing gain controller in patient SD would be predicted to be much lower (i.e. a stronger adaptive effect) than the time constant of the increasing gain controller. In contrast, the actual presence of overshooting saccades may not be the important factor, but rather the deviation of the actual error (visual or motor) from the predicted error. Becker and Jürgens (1979) proposed that the saccadic system makes a comparison of predicted and real error in order to control the generation of corrective saccades. In this case, if the saccadic system were deliberately undershooting the target by a larger than normal amount (for whatever reason) it would work to maintain this degree of undershoot, even though it appears abnormal.
7.4.3 Neuroanatomical substrates of saccadic dysmetria

The finding of different types of dysmetria is interesting as hypermetria and hypometria are thought to be caused by lesions to distinct regions of the cerebellum and fastigial nucleus.

The oculomotor vermis (lobules VI and VII) and its immediate output structure, the caudal fastigial nucleus (fastigial oculomotor region, FOR) are known to be intimately involved in the accuracy of saccades in monkey (Optican and Robinson, 1980) and in the adaptive control of saccadic amplitude in monkeys in intrasaccadic target perturbation experiments such as the one described in this experiment (Goldberg et al., 1993; Takagi et al., 1998). In humans, saccadic hypermetria has been reported in patients with large cerebellar hemisphere or midline lesions (Selhorst et al., 1976).

Evidence from both experimental and clinical studies in both human and monkeys has led to in-depth knowledge of the main effects of lesions of the vermis and FOR. Lesions of the oculomotor vermis have the opposite effect to lesions of the FOR. Unilateral vermis lesions cause hypometric saccades to the ipsilateral side and hypermetric saccades to the contralateral side. Bilateral vermis lesions lead to hypometric saccades in both directions, while bilateral lesions to the FOR lead to hypermetric saccades in both directions (see Büttner and Straube, 1995). These relationships can be understood in the context of the physiology of the cerebellum and its pathways. In common with all the output cells of the cerebellum, the vermal projections to the FOR are inhibitory in nature. Thus, lesions to the vermis cause a disinhibition to the FOR. The output of the FOR to the saccadic centres in the brainstem is itself inhibitory. Thus, lesions to the vermis causes disinhibition of the FOR and greater inhibition of the brainstem (hypometria). In contrast, lesions to the FOR release the brainstem from its inhibition, causing hypermetria.

Given that the hypometria and hypermetria seen in 4 of our DES patients was not due to a specific compensatory strategy, but probably resulted from deficits in the
saccadic control system; the reported distinctions in the neuroanatomical site of hypometria and hypermetria may indicate that our patients have persistent deficits in different, though related areas. This may be a result of random variation in the effect of the disease process on the cerebellum and cerebellar nuclei, or a systematic effect dependent on other, as yet unspecified, factors such as age of onset or treatment protocols.

7.4.4 Neuroanatomical origin of opsoclonus

Opsoclonus occurs not only as part of DES, but can also occur in isolation as a paraneoplastic, post-infectious, toxic-metabolic or idiopathic phenomenon (see Leigh and Zee, 1991). It is likely, though not certain, that the opsoclonus apparent as part of DES, has the same underlying anatomical substrate as isolated opsoclonus. There have however been no conclusive or consistent findings regarding the underlying pathology.

The normal generation of saccades involves a complex relationship between inhibitory and excitatory burst neurons, pause neurons and omnipause neurons within the brainstem. Excitatory burst neurons have projections directly onto the oculomotor neurons. These burst neurons are under inhibitory control by tonically active pause and omnipause neurons. Pause and omnipause neurons receive inputs primarily from the superior colliculus, the frontal eye fields and the mesencephalic reticular formation (Büttner-Ennever and Büttner, 1988). Burst neurons are activated themselves, either directly or indirectly, by saccade-related burst neurons in the superior colliculus and frontal eye fields (Chimoto et al., 1996; Spark and Mays, 1990). The cerebellum has also been shown to have input pathways to the pre-motor saccade generator in the paramedian pontine reticular formation (PPRF) in the brainstem (Asanuma et al., 1983). The connections are represented schematically in Figure 7.4.
Opsoclonus clearly reflects some sort of hyperactivity within the saccadic system. This could be due to either excitatory or disinhibitory mechanisms. The diffuse and complex connections between the saccade generating areas shown in Figure 7.4 suggest that there are a number of routes by which excessive activity in the premotor burst neurons could occur, causing excess saccades as observed in opsoclonus. Abnormal burst neuron discharge could result directly from either a loss of tonic inhibition from the pause cells, or from abnormal excitatory input direct from the superior colliculus, frontal eye fields or FOR. Abnormal activity in the superior colliculus and frontal eye fields could also result in a loss of tonic excitation that usually maintains pause cell discharge during fixation.

Zee and Robinson (1979) originally proposed that opsoclonus reflected repetitive alternating discharges by different populations of burst neurons. This proposal was based on a model of saccade generation. Three factors were believed to contribute to these saccadic oscillations: 1) the extremely high discharge rates of saccadic burst neurons, 2) the existence of central processing delays due to the eye position feedback loop, making the system susceptible to oscillations, and 3) abnormalities of the brainstem pause neurons, or their inputs, which normally inhibit burst neurons during periods of fixation.

Pause cell dysfunction as the underlying cause of opsoclonus has received little support in spite of its theoretical simplicity. Autopsy findings of some patients who had
had opsinclonus showed no abnormalities in the region of the brainstem where the pause neurons are located (Ridley et al., 1987). Furthermore, experimental lesions of the pause cell region in monkeys does not produce opsinclonus, but slow saccades (Leigh and Zee, 1991). Their lesions may however not have been restricted to the pause cell region. Finally, an MRI study has shown that patients with lesions in the area of the omnipause neurons in the pontine tegmental raphe of the PPRF have slow saccades (Bronstein et al., 1990), not opsinclonus.

There is no evidence that lesions in the area of the pause cells themselves may produce opsinclonus, however it is possible that abnormal inputs to the pause cells, as mentioned above, or directly on to the burst cells themselves, may cause opsinclonus. It has been proposed that input driving the burst cells can also lead to inhibition of the pause cells via inhibitory burst neurons (Scudder, 1988).

The cerebellum has been implicated in opsinclonus, not only by reports of dysmetric eye movements but also in post-mortem morphological and brain imaging studies. In fact, Cogan (1954) was the first to suggest that opsinclonus was associated with cerebellar lesions or disease although supporting evidence has since been elusive. Childhood neuroblastoma cases of opsinclonus have suggested a loss of Purkinje cells (Henson and Urich, 1982). Post-mortem cases of adult paraneoplastic opsinclonus have revealed mild to severe loss of Purkinje cells, changes in the dentate nucleus and peridental demyelination (Ellenberger et al., 1968; Kilgo and Schwartze, 1984; Hunter and Kooistra, 1986; Graus et al., 1988). A post-mortem of a child with DES was however found to be normal (Lemerle et al., 1969). A CT study in an infant with DES revealed an acute cerebellar lesion which subsequently resolved with residual cerebellar atrophy (Willis et al., 1983).

More recently a SPECT study in two children with DES has implicated the vermis of the cerebellum in particular with the generation of opsinclonus (Oguro et al., 1997). One child was scanned three times, once when the symptoms of opsinclonus and
myoclonus were marked, at which time there was hyperperfusion in the cerebellum and in particular the vermis. The following two scans were performed when the symptoms had subsided; the area of hyperperfusion in the vermis had disappeared while the activity in the rest of the cerebellum appeared the same. In the second case, SPECT was performed three years after the onset of symptoms in a child with persistent occasional opsoclonus, myoclonus and ataxia. Hypoperfusion was noted in the cerebellum and particularly in the vermis. The contrast between finding hyperperfusion in the acute stage of a disease and hypoperfusion in the chronic stage has been reported previously in sequential SPECT studies in children with encephalitis (Launes et al., 1988) and thus may represent the normal evolution of some brain diseases.

