Head-Unrestrained Primate Gaze Adaptation

by

Aaron Lee Cecala

Submitted in Partial Fulfillment

of the

Requirements for the Degree

Doctor of Philosophy

Supervised by

Edward G. Freedman

Department of Neurobiology and Anatomy
School of Medicine and Dentistry

University of Rochester
Rochester, New York

2009
Dedication

I would like to dedicate this thesis to my wife Rebecca and my parents Donald and June Cecala whose unwavering emotional support has allowed me to complete this stage of my academic journey.
Curriculum Vitae

The author was born in Springville, New York on August 12, 1980. He attended Allegheny College from 1998 to 2002, and graduated with a Bachelor of Science degree in neuroscience and psychology in 2002. He came to the University of Rochester in the fall of 2002 and began graduate studies in the Interdepartmental Graduate Program in Neuroscience. He was awarded funding from the Interdepartmental Neuroscience Training Grant (NINDS T32 NS07489) in 2002 and 2003, and the Center for Visual Sciences Training Grant (NEI T32 EY07125) in 2004 and 2005. He pursued his research in Neurobiology and Anatomy under the direction of Professor Edward G. Freedman and received the Master of Science degree from the University of Rochester in 2006.
Acknowledgements

I would like to thank Edward G. Freedman for his constant support of career goals and his critical assessment of my work. I would also like to thank the members of the Freedman lab for contributing to the intellectual environment in which this work was carried out and their support of my work. Finally, I would like to acknowledge the efforts of Drs. Marc Scheiber, David Pinto, David Knill, and William Merigan (chair) for serving on my thesis committee.
Abstract

Changing the direction of the line of sight (gaze) allows primates to gather visual information from their surrounding environment. Gaze shifts can result from movements of the eyes, head, and/or body. In order to efficiently obtain information from the environment, the central nervous system must maintain the accuracy of gaze shifts by adjusting the metrics of these effectors in response to persistent changes in sensory input (sensorimotor adaptation) that result from aging, disease, or changes to the reliability of sensory cues. Studies of primate gaze adaptation have emphasized changes in eye movement amplitude in response to small (<5°) visual errors in head-restrained subjects. The work presented in the current thesis investigated the mechanism by which the central nervous system adjusts gaze amplitude in response to large (>20°) residual visual errors in head-unrestrained subjects. I tested hypotheses describing the nature of this mechanism in two primate species using behavioral (in humans and monkeys) and neurophysiological (in monkeys) methods that allowed gaze, eye, and head motor commands to be dissociated.

Three results from my behavioral experiments support a hypothesis that a gaze command signal is adjusted to maintain the accuracy of gaze shifts towards visual targets: 1) changes in gaze amplitude in response to large visual errors were the result of alterations to both eye and head
movement amplitudes; 2) modifications to eye and head movements were dependent upon the position of the eyes at gaze onset, and; 3) changes to gaze amplitude at one initial eye position transferred to gaze shifts initiated from other eye positions. A neurophysiology experiment was designed to test the hypothesis that a modification to a gaze command generated by the superior colliculus (SC) could account for these behavioral observations. Our results suggest that gaze shifts evoked by microstimulation of the SC can be modified in response to large visual errors. The combined results of the experiments described in the current thesis are consistent with the hypothesis that a gaze command is altered prior to being decomposed into separate eye and head movement commands during gaze adaptation.
# Table of Contents

Chapter 1  
**General Introduction**  
1.1  
**Primate Visual Orienting Movements**  
1.1.1  
Saccades  
2  
1.1.2  
Eye-Head Coordination  
3  
1.2  
Primate Gaze Amplitude Adaptation  
1.2.1  
Saccades  
5  
1.2.2  
Coordinated Eye-Head Movements  
6  
1.3  
Superior Colliculus involvement in Gaze Control  
8  
References  
13

Chapter 2  
**Human Head-Unrestrained Gaze Adaptation**  
2.1  
Introduction  
22  
2.2  
Material and Methods  
27  
2.3  
Results  
34  
2.4  
Discussion  
55  
References  
64

Chapter 3  
**Monkey Head-Unrestrained Gaze Adaptation**  
3.1  
Introduction  
88  
3.2  
Material and Methods  
92
3.3 Results