The lack of persistent oculomotor symptoms in some of our patients does not exclude the likelihood of cerebellar involvement in DES. The symptoms of cerebellar disease can improve remarkably over time, as long as the underlying disease process is not progressive, especially if the lesion occurs in childhood (Wania and Walsh, 1959). This clinical observation has been supported by experimental work in monkeys. Neonatal monkeys with cerebellar ablations were virtually asymptomatic as long as the cerebellar nuclei were intact (Eckmiller and Westheimer, 1983). This suggests that the functions of the cerebellum may be adopted by other parts of the brain when the cerebellum is unable to perform its functions properly.

Dynamic overshoot was noted to be prominent only in our patients with hypermetric saccades. Dynamic overshoot could also be seen in the eye movement traces of the patients with DES in the study of Shawkat et al. (1993). Dynamic overshooting is regularly observed in the saccades of normal subjects, particularly in the abducting eye and after saccades of less than 10° (Kapoula et al., 1986). Our data come from adducting saccades made by the left eye and so are not readily explained by these normal patterns. The presence of dynamic overshoot, in addition to the hypermetria, suggests that these
patients were perhaps still being affected by processes which were also active during the acute phase of DES.

Opsoclonus consists of both horizontal and vertical saccades. The burst cells controlling the horizontal and vertical saccades are in distinct areas, the PPRF and the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) respectively. These areas are not near each other in the brainstem (see Figure 1.5 in the introduction) so it is unlikely that lesions directly to the burst cells themselves would cause opsoclonus as a mechanism that would specifically target these two distinct areas would be hard to imagine unless it were a neurotransmitter and biochemically-mediated disorder. It seems more likely that it is an area that projects to both the horizontal and vertical burst cell areas that may cause opsoclonus. Areas that input to the burst cell region of the PPRF are superior colliculi, the vestibular nuclei, the frontal eye fields, the riMLF, the cerebellum and the perihypoglossal nuclei (see Hepp et al., 1989). Areas that project to the riMLF have not been systematically studied but are thought to include the rostral part of the PPRF, the vestibular nuclei, and the frontal eye fields.

How the cerebellum could be involved in the generation of opsoclonus is unclear. It is reported to have inputs to both the PPRF, and indirectly to the riMLF (Hepp et al., 1989). It is possible that if the cerebellum does not turn off the input to the burst neurons at the correct time an excessive form of dynamic overshoot could result, which may appear like opsoclonus.

7.4.5 Cognitive deficits and the vermis

Many children with DES are found to have long term cognitive deficits (Hammer et al., 1995; Papero et al., 1995; Pohl et al., 1996; Russo et al., 1997), primarily learning difficulties and speech abnormalities. Only 12% of a study of 49 patients were considered neurologically normal (Pohl et al., 1996). There was no correlation however with the time of onset, severity or course of their symptoms. We performed no formal assessments
of cognitive outcome in the patients in our study. Reports from parents regarding the abilities of their children indicated that five of the seven patients in our study have some form of learning disability and residual cognitive problems, usually requiring special attention at school. Two patients were considered to be neurologically normal, one of which was the oldest patient (19 years old) and was in higher education. The number of patients investigated in our study were too few to be able to make associations between residual oculomotor deficits and cognitive deficits. The finding that the patient with no neurological sequelae (JG) had marked saccadic dysmetria while a patient with quite severe learning difficulties (AR) had no saccadic dysmetria or adaptive control deficits does not support a predictable relationship between oculomotor deficits and cognitive deficits.

The association of dysmetria with the cognitive abilities of children has not been formally investigated. The cerebellum had traditionally been regarded as primarily involved in motor control mechanisms, however, the role of the cerebellum in higher cognitive abilities, particularly in language skills, has more recently been acknowledged (e.g., Leiner et al., 1993; Bloedel and Bracha, 1997). Vermis lobules VI and VII (i.e., the oculomotor vermis) have been noted to be preferentially affected in at least two neurological disorders of childhood with prominent cognitive aspects: autism and fragile X syndrome.

Autistic children, who are severely impaired in both language and cognitive development, have been reported to show developmental hypoplasia of vermis lobules VI and VII on MRI (Courchesne et al., 1988; Courchesne et al., 1994) and bilateral Purkinje and granule cell loss in the cerebellar hemispheres and vermis and deep cerebellar nuclei at autopsy (Bauman, 1991; Bauman and Kemper, 1985). There have been few investigations of oculomotor function in children with autism. Reports have been contradictory with a recent well-controlled study reporting no abnormalities in the metrics or dynamics of visually-guided saccades (Minshew et al., 1999) while a previous study
reported saccadic hypometria and reduced velocities in the voluntary saccades of some autistic children (Rosenhall et al., 1988).

Similarly, children with fragile X syndrome are characterised by cognitive and behavioural abnormalities have been found to have a decreased size of the posterior vermis (Reiss et al., 1991; Mostofsky et al., 1998).

It has been put forward that the cerebellum, and particularly the vermis, may be more vulnerable to developmental abnormalities, or the effects of early insults, due to its protracted course of post-natal development (Ciesielski et al., 1997). Vermal lobules VI and VII are amongst the final areas of the vermis to develop in humans and are ontologically and developmentally distinct from lobules I to V (Isumi et al., 1997). Further evidence for the vulnerability of lobules VI and VII can be found in the examination of the neurological sequelae of survivors of acute lymphoblastic leukaemia. These patients, treated with chemotherapy and radiotherapy, were found to have marked hypoplasia of vermis lobules I through VII but particularly VI and VII on MRI in relation to rigorously selected controls (Ciesielski et al., 1994, 1997). This apparent vulnerability of the posterior vermis may be the cause of the oculomotor deficits that are prominent in DES. The process that effects this damage to the vermis in DES is as yet unknown though it is popularly believed to be an autoimmune process at present (Pranzatelli 1996).

The two examples above of neurological diseases with prominent cognitive deficits and associated vermis abnormalities do not necessarily indicate a causal link between vermis abnormalities and cognitive disorders. Cognitive abilities are diffuse and specialised. The vermis itself may play an as yet unknown role in certain cognitive abilities, particularly given the widespread input and output connections of the cerebellum (see Keller, 1989). Alternatively, processes which preferentially cause damage to the posterior vermis may also affect other areas of the brain that play a role in cognition. Such processes could be autoimmune effects or the result of neurotransmitter imbalances.
Vermis signs such as saccadic dysmetria may be indirectly associated with cognitive abilities due to the importance of accurate eye movements in cognitive tasks with a particular visual dependence such as reading (see Rayner, 1998). The serial fixation of words and the resetting of the eye to the beginning of a new line both require precise saccades.

7.5 Conclusions

Saccadic dysmetria and adaptive control capabilities were assessed in 7 children and young adults with DES. Two patients had persistent hypermetria, two had persistent hypometria and 3 were normal. Only one patient had apparently absent adaptive control. This may have been related to the particularly low gain of primary saccades in this patient, or reflect the previously proposed dissociation between the mechanism that determines the time constants of the adaptive elements themselves. No consistent relationships were found between the presence of persistent saccadic dysmetria and the ability to adaptively decrease gain. This suggests that the ability to manipulate gain and the ability to generate saccades of the optimal gain are functionally, and perhaps also anatomically, distinct from each other.

Long-term neurological sequelae are prominent in DES. These are well reported in the cognitive domain, while oculomotor sequelae are documented here for only the second time. Four out of the seven patients in this study were found to have oculomotor sequelae. The presence of cognitive deficits was not found to be directly related to either persistent saccadic dysmetria or adaptive control capabilities, although this was not formally tested.

Saccadic dysmetria and adaptive control capabilities are believed to be intimately related to the vermis of the cerebellum and the oculomotor region of the fastigial nucleus. These areas have been previously implicated in the pathogenesis of DES, most recently in
a serial SPECT study. Our findings suggest a heterogeneous developmental pattern of symptoms in children with DES with some support for the involvement of vermis and FOR in their oculomotor outcome.

This is the first time that an intrasaccadic adaptive control paradigm has been successfully used to test adaptive control in a group of young patients and control subjects. This technique has been used previously as a research tool only. However, this experiment has demonstrated its use as a valuable clinical tool for the future.
Chapter 8. General Discussion and Conclusions

The saccadic flight-time minimisation hypothesis

This thesis brings together evidence from a diverse range of experiments to support predictions made by the saccadic flight-time minimisation hypothesis (SFM) (Harris, 1995). The SFM hypothesis proposes that the gain of saccades is determined by the drive to minimise saccadic flight-time, and provides an explanation for the well-known undershoot bias of saccades to visual targets. Saccades that overshoot the target are believed to incur a cost to the saccadic system in terms of flight-time. In order to minimise saccadic flight-time over sequences of saccades, the number of overshooting saccades must be kept to a low level, though not completely eliminated; in turn the majority of saccades will undershoot the target. The undershoot bias is a subtle effect in normal children and adults (see Table 8.1), however, its strong presence in infants (Harris et al., 1993), and as shown in these experiments, in antisaccades, express saccades, and patients with homonymous hemianopia (see Table 8.2), suggests that it is not a chance effect but a deliberate strategy that must exist for a reason. The normal level of gain and standard deviation in adults and children was, on average, very consistent between subjects and between experiments, in spite of the variations in protocol. This can be seen in Table 8.1.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>n</th>
<th>TE</th>
<th>Mean Gain</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 3. Saccades made by hemianopic patients into the seeing hemifield</td>
<td>7</td>
<td>15°</td>
<td>0.932</td>
<td>0.04</td>
</tr>
<tr>
<td>Chapter 3. Saccades made by control subjects</td>
<td>7</td>
<td>15°</td>
<td>0.927</td>
<td>0.06</td>
</tr>
<tr>
<td>Chapter 4. Prosaccades</td>
<td>5</td>
<td>10°</td>
<td>0.931</td>
<td>0.04</td>
</tr>
<tr>
<td>Chapter 6. Non-express type saccades made by an express-saccade maker</td>
<td>1</td>
<td>10°</td>
<td>0.949</td>
<td>0.05</td>
</tr>
<tr>
<td>Chapter 7. Saccades made in the pre-adaptation phase</td>
<td>7</td>
<td>10°</td>
<td>0.94</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 8.1. The mean gain and standard deviation for ‘normal’ saccades. n - the number of individual results contained within the mean; TE - target eccentricity; SD- standard deviation of the mean.
8. Conclusion

One of the main predictions of the SFM hypothesis is that that the gain of saccades is fundamentally linked to their standard deviation. If the standard deviation is high the average gain of saccades is predicted to be low. This is believed to be an adaptive strategy that functions to prevent too many overshooting saccades, and thus minimises saccadic flight-time.

It has been demonstrated that a high standard deviation can occur under both normal (antisaccades, express saccades) and abnormal (hemianopia) circumstances, and that this is generally associated with a low gain.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>n</th>
<th>TE</th>
<th>Mean Gain</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 3. Saccades made by hemianopic patients into the blind hemifield</td>
<td>7</td>
<td>15°</td>
<td>0.644</td>
<td>0.33</td>
</tr>
<tr>
<td>Chapter 4. Antisaccades</td>
<td>5</td>
<td>10°</td>
<td>0.825</td>
<td>0.09</td>
</tr>
<tr>
<td>Chapter 6. Express type saccades made by an express-saccade maker</td>
<td>1</td>
<td>10°</td>
<td>0.846</td>
<td>0.13</td>
</tr>
<tr>
<td>Chapter 7. Saccades made by a patient with Dancing Eye Syndrome</td>
<td>1</td>
<td>10°</td>
<td>0.63</td>
<td>0.09</td>
</tr>
<tr>
<td>Chapter 7. Saccades made by a patient with Dancing Eye Syndrome</td>
<td>1</td>
<td>10°</td>
<td>0.80</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Table 8.2. The mean gain and standard deviation for subjects with low gain saccades

The high standard deviation of saccades into the blind hemifield in hemianopic children can be attributed to the lack of knowledge regarding the target location within the blind hemifield. Hemianopic children were found to generate very low gain saccades into the blind hemifield which required numerous corrective saccades. This gives the saccadic eye movement trace the characteristic staircase appearance. Normal adults produce saccades with a high standard deviation and a low gain in the antisaccade task. This can again be attributed to uncertainty with respect to the location of the visual goal as there is no direct visual stimulus. Express saccades generated by one normal adult (an ‘express saccade maker’) also showed the association. Finally, there were two patients with Dancing Eye Syndrome (DES) who were noted to have low gain saccades. These patients in contrast did not have remarkably high standard deviations. Thus a low gain does not
depend necessarily on a high standard deviation. The low gain in these patients may have been due to the nature of the neurological damage caused by DES, i.e. the low gain was not an adaptive strategy in the face of a high standard deviation, but a result of a lesion somewhere within the oculomotor control system. Table 8.2 shows examples of low gains in association with a high standard deviation (except for DES patients).

Further support for the SFM hypothesis was obtained in Chapter 5. This experiment investigated an additional prediction of the SFM hypothesis, that the gain of saccades is related to their main sequence for duration. Normal subjects are known to show stereotypical main sequences and gain characteristics, thus any correlations between subjects were expected to be subtle. Correlation analyses were performed on data from 20 subjects. Highly significant correlations were found when the gain was quantified in such a way that the effects of a poor calibration, or slow eye movement components were excluded.

Although we have provided empirical support for the two main predictions of the SFM hypothesis, this does not of course necessarily mean that this hypothesis is valid. However, few other hypotheses have been put forward to explain the gain characteristics of saccades, and in particular the undershoot bias. One of the most persistent theories has been the hemispheric facilitation theory first put forward by Robinson (1973). This theory proposes that the undershoot bias functions to prevent an increase in the intersaccadic interval (ISI) associated with switching the representation of a target from one hemisphere to the other, as would occur if the saccade overshot the target. With the data in Chapter 5 we were able to reject this hypothesis: we found no significant difference between the ISI of onwards or backwards corrective saccades in robust analyses. In the absence of any other robust and testable theories to account for the undershoot bias, flight-time minimisation can be currently considered as the most plausible explanation for the undershoot bias and the gain of saccades under different circumstances.
Adaptive control

The saccadic system is traditionally believed to strive to minimise post-saccadic retinal error, despite the known bias to undershoot. The use of retinal error to drive the adaptive control system appears to be a direct and parsimonious means to manipulate gain. The adaptive control of gain using the intrasaccadic target displacement paradigm proved a successful way in which to investigate the goal of the saccadic system. Our data show that the goal of the adaptive control system does not appear to be the minimisation of average post-saccadic retinal error over the course of the experiment. The results again support the SFM hypothesis, as the gain was found to decrease when the standard deviation of the gain was artificially increased by a random onwards and backwards intrasaccadic target step. These results could also be compatible with the idea that retinal error drives an adaptive control system in which the gain decreasing element is more potent than the gain increasing element and that retinal error is assessed on a trial-to-trial basis.