3.4 Discussion

References

Chapter 4 Superior Colliculus Stimulation and Conclusion

4.1 Introduction

4.2 Methods

4.3 Preliminary Results and Discussion

4.3.1 Alternative Loci for Adaptation

4.3.2 Brainstem Control of Primate Eye and Head Movements

4.3.3 Cerebellar Involvement in Primate Gaze Control

References

Chapter 5 General Synthesis

References
## List of Tables

<table>
<thead>
<tr>
<th>Table</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 2.1</td>
<td>Transfer of gaze, saccade, and head contribution between pre- and post-transfer phases</td>
<td>87</td>
</tr>
<tr>
<td>Table 3.1</td>
<td>Transfer of gaze, saccade, head contribution, and total head amplitude between pre- and post transfer phases</td>
<td>165</td>
</tr>
<tr>
<td>Table 3.2</td>
<td>Gaze Adaptation Trial Constants</td>
<td>166</td>
</tr>
<tr>
<td>Table 3.3</td>
<td>Head-Restrained Summary Data</td>
<td>167</td>
</tr>
<tr>
<td>Table 3.4</td>
<td>Changes to gaze, saccade, head contribution, and total head amplitude during head-restrained transfer experiments</td>
<td>168</td>
</tr>
<tr>
<td>Figure</td>
<td>Title</td>
<td>Page</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Figure 1.1</td>
<td>Characteristics of primate gaze shifts.</td>
<td>20</td>
</tr>
<tr>
<td>Figure 2.1</td>
<td>Schematic diagrams of trial types.</td>
<td>71</td>
</tr>
<tr>
<td>Figure 2.2</td>
<td>Example human forward adaptation from centered eye position.</td>
<td>73</td>
</tr>
<tr>
<td>Figure 2.3</td>
<td>Example human backward adaptation from centered eye position.</td>
<td>75</td>
</tr>
<tr>
<td>Figure 2.4</td>
<td>Summary human data- centered eye position.</td>
<td>77</td>
</tr>
<tr>
<td>Figure 2.5</td>
<td>Example human adaptation from eccentric eye positions.</td>
<td>79</td>
</tr>
<tr>
<td>Figure 2.6</td>
<td>Summary human data- forward adaptation from eccentric eye positions.</td>
<td>81</td>
</tr>
<tr>
<td>Figure 2.7</td>
<td>Summary human data- backward adaptation from eccentric eye positions.</td>
<td>83</td>
</tr>
<tr>
<td>Figure 2.8</td>
<td>Example human head-unrestrained adaptation transfer experiments.</td>
<td>85</td>
</tr>
<tr>
<td>Figure 3.1</td>
<td>Schematic diagrams of trial types, targets, and reward windows.</td>
<td>143</td>
</tr>
<tr>
<td>Figure 3.2</td>
<td>Example monkey backward adaptation</td>
<td></td>
</tr>
</tbody>
</table>
from centered eye position. 145

Figure 3.3 Example monkey forward adaptation from centered eye position. 147

Figure 3.4 Summary monkey data- centered eye position. 149

Figure 3.5 Example monkey backward adaptation from eccentric eye positions. 151

Figure 3.6 Example monkey forward adaptation from eccentric eye positions. 153

Figure 3.7 Summary monkey data-backward adaptation from eccentric eye positions. 155

Figure 3.8 Summary monkey data- forward adaptation from eccentric eye positions. 157

Figure 3.9 Transfer of gaze adaptation state to novel eye positions. 159

Figure 3.10 Comparison of relative eye and head-contribution to gaze shifts of equal amplitude. 161

Figure 3.11 Large amplitude head-restrained adaptation. 163

Figure 4.1 Schematic diagrams of trial types. 191

Figure 4.2 Modification of stimulation evoked gaze shifts. 193
Chapter 1: General Introduction

The ability of chordates to actively acquire high quality sensory information from their environment depends upon a species’ ability to orient specialized sensory receptors toward stimuli of interest. Reorientation of sensory receptors may be accomplished by voluntary, goal-directed movements involving multiple body segments. For example, visual information is obtained by changing the orientation of a photoreceptor sheet and can be accomplished by movements of the eyes, head, and/or body depending on the species specific mobility of these effectors. In primates, accurate and precise movements of the line of sight (gaze) allow for the placement of the fovea, a specialized region of the retina, on objects of interest. An adaptive mechanism is believed to maintain gaze accuracy in response to dynamic internal (e.g. senescence of the motor plant) and external (e.g. changes to the reliability of visual information) environments thereby allowing a primate to efficiently acquire visual information throughout its lifetime. The primary goal of this thesis was to test hypotheses concerning the type of motor command modified during primate gaze adaptation when the eyes and head are used to orient towards visual stimuli.
1.1 Primate Visual Orienting Movements

1.1.1 Saccades

When the head is prevented from moving, changes in the line of sight are accomplished by high velocity, conjugate rotations of the eyes known as saccades. Figure 1A shows data collected from a rightward saccade produced by a head-restrained monkey towards a target displaced ~18° from the subject’s initial fixation position. In this case, the primary saccade undershoots the peripheral target ($T_1$). Saccades are defined by a set of metrical relationships between amplitude-peak velocity-duration (Bahill, Clark, & Stark, 1975; Baloh, Sills, Kumley & Honrubia, 1975; vanGisbergen, Van Opstal, & Ottes, 1984). For example, the relationship between peak eye velocity and movement amplitude is described by a saturating function and there is a linear relationship between saccade duration and movement amplitude (Fig 1.1B). In addition to these stereotyped relationships, saccade kinematics (temporal progression) are predictable given information about movement amplitude (vanGisbergen et al. 1984). Movements that do not meet these criteria are indicators of severe neuromechanical deficits (Leigh & Zee, 1999).

The optimal orienting response to the sudden appearance of a visual target of interest in the periphery is an eye movement that rapidly reaches and ends on the target. However, as shown in Fig. 1.1A, primate
subjects frequently show small degrees of saccadic dysmetria, most commonly undershooting (hypometria) of the target. The difference between the final position of the primary movement and the target location (i.e. retinal error at the end of the primary movement) is then often reduced by a corrective saccade (Fig. 1.1A). The degree of dysmetria is usually relatively small, about 10% of the amplitude of the saccade for non-predictable targets (Becker & Fuchs, 1969; Troost et al, 1974). The accuracy and precision of primary saccades can be influenced by the size and direction of target displacement (Kowler & Blaser, 1995), age of the subject (Bono et al, 1996; Hotson & Steinke, 1988; Huaman & Sharpe, 1993; Irving et al, 2006; Jagla et al, 1992; Munoz et al, 1998; Sharpe & Jackson, 1987; Shupert & Fuchs, 1988), the nature of the stimuli (e.g. target size or luminance, Deubel, 1989), intra-saccade target displacement (McLaughlin, 1967) or neurological impairment (Leigh & Zee, 1999).

1.1.2 Eye-Head Coordination

When a primate’s head is allowed to move, changes of the line of sight can be accomplished by coordinated movements of the eyes and head. Figure 1.1C shows position traces for eye, head, and gaze for a 45.1° horizontal gaze shift in a monkey. In this case: 1) the subject uses both the eyes and head to produce a ~45° change in gaze; 2) the eyes
begin deviated -2.0° in the orbits with respect to movement direction; 3) both eye and gaze movement onset occur simultaneously; 4) head onset occurs after eye/gaze onset; 5) due to the vestibulo-ocular reflex (VOR) the eyes immediately begin to counter rotate when the gaze shift ends; and 6) head movement offset occurs after the gaze shift has terminated.

In primates, the metrics of gaze, eye and head movements used to re-orient the line of sight towards visual targets are predictable and dissociable (monkeys: Freedman & Sparks, 1997a, Freedman, 2005, Freedman, 2008a, Freedman & Cecala, 2008; humans: Volle & Guitton, 1993; Stahl, 1999). For example, for gaze shifts with the same amplitude and direction, the contributions of the eyes and head vary inversely as a function of the initial position of the eyes in the orbits; the head tends to contribute more when the eyes are deviated towards (head deviated away) from the ensuing target (Figure 1.1D). Furthermore, like head restrained saccades described above, the amplitude, duration, and peak velocity relationships for gaze, eye, and head movements are highly stereotyped given knowledge about the initial eye position and gaze movement amplitude (see Freedman, 2008b for review).

Head-unrestrained gaze shifts towards visual targets are accurate in both humans (e.g. Guitton & Volle, 1987) and monkeys (e.g. Freedman & Sparks, 1997a), although the same slight hypometria described for
saccadic eye movements above is also typical for head-unrestrained gaze shifts. For example, in two monkey subjects, Freedman & Sparks (1997a) reported that horizontal gaze amplitude was >90% of target displacement amplitude. The effects of aging and target characteristics on gaze accuracy in head-unrestrained subjects have not been thoroughly explored; however, the accuracy of head unrestrained gaze shifts can be impaired as a result of diseases that affect cerebellar and brainstem function (e.g. cerebellar ataxia, Shimizu et al, 1981).

1.2 Primate Gaze Amplitude Adaptation

1.2.1 Saccades

Maintaining the accuracy and precision of visual orienting movements is a crucial function of the nervous system. Within the context of visual orienting movements, investigation of the mechanisms responsible for the adjustment of motor output given persistent changes in sensory input (sensorimotor adaptation) has centered on the experimental introduction of visual errors at the end of saccades when the head does not move. McLaughlin (1967) demonstrated that the amplitude of a saccade towards a visual target (T₁) in a particular location can be gradually altered by repeatedly shifting the location of the target during the saccade. The resultant visual error (between the retinal image of the displaced target (T₂) and the fovea) drives
adaptation so that the amplitude of saccades become either smaller (backward adaptation) or larger (forward adaptation) than saccades made before adaptation (Wallman & Fuchs, 1998).