The inconclusiveness of our results with respect to the goal of the adaptive control system may in fact indicate that the adaptive controller is more complex than predicted. There is evidence that there are distinct short- and long-term adaptive processes i.e. slow adaptation in response to muscle weakening, and fast adaptation in the intrasaccadic target displacement paradigm. There is also evidence that different types of saccades can be separately adapted eg voluntary saccades and reflexive saccades. We have additionally shown that express saccades can possibly be separately adapted from normal reflexive saccades. It is possible that flight-time minimisation and retinal error minimisation may work in parallel to maintain the gain at an optimal level. The minimisation of retinal error would be most suited to work on a short-term basis, trial-to-trial, in which saccadic overshoots cause a decrease in gain and saccadic undershoots cause an increase in gain. The undershoot bias could result from the relative strengths of the adaptive elements such that an overshoot would induce a stronger drive to decrease the gain than an undershoot.
would to increase the gain. The different strengths, or time constants, of the gain increasing and decreasing elements could be set by a long-term adaptive processes that functions to minimise saccadic flight-time. In this sense, flight-time minimisation acts as a supervisory mechanism to determine the dynamic equilibrium of the adaptive system.

As mentioned previously, it is also a possibility that the goal of the saccadic system is affected by the circumstances in which saccades are generated. The minimisation of retinal error as the goal of the adaptive processes may be a special situation imposed, or perhaps facilitated, by the unnatural visual environment in which laboratory saccades are elicited. Most saccades made in a natural context are part of a scanning sequence within a rich visual environment. The adaptive control of scanning saccades on the basis of a post-saccadic visual error is greatly complicated by the need for reliable and rapid re-identification of the visual target at its new retinal location after the saccade. In the context of saccades induced to single targets in the laboratory however, post-saccadic target identification is no longer an important issue as there would be automatic re-identification due to there only being one target. As such, the visual error signal would be easily obtained by the adaptive control system.

The idea of the minimisation of saccadic flight-time as a long-term adaptive process also fits with the proposed mechanisms behind SFM. Minimisation of saccadic flight-time is only effective over a series of saccades and cannot make meaningful adjustments on a single trial basis. This is because the minimum flight-time for any saccade amplitude cannot be known in advance in order to calculate a flight-time error signal, unless the brain contains some sort of hard-wired look-up table for the minimum for each possible combination of eye movement amplitude and start and finish position in the orbit. It is difficult to imagine the physiological plausibility of such a system as it would have to be present from birth with the appropriate minimum durations already programmed, and continually updated over time. The saccadic system is known to be able to integrate information over both space and time, for example in the range effect in
which the behaviour of the saccadic system responds to the particular pattern of target presentation in space and time. It may be possible that minimisation of flight-time is employed preferentially when multiple saccades are being made in sequence, such as in the context of visual scanning, so that over time the optimal gain of the system can be determined.

The evolution of the distinct saccade generating circuits may have facilitated, or necessitated, the development of independent adaptive mechanisms. The ability to separately adapt different types of saccades could be beneficial due to their distinct uses. Internally generated scanning saccades may have a lesser requirement for accuracy in favour of rapid information accumulation regarding the gross features of the environment, while reflexive saccades, generated to specific visual targets may have a greater need for accuracy to provide the visual system with detailed information about sudden changes in the environment. At least partially separate adaptive controllers would be required to maintain the distinct parameters of such saccades. On the other hand, the ability to transfer gain changes from one type of saccade to another would be beneficial if the saccadic system were affected by a peripheral process, e.g. an extra-ocular muscle paresis, that changes the input/output relations of all saccades, irrelevant of their central generating pathways.

Although we have provided much evidence that supports the SFM hypothesis, none is conclusive. There are many further experiments that could be undertaken to seek further support for the SFM hypothesis but an experiment to provide conclusive evidence regarding this hypothesis is elusive. The relationship between gain and the main sequence for duration deserves further investigation. In the experiment in Chapter 5 the gain of saccades within individuals was complicated by the influence of the range effect. Investigating saccades to one eccentricity only, or comparing centrifugal and centripetal saccades, would be useful to provide further support for the predicted relationship between gain and the main sequence. It would also be interesting to test subjects with
abnormal main sequences, i.e. saccades with abnormal flight-times. For example, Gaucher patients have slow saccades, and myasthenic patients have fast saccades. A patient who makes very slow saccades maybe expected to strive to make very accurate saccades in order to prevent the need to make more than one saccade. This would depend though on whether saccades were slowed across the complete spectrum of saccade amplitudes, or whether it was an amplitude-dependent phenomenon.

**Neurological aspects**

As discussed, the cerebellum is believed to be the main area involved in the adaptive control of saccades. Exactly what forms of adaptive control exist, and whether the cerebellum is directly involved in them all is unknown. No differences have been found in the activity of neurons in the fastigial oculomotor region (FOR) during externally triggered, visually guided, spontaneous saccades in the light, or the fast phases of nystagmus (Helmchen et al., 1994; Ohtsuka and Noda, 1991, Fuchs et al., 1993). This implies that the cerebellum is involved in the adaptive control of all saccades. It is possible that additional input may fine tune this cerebellar output on the basis of the type of saccade triggered, by a parallel output from the cortical areas involved to the cerebellum. The involvement of higher levels in the adaptive control process has been suggested by Frens and van Opstal (1994). They suggested that short-term adaptation may involve a change in activity of the specific ensemble of cells in the area responsible for the generation of the adapted saccade in the frontal eye fields (FEF). This change may not be detected in the superior colliculus (as reported by Fitzgibbon et al., 1986)) due to the direct pathway from the FEF to the brainstem.

Experiments that dissociate the adaptive control abilities of different types of saccades (eg Erkelens and Hullemman, 1994; Deubel, 1995) suggest that adaptive gain modification may also occur in higher oculomotor centres before the signals from different parts of the cortex and the superior colliculus have converged. Thus in addition
to a cerebellar-based adaptive control system there may be one or more adaptive control systems which can be implemented further upstream.

Clinical relevance

Aside from the theoretical implications of this work, we propose that undershooting strategy seen in hemianopic children in fact represents a normal adaptive strategy of the saccadic system. This multiple hypometria reflects the working of a healthy adaptive control system in the face of other neurological damage. Furthermore, we have shown the feasibility of applying the adaptive control paradigm to clinical populations, including children. As a clinical tool, this technique may enable the functioning of the adaptive control system to be assessed longitudinally in children with known or suspected cerebellar pathology. Abnormality in the adaptive control system may have long-term implications for children with disorders affecting the cerebellum. In the future, if the localisation and specialisation of the adaptive control system can be better understood, the adaptive control paradigm could be used as a means of early detection of cerebellar deficits, before they are likely to show up on a brain scan, and may allow early intervention.
References


Appendix A.


3050 — B740

SACCADE EYE MOVEMENT STRATEGIES IN CHILDREN WITH HOMONYMOUS HEMIANOPIA. ([L.E.Meze, C.M.Harris, F.S.Sawkat, A.Kriss, P.West, C.Turns, D.Taylor]) Department of Ophthalmology, Great Ormond Street Hospital for Children, London WC1N 3JH, UK.