The majority of studies describing primate behavior during the McLaughlin task have characterized the magnitude of adaptation in response to visual errors that are typically 20-30% of the primary saccade (for review see Hopp & Fuchs, 2004). Since the amplitude of saccades during the pre-adaptation phase of these experiments is often between 8-15°, the 20-30% target shift amounts to approximately a 2-5° visual error at the end of the primary movement. The magnitude of saccadic adaptation often does not reduce visual error at the end of the primary saccade to zero, is highly variable across subjects and across experiments in the same subject, resulting in saccade amplitudes that are reduced or increased by ~2-4° (Fuchs, Reiner, & Pong, 1996; Straube et al, 1997; Robinson, Noto, & Bevans, 2003). Few studies of saccadic adaptation have attempted to alter large amplitude gaze shifts using large intra-saccade target displacement (but see Robinson, Noto, Bevans, 2003).

1.2.2 Coordinated Eye-Head Movements

Although motility of both the eyes and head increases the range of the visual world that a primate is permitted to explore in a single gaze
shift, an adaptive gaze control system in this context is faced with the problem of coordinating both effectors to maintain gaze accuracy. There are at least three alternative hypotheses that describe the mechanism by which an adaptive gaze control system could adjust gaze amplitude in response to visual errors. An “eye-only” or “head-only” hypothesis states that only one of the two effectors is modified at any time to alter gaze amplitude in order to produce more accurate gaze shifts. For example, if a gaze shift falls short of its intended target the adaptive control mechanism would increase only the head (or eye) contribution to the movement. A third alternative hypothesis states that the gaze command used to direct the line of sight, upstream from the commands to separately move the eyes and head, is modified during gaze adaptation. This “gaze command hypothesis” makes several explicit predictions concerning the adaptive control of gaze shifts: 1) changes in gaze amplitude may result from changes to both eye and head contributions to gaze; 2) changes in eye and head contribution to gaze will vary as a function of the orbital eye position at gaze onset and the magnitude of gaze adaptation; and 3) changes in gaze amplitude, induced at one eye position, will transfer to gaze shifts initiated from novel eye positions. The observation that the relative contribution of the eyes and head used to re-direct the line of sight can be predicted based on the position of the eyes at gaze onset and the gaze vector during
visually guided movements (humans: Volle & Guitton, 1993; Stahl, 1999; monkeys: Freedman & Sparks, 1997a; Freedman, 2005; Freedman, 2008a) will allow us to dissociate these alternative hypotheses in each of the experiments described in this thesis. The behavioral experiments described in chapters 2 and 3 will provide evidence that supports the gaze hypothesis described above.

1.3 Superior Colliculus involvement in Gaze Control

Evidence gathered from microstimulation (Freedman et al, 1996), inactivation (Walton et al, 2008), and single unit recording (Freedman & Sparks, 1997b) experiments in rhesus monkeys support a hypothesis (Freedman, 2001) that activity in the primate superior colliculus (SC) encodes a gaze displacement command which is parsed downstream from this structure into commands to move the eyes and/or head. For example, suprathreshold stimulation of the deeper layers of the SC produces contraversive gaze shifts whose metrical relationships are comparable to visually guided gaze shifts matched for amplitude, direction, and initial eye position (Freedman et al, 1996). The relative eye and head contributions for gaze shifts evoked from a particular SC location vary as a function of initial eye position in a fashion similar to visually guided movements. When using suprathreshold stimulation, the amplitude and direction of gaze shifts are a function of the site of
stimulation in the SC with movement amplitudes increasing from rostral to caudal, and changing direction from upward to downward from medial to lateral (Robinson, 1972; Freedman et al, 1996). Gaze related burst neurons recorded from the intermediate and deep layers of a particular SC location produce a high frequency burst of activity associated with gaze shifts of a particular vector, not the eye or head components of gaze (Freedman & Sparks, 1997b). Gaze related burst neurons are arranged in a topographic motor map that corresponds to that produced by microstimulation (Freedman & Sparks, 1997b). In short, the locus of neural activity in the SC motor map specifies the amplitude and direction of a gaze shift, not the relative contributions of the eyes or head to that gaze shift.

Two alternative hypotheses describing collicular activity could account for a change in gaze output during the McLaughlin paradigm. First, as gaze amplitudes change, the locus of SC motor activity could change systematically. For example, during backward adaptation, as gaze amplitude gradually decreases, the locus of activity specifying the observed gaze shift would gradually become more and more rostral in the SC motor map. In this case, the output of the SC specifies the motor output that is actually observed. Alternatively, the locus of SC motor activity could remain constant throughout adaptation. In this instance, SC activity specifies a change in the line of sight towards the first
peripheral visual target ($T_1$) presented to the subject, not the actual movement produced. In the latter case, the collicular command must be altered at a location other than the SC to account for the change in gaze amplitude. Both single unit recording and microstimulation experiments used to address these hypotheses in the head-restrained monkeys have failed to clearly dissociate these hypotheses.

Single unit neural recordings have provided support for both hypotheses described above. Frens & van Opstal