Purpose. To investigate saccadic eye movement strategies in children with homonymous hemianopia (HH) and compare to simulations that minimise saccadic flight time or total time to target fixation. Previous investigations have been limited to adults. Methods. Saccadic eye movements were recorded in 10 subjects (aged 6-16yrs) with HH using dc-EOG. HH was diagnosed with perimetry and/or pattern VEPs. Saccades were elicited to red LEDs at amplitudes of 10 or 20 degrees, randomised to the left or right of the central fixation target in a no-gap paradigm. Patients with cerebellar symptoms, ocular motor apraxia, or basal ganglia disease were excluded. Results. All subjects made multiple hypometric saccades into their blind field, with a maximum of 5 saccades required to acquire the target, while saccades into their preserved hemifield were rarely of this type. Nine subjects made occasional hypermetric saccades, into both the blind and preserved hemisfields. One subject showed more consistent hypermetria into the blind field, although there was an equal tendency to make multiple hypometric saccades as well. Conclusion. Hypermetria has been described as a compensatory strategy in adults with HH. We have found little support for this in children. Although simulations show that hypometria is an optimal strategy to minimise total flight time, if the subject has an expectation of target position then hypermetria may become optimal. Despite non-randomisation of target amplitude, allowing subjects to build up an expectation of target position, our subjects paradoxically did not adopt hypermetria as a consistent compensatory strategy.
SACCADIC STRATEGIES IN HEMIANOPIC CHILDREN

L.E. Mezey, F.S. Shawkat, A. Kriss, P. West, C. Timms, D. Taylor, C.M. Harris

Department of Ophthalmology, Great Ormond Street Hospital for Children, London WC1N 3JH

This study reports the saccadic eye movement strategies seen in children with homonymous hemianopia (HH) and attempts to reconcile these findings with simulations concerning saccadic flight time and total time-to-fixation. **Method.** Saccadic eye movements were recorded in 10 children (aged 6-16 yrs) with HH using dc-EOG. HH was diagnosed with perimetry and/or pattern VEPs. Saccades were elicited to red LEDs at amplitudes of 10 or 20 degrees, randomised to the left or right of the central fixation target in a no-gap paradigm. Children with cerebellar symptoms, ocular motor apraxia, or basal ganglia disease were excluded. **Results.** All children made multiple hypometric saccades into their blind field while saccades into their preserved field were mostly normometric. Nine children made occasional hypermetric saccades, though into both the blind and preserved hemifields. One child showed more consistent hypermetria into the blind field, but with an equal tendency to make multiple hypometric saccades. **Conclusion.** Although hypermetria has been described as a compensatory strategy in adults with HH, we have found little support for this in children. Computer simulations suggest that the optimal strategy to minimise either saccadic flight time or total time-to-fixation depends whether the subject holds an expectation of target location. With no expectation hypometria is optimal. With a strong expectation hypermetria may become optimal. Despite non-randomisation of target amplitude, allowing the build up an expectation of target position, the children in this study paradoxically did not adopt hypermetria as a consistent compensatory strategy.
Saccadic strategies in children with hemianopia

L E Mesey* BSc;
C M Harris PhD;
F S Shawkat PhD;
C Tums DBO(T);
A Kriss PhD;
P West;
D S Taylor FRCS FRCOPth; Department of Ophthalmology, Great Ormond Street Hospital for Children, London WC1N 3JH, UK.

*Correspondence to first author.

Multiple hypometric (undershooting) saccades are generally reported as a compensatory strategy in adults with homonymous hemianopia. However, hypermetric (overshooting) saccades have been reported to develop spontaneously as a beneficial strategy in response to predictable targets. We examined the saccades of 10 children (aged 5 to 16 years) with homonymous hemianopia to determine the type of compensatory eye-movement strategies employed 6 months to 16 years after hemianopia onset. Homonymous hemianopia was identified using perimetry and/or pattern visual evoked potentials and supported with results of neuroimaging. Eye movements were recorded using bifoveal electrocugulography. Saccades were elicited to a red light source in a semipredictable paradigm. We found that hypermetria was not a consistent compensatory strategy in our patients. In spite of the predictability of our paradigm and the long follow-up period, multiple hypometric saccades into the blind field appeared to be the preferred strategy.

Saccades are fast eye movements used to redirect the line of vision to bring objects of interest onto the fovea. This is normally achieved with a single saccade, or a saccade which stops slightly short of the target (undershooting/hypometric saccade) with a small onward 'corrective' saccade to reach the target. Saccades which overshoot the target (hypermetric saccades), requiring a backward corrective saccade, are less commonly observed. Understanding the saccadic response of patients with homonymous hemianopia—the loss of one visual hemifield—is not only important for revealing the underlying mechanisms of the saccadic system, but may also be important in rehabilitation. Staircase-like sequences of hypometric (undershooting) saccades into the blind field have frequently been reported in patients with homonymous hemianopia (Gasgel and Williams 1963, Meienberg et al. 1981, Meienberg et al. 1986, Zangemeister et al. 1986, Zangemeister et al. 1995). However, spontaneous hypermetria (overshooting) has also been reported in response to predictable targets (Meienberg et al. 1981). It has been proposed that hypermetria is a more efficient strategy of reaching a predictable visual target in the blind field than the 'safe but slow' (Zangemeister et al. 1986) though 'very reliable' (Meienberg et al. 1981) strategy of undershooting. This is because a hypermetric saccade rapidly brings the target into the seeing field, allowing the target to then be accurately fixated under visual guidance (Meienberg et al. 1981). Such findings have been used to support the use of cognitive rehabilitation training for hemianopic patients, who are trained to look large saccades to targets in their blind field, and in whom subjective improvement has been reported (Zihl 1988, Kerkhoff et al. 1992, Kerkhoff et al. 1994).

Although in our experience children are generally found to compensate extremely well for their visual-field deficits, adults with homonymous visual-field disorders have often been reported to have a poor functional rehabilitation outcome (Savir et al. 1977, Reding and Potes 1988, Grosswasser et al. 1990). Could the compensation shown in children be due to the natural development of compensatory eye movements (such as hypermetria), enabled by greater plasticity of the young central nervous system?

To our knowledge, saccadic strategies in children with hemianopia have not been investigated. Therefore, we undertook a retrospective study of the saccadic eye-movement recordings of 10 children with homonymous hemianopia due to various causes, and in whom there had been a wide range of postlesion experience.

Method

PATIENTS

Ten children aged between 5 and 16 years at the time of eye-movement recordings were studied. They were seen at the Ophthalmology Department at Great Ormond Street Hospital for Children as part of their routine clinical investigations. Homonymous hemianopia was diagnosed using visual field testing, either Goldmann perimetry or confrontation, and pattern visual evoked potentials (Bluthardt et al. 1992), especially for those children who were unable to carry out visual-field testing reliably. Field-defect results were supported in nine patients with neuroimaging findings. Homonymous hemianopia had a variety of causes, and was probably congenital in two children, and acquired during childhood in the others. Testing was performed between 6
months and 16 years after onset of hemianopia (see Table I).

None of the patients had cerebellar signs such as ataxia or nystagmus. No formal testing for visual neglect was carried out, however, none of the patients exhibited signs of neglect such as ignoring contralesional space or failing to search for objects in the contralesional hemifield (Rafal 1994).

**EYE-MOVEMENT RECORDING**

Horizontal eye movements were recorded using bitemporal dc-coupled electrooculography (EOG). Younger patients sat on their parent’s lap with their head held as still as possible without upsetting the child. Older children sat alone with their head against a headrest and, when necessary, their head was held still by the experimenter. All patients were tested under standard room-lighting conditions. Simultaneous video monitoring of the eyes was made throughout testing to confirm fixation before each trial began (Harris et al. 1992).

Saccades were elicited to a red light source, subtending a visual angle of 17 minutes of arc, mounted against a flat black background and placed 1 m away from the subject. Patients were tested with target eccentricities of 10° (six patients), 20° (three patients), or both (one patient). Each eccentricity was tested separately with the direction randomized to the left or right of the central fixation target (semipredictable paradigm). The central light went off as the peripheral light came on. The location of the non-illuminated target was visible. Patients made varying numbers of saccades according to their individual tolerance to the task. They were asked to follow the light with their eyes wherever it went. Thus when the light disappeared from their seeing field, they would look for it in their blind field.

**ANALYSIS**

Each trial elicited a ‘saccadic sequence’ in which the target was fixated by a sequence of one or more saccades, called ‘multiplicity’ (singlets, doublets, etc.). The magnitude and direction of each saccade in a sequence was measured from off-line plots on a high-resolution chart recorder. To interpret the results correctly, it is important to recognize that due to inevitable EOG drift, intertrial head movements, and uncertain fixation consistency, i.e. not fixing with precisely the same retinal locus (see Hainline et al. 1990), it is not possible to acquire reliable absolute intertrial calibrations. Therefore, each trial was considered separately, where the net displacement of the eye-movement record of a trial was assumed to correspond to the stimulus target eccentricity. However, this creates a bias in the measurement of saccadic gain (the ratio of saccadic amplitude to target eccentricity) because any saccade without a following resolvable corrective saccade is deemed to be on target, i.e. have a gain of 1.0 if it is a primary saccade. Thus the final saccade in a sequence (or the primary saccade in a singlet) cannot necessarily be considered precisely orthometric due to inconsistent fixation and the limits of EOG resolution which will obscure small saccadic and non-saccadic corrections.

We report the joint analysis of 10° and 20° trials because no significant differences were found in either the multiplicity or the primary gain between subjects, or within the one subject who was tested with both eccentricities. With due awareness of the confounding factors outlined above, trials were nominally classified, according to their gain, into one of four groups: (1) Normometric, for fixations without a secondary saccade or with a multiplicity of two in which the primary gain is between 0.9 and 1. This amount (up to 10%) of undershoot is generally believed to be physiological (Troost et al. 1974); (2) Hypometric, with a primary saccade gain <0.9; (3) Hypermetric, where a secondary saccade was made in the direction opposite to the movement of the target (primary saccade gain >1); (4) Wrong direction, for primary saccades made in the direction opposite to that of the target.

Responses to targets in the blind field were compared to those in the seeing field to determine any significant differences.

**Results**

A total of 288 saccadic sequences were made by the 10 patients involved in this study (see Table II for summary). Overall 64% of saccades made into the blind field were hypometric, which is significantly more than the 15% of hypometric saccades made into the seeing field (P<0.005, Wilcoxon matched-pairs

---

Table I: Summary of patient data

<table>
<thead>
<tr>
<th>Patient nr</th>
<th>Age at onset (y)</th>
<th>Age at lesion</th>
<th>Diagnosis</th>
<th>pVEP</th>
<th>Fields</th>
<th>Neuroimaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>Perinatal</td>
<td>L. Cerebral palsy</td>
<td>Yes</td>
<td>G</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>7 y</td>
<td>R. Sturge-Weber + L occipital angioma</td>
<td>No</td>
<td>G</td>
<td>MRI</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>11 y</td>
<td>L. Epilepsy, hemiplegia, R occipital defect</td>
<td>Yes</td>
<td>C</td>
<td>MRI</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>Perinatal</td>
<td>L. Cerebral palsy, L temporal-lobe damage</td>
<td>Yes</td>
<td>G</td>
<td>CT</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>2 y</td>
<td>R. L temporal-lobe cystic astrocytoma</td>
<td>Yes</td>
<td>None</td>
<td>MRI</td>
</tr>
<tr>
<td>6</td>
<td>11</td>
<td>14 mo</td>
<td>R. L occipital-lobe lesion</td>
<td>Yes</td>
<td>C</td>
<td>CT</td>
</tr>
<tr>
<td>7</td>
<td>11</td>
<td>1 y</td>
<td>L. R suprasellar astrocytoma</td>
<td>Yes</td>
<td>C</td>
<td>MRI</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>14 mo</td>
<td>R. Temporal-M strobalastoma</td>
<td>Yes</td>
<td>G</td>
<td>MRI</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
<td>9 y</td>
<td>R. Epilepsy, L temporal-lobe</td>
<td>Yes</td>
<td>C</td>
<td>MRI</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>6 mo</td>
<td>R. Epilepsy, cerebral palsy, L temporal-lobe</td>
<td>Yes</td>
<td>G</td>
<td>MRI</td>
</tr>
</tbody>
</table>

pVEP pattern visual evoked potentials; G. Goldmann perimetry; C, to confrontation; L, left; R, right.

---

Saccades in Children with Hemianopia. L. Bley et al. 62*
test). Seven of the 10 patients made some (range 8 to 43%) hypermetric saccades into their blind field, however, only two of these patients (patients 1 and 7) made significantly more hypermetric saccades into their blind field than their seeing field (χ² test with Yates’ correction for continuity; P < 0.05) (see Table II). The other three of the 10 patients made no hypermetric saccades into either their blind or seeing fields. Only two patients (patients 4 and 10) made hypermetric saccades into their seeing fields. Nine patients made normometric saccades into their blind field (average 15%). Most saccades (82%) into the seeing field were normometric. A small number of sac- cades to targets in the blind hemifield were initially made in the wrong direction.

The multiplicity of all saccades into the blind field ranged from 1 to 7. There were 15% singles, 37% doubles, 24% triplets, 16% quadruplets, and 6% quintuplets. There was also one sextuplet and one septuplet (0.7% each). The longer sequences of five or more steps usually resulted from seemingly confused sequences of saccades, for example, making a small saccade into the blind field followed by a large saccade back into the seeing field before continuing the search in the blind field. Such sequences may have been the result of lack of attention. The multiplicity of saccades into the seeing field ranged from one to three. There were 82% singles, 17% doubles, and 0.7% triplets.

There was clearly a large variation in the amplitude of the primary saccade of each hypometric sequence, both between and within patients. This variation was however not symmetrical around a gain of 1. There was a bias toward undershooting. This is demonstrated in Figure 1, showing the gain of the primary saccade in each trial for one patient (patient 6). It can be seen that although there is a large degree of variation below the unity line (gain=1), and a number of points lying directly on the line, i.e. sequences without a resolvable secondary saccade (see analysis), there is no spread above the unity line. It can also be seen that there is no apparent trend over time for a systematic change in the gain of the primary saccade. None of our patients showed evidence of improvement during the course of the experiment.

Figure 2 represents a comparison of the primary and sec-ondary saccades into the blind field for all sequences with a multiplicity of two or more. Sequences in which the primary saccade was in the wrong direction have not been plotted. Both amplitudes have been normalized by dividing by the total saccadic component in the sequence. The oblique dashed lines represent two deterministic mechanisms for interpreting saccade amplitude. The ‘fixed magnitude’ line describes sequences in which the amplitudes of the primary and secondary saccades are equal. Relatively few points lie directly on this line indicating that the primary and secondary saccades were rarely of the same magnitude. The ‘corrective’ line describes sequences in which the secondary saccade is equal to the remaining target eccentricity left by the primary saccade. All sequences with a multiplicity of two lie on this line due to our means of calibration. The absence of primary saccades with a gain of between 0.93 and 1.10 represents the resolution to which we were able to measure. Apart from those points lying on the corrective line, the other points do not show any clear pattern in the relation between the primary and secondary saccades. It can be seen that hypermetric primary saccades overshoot the target by as much as 50%, the average being 31%.

Discussion
Our observations show that children with homonymous hemianopia do not develop a consistent strategy of saccadic hypermetria into their blind fields. On most trials (64% across all subjects) saccades were hypometric taking from 2 to 7 saccades (mean = 3) to reach the target. Although hypermetria did occasionally occur in seven of the 10 cases, it always occurred less frequently than hypometria (except in patient 7), and there was no indication of a consistent strategy or an adaptive trend towards hypermetria (see Fig. 1).

With targets of predictable eccentricity and timing, Meienberg et al. (1981) reported hypometria in the first trials, but once the target position had been learned, the target was fixated with one overshooting saccade followed by a backward glissade or saccadic movement. In our patients this was not seen (subject to the resolution of EOG) in spite of the availability of consistent information about the target location and central fixation cue in our paradigm.

Table II: Comparison of percentage of types of saccades made by each patient into the blind and seeing fields

<table>
<thead>
<tr>
<th>Patient</th>
<th>Seeing field</th>
<th></th>
<th></th>
<th></th>
<th>Blind field</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>nr</td>
<td>% total number of saccades</td>
<td>N</td>
<td>Wrong</td>
<td>Normometric</td>
<td>Hypometric</td>
<td>N</td>
<td>Wrong</td>
<td>Normometric</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------</td>
<td>---</td>
<td>--------</td>
<td>-------------</td>
<td>------------</td>
<td>---</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>1</td>
<td>79</td>
<td>14</td>
<td>0</td>
<td>21</td>
<td>7</td>
<td>15</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td>94</td>
<td>16</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>10</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>94</td>
<td>4</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>75</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>100</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>13</td>
<td>8</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>6</td>
<td>66</td>
<td>3</td>
<td>0</td>
<td>34</td>
<td>19</td>
<td>31</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>7</td>
<td>100</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>8</td>
<td>100</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>9</td>
<td>75</td>
<td>10</td>
<td>0</td>
<td>25</td>
<td>20</td>
<td>11</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>10</td>
<td>60</td>
<td>15</td>
<td>0</td>
<td>20</td>
<td>15</td>
<td>10</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>11</td>
<td>82</td>
<td>15</td>
<td>3</td>
<td>137</td>
<td>6</td>
<td>15</td>
<td>3</td>
<td>137</td>
</tr>
</tbody>
</table>

N, Number of trials.

* P < 0.05, comparison of hypermetric saccades made into the blind and seeing fields.

628 Developmental Medicine & Child Neurology 1998, 40: 626-630
allowing target position prediction.

We emphasize that there were potentially significant differences between Meeningberg's paradigm and ours. While the eccentricity of the target was fully predictable in both paradigms, in our paradigm the side of target presentation was randomized, rather than predictably alternating between left and right. In Meeningberg's study the targets were also predictable in time, while they were variable in ours, although the central fixation light always extinguished at target onset thus giving a cue that a peripheral target had been lit. A more predictable paradigm could have facilitated more hypermetric saccades. It is possible that Meeningberg's fully predictable paradigm could have been generating voluntary saccades, rather than the reflexive saccades that were elicited in our paradigm. Voluntary (internally triggered) and reflexive (externally triggered) saccades are known to be generated by at least partially different neural pathways and have been shown to be separately adaptable in humans (Erkelens and Hulleman 1993, Deubel 1995). Whether these experimental differences can explain our results remains to be tested.

Meeningberg et al. (1981) also reported a follow-up recording of one patient 3 months after the previous recording session (7.5 months postlesion). In these later recordings, saccades showed a greater degree of hypermetria into the blind hemifield, often by 50% or more, even on the first trial, and even when the eccentricities were large and randomized. This implies that adults may spontaneously develop hypermetria as a long-term compensatory strategy. However, this clearly did not occur in our testing, in spite of the considerable (6 months to 16 years postlesion) everyday visual experience of our patients. Thus we have no evidence that hypermetria is a spontaneously acquired strategy, at least in the first two decades of life.

This leads us to question whether hypermetria is always a beneficial strategy. If there is no information about the target location (that is, it could be anywhere in the blind field), then always making a large saccade into the blind field would be a poor strategy for locating a target that is parafoveal as a large return saccade would be needed. Whereas at the other extreme, making very small saccades would be time consuming for a peripheral target. On the other hand, if the patient expected the target to appear at an approximately known eccentricity it would pay to overshoot slightly the expected eccentricity so that only a small return saccade would be needed, in which case hypometria would be suboptimal. In the absence of any form of residual vision the best strategy would depend on the patient's expectation. It would also depend on whether the constraining saccadic variable is total time to reach the target or just the duration of the saccadic component (Harris 1995). In spite of allowing our patients to build up an expectation of target position, hypometria was still the preferred strategy.

One surprising finding in our data was a large degree of variability from one trial to the next. If a fixed deterministic strategy were adopted, we would expect approximately the same gain for each saccade both between and within trials. Clearly this did not happen. Figure 2 not only shows a wide range (0.07 to 1.50) of primary saccadic gains between trials, with no apparent systematic relation to the secondary saccades, but also how few points lie on the 'fixed magnitude' line. This demonstrates that saccades of a fixed magnitude are not generated repeatedly within trials until the target is reached. Nor can the apparent randomness of the primary saccadic gain be explained by a systematic change in strategy, or memorization of the target position. If this were the case, one would expect to see a gradual, directional change in saccadic gain.

Hypometria and a greater variable error have also been reported for saccades to predictable (Bronstein and Kennard 1987) and remembered (Bracewell et al. 1990, White et al. 1994) targets. Such predictive or remembered saccades are
made without a visible target. Our patients with hemianopia were also making saccades in the absence of a visible target. Although such reports may partly account for the hypometria observed, they are unlikely to account for the staircase pattern of saccades as the degree of hypometria reported was far less than that observed in our patients with hemianopia.

Hypometria and variability in saccades have also been reported in infants (Harris et al. 1993). However, in spite of this variability, there is a clear bias to undershoot. It has been proposed that when the saccadic system cannot program a saccade accurately enough, as for example in the case of infants, the system avoids overshooting by aiming for a hypometric position, which is near-optimal for minimizing total saccade flight-time (including corrective saccades) (Harris 1995). A similar theory could explain the low gains in the patients with hemianopia. However, while the variability in infants may be explicable in terms of immaturity, in adults with hemianopia it is unexplained. At present it is not clear whether the variability represents a normal stochastic strategy in the face of incomplete target uncertainty in the hemianopic field (see Harris 1998), or whether the lack of visual input disturbs the cerebellar saccadic gain controller (Optican and Robinson 1980).

Hypometria, though not consistent, was nevertheless observed into the blind field of seven patients. Hypometric saccades are generally associated with diseases of the cerebellum (Leigh and Zee 1983), however, we detected no cerebellar abnormalities in our patients. Thus we suggest that homonymous hemianopia should be considered as a differential diagnosis when saccadic hypometria is observed.

In conclusion these data show that multiple hypometric saccades into the blind field are a persistent 'strategy' in children with hemianopia even with many years of post lesion experience. This suggests that the relatively good compensation seen in these children with hemianopia is not due to a strategy of saccadic hypometria. It follows that, for the findings from this limited data set at least, intervention in the form of hypometric saccadic training may not be appropriate. Whether the hypometria we observed represents the upper end of the primary saccadic distribution or a separate distribution representing a distinct strategy is yet to be determined. Clearly our data raise more questions than answers, but at present we have no empirical evidence or even conceptual framework to support the notion that hypometria should be a beneficial compensatory strategy for reflexive saccades in hemianopic children.

Accepted for publication 25th March 1998.

Acknowledgements

We thank the charities Child Health Research Appeal Trust, Help a Child to See, and the Iris Fund for their support.

References


Letters to the editor

'Saccadic strategies in children with hemianopia'

SIR—We would like to commend Mezy et al. for their report in Developmental Medicine and Child Neurology volume 40 in which they reported on the saccadic strategies of 10 children with hemianopia. They concluded that 'multiple hypometric saccades into the blind hemifield are a persistent "strategy" in children with hemianopia... and that children with homonymous hemianopia do not develop a consistent strategy of saccadic hypermetria into the blind hemifield. We would like to indicate an interesting trend in the authors' data and ask the authors to comment on an additional clinical feature.

We reported the concurrence of an anomalous face turn toward the blind hemifield in 10 children with early onset hemianopia, with a range of onset between in utero and 1 year 6 months of age. We postulated that children with early onset hemianopia adopted an anomalous head posture to enlarge the 'functional' visual field on the blind side by allowing a larger saccade into the blind hemifield. Zangemeister et al. reported through the use of infra-red recordings that patients with early onset or congenital homonymous hemianopia use large 'overboosting' saccades into the blind hemifield. Although we did not formally test the saccades in our patients, we believed that the anomalous face turn allowed affected children to take better advantage of adaptive strategies such as hypermetric saccades, as Zangemeister et al. described. While none of the authors' patients used a preponderance of hypermetric saccades in the blind hemifield, the four patients with onset of the hemianopia during the first year of life used a greater percentage of hypermetric saccades than patients with onset after 1 year of age. The ages of patients who showed a greater percentage of hypermetric saccades are similar to those of the patients that we reported with anomalous face turns toward the blind hemifield.

We would be interested to know whether the authors noted anomalous head postures in any of their patients. Additionally, we would be interested to know whether any correlation between the presence of a face turn toward the blind hemifield and increased use of hypermetric saccades occurred. If such a correlation exists, this would provide some support for the theory that only children with the most immature visual systems are likely to develop and use these adaptive mechanisms. The authors' work provides valuable new information which may be important implications in the evaluation and treatment of children with childhood-onset hemianopia, and we hope they will continue this important work.

David K Coats MD
Evelyn A Paysse MD

Cullen Eye Institute
Baylor College of Medicine
Texas Children's Hospital
Houston, TX, USA

References

Laura Mezy et al. reply

SIR—We thank Coats and Paysse for their interest in our work and their suggestions regarding the relationship between the development of adaptive saccadic strategies and the occurrence of an anomalous face turn towards the blind field in early onset homonymous hemianopia. We cannot provide reliable information regarding the presence of anomalous face turns in our patients because our data were obtained retrospectively and the medical records of our patients showed no clear evidence of such face turns. However, a general body orientation was noted in one patient (patient 1) with cerebral palsy. Of course, a subtle face turn may have gone unnoticed or may not have been recorded. Thus we cannot comment on the relationship between hypermetric saccades and the use of a face turn in our patients, or how the time of onset of the hemianopic defect may affect any adaptive strategy.

The use of ipsilateral face turn in hemianopic patients is open to a number of intriguing interpretations. Firstly, if the face is turned ipsilateral to the blind field while the eyes are kept looking straight ahead, a greater ocuulomotor range into the blind field is made available, as proposed in Coats and Paysse's letter. This greater ocuulomotor range would facilitate the generation of hypermetric saccades into the blind field because smaller saccades made ipsilaterally to the blind field from the primary position would reach 'deeper' into the blind field.

Alternatively, a face turn could allow saccades of a visual scanning sequence to incorporate more of the otherwise unseen field. Most saccades of a scanning sequence are distributed around the primary position. So, while there would be a bias towards scanning on one side of body-centred space, information from the other side would still be available in the intact peripheral visual field.

A third benefit of an anomalous face turn could come from an improved optic flow field during natural locomotion. The optic flow field is the fluctuating patterns of reflected light that pass across the retina as a result of any relative movement between the observer and the environment. These patterns radiate from the centre of expansion when moving in the forward direction. If the face and eyes are turned to the side, the centre of expansion and a more symmetrical optic flow field would be regained. This would be expected to aid the control of speed and direction of locomotion. These are just three examples of how a face turn might be beneficial in different contexts.


258
Without further research it is difficult to postulate which, if any, of these interpretations of an anomalous face turn is valid. We are continuing with our research in this field, using more accurate eye movement recording techniques, and we shall certainly make an effort to address this interesting question in the future.

Laura E Mezey
Christopher M Harris
Fatima S Shaukat
Chris Timms
Anthony Kritis
Peter West
David S Taylor

Department of Ophthalmology
Great Ormond Street Hospital for Children NHS Trust
Great Ormond Street
London WC1N 3JH, UK.

‘Multidisciplinary Appraisal of the British Institute for Brain Injured Children, Somerset, UK’

Sir—I am writing in response to Dr Richard Morton’s letter in Developmental Medicine and Child Neurology (41: 211–2) concerning an assessment of the British Institute for Brain Injured Children (BIBIC). This appraisal was undertaken in 1995 and 1996 and was the instrument that the BIBIC needed to make changes that were already thought to be necessary. We no longer practise the Doman–Delocato approach to neurodisability, but have restructured our programme to reflect more up-to-date methods. A physiotherapist, nursery nurse, and teachers of special needs have been recruited to enrich the skills available. Furthermore, continuing training of the staff has taken place. Some of this training has been conducted with the assistance of the original assessment team.

We extend our thanks to Dr Morton and his team and look forward to his visit later this year so that he may see for himself the progress we have made and continue to make.

Jo Judge MRCPCH, Medical Director, BIBIC
The British Institute for Brain Injured Children
Knowle Hall
Bridgwater
Somerset
TA7 8PJ

Mac Keith Meetings

Transition to Adulthood (Open meeting)
Royal Society of Medicine, London. Monday 28th June 1999
Organised by Martin Bax and Greg O’Brien

Non-accidental Head Injury (Open meeting)
Royal Society of Medicine, London. Friday 9th July 1999
Organised by Bob Minns and Keith Brown

Neuroprotection of the Infant (Closed research workshop)
Royal Society of Medicine, London. Thursday 7th to Friday 8th October 1999
Organised by Martin Bax, Murray Goldstein, Philippe Evrard, and David Edwards

Rett Syndrome (Open meeting)
Royal Society of Medicine, London. Friday 15th October 1999
Organised by Alison Kerr

Specific Learning Disorders (Open meeting)
Royal Society of Medicine, London. November 1999 – date to be confirmed
Organised by Martin Bax and Greg O’Brien

Disordered Auditory Processing (Closed research workshop)
Royal Society of Medicine, London. December 1999 – date to be confirmed
Organised by Anne O’Hare

For further information, and to book places at open meetings, contact Vesna Milenkovic, CME Department, The Royal Society of Medicine, 1 Wimpole St, London W1M 8AE.
Tel. 0171 290 2988
E-mail: Vesna.Milenkovic@roysocmed.ac.uk
SUPPORT FOR THE SACCADIC FLIGHT TIME MINIMISATION HYPOTHESIS

C.M.Harris, L.E.Meze
Dept of Ophthalmology and Visual Sciences Unit, Great Ormond Street Hospital and the Institute of Child Health, London WC1N 3JH

Aim It is well known that saccades undershoot their targets. This undershoot bias is particularly prominent in infancy. It has been proposed that this bias reflects an economic strategy to minimise total saccadic flight time in the presence of target uncertainty as opposed to a simple retinal error feedback control mechanism. We attempted to distinguish between these hypotheses using adaptive control paradigms in which an intrasaccadic secondary target displacement was elicited by the primary saccade. In the critical experiment the intrasaccadic target displacement was randomised so that average retinal error over the course of the experiment was zero. According to the retinal error hypothesis we would expect no adaptive change in the gain of saccades during the random paradigm while the saccadic flight time minimisation hypothesis would predict a decrease in gain.

Methods Subjects were 6 adults (age range 24-44). Adaptation was elicited to initial target displacements of $+10^\circ$, with an intra-saccadic target step of $2^\circ$. Three separate experiments were performed by each subject in which the intra-saccadic target step was either onwards ($+2^\circ$), backwards ($-2^\circ$) or randomised onwards and backwards. Experiments consisted of 200 adaptive trials (with the intra-saccadic target displacement) and 50 standard trials before and after adaptation to assess gain changes over the course of the experiment. Eye movements were recorded with an infra-red eye tracker. Saccades were elicited to a red laser spot front-projected onto a white screen in front of the subject.

Results All subjects were able to appropriately adaptively adjust the gain of their saccades over the course of the gain increasing and gain decreasing experiments. Average gain decreases were larger in magnitude (-0.103) than gain increases (+0.051). In the random paradigm all subjects showed a decrease (-0.078) in the gain of their saccades in spite of there being no retinal error on average. One subject was found to be an 'express saccade maker'. Both express saccades and normal reflexive saccades were found to change their gain over the course of the experiment.

Conclusion A decrease in gain when the average retinal error over the course of the experiment was zero supports the saccadic flight time minimisation hypothesis. Although not proven, the saccadic flight time minimisation hypothesis is consistent with the low gain of saccades observed in infancy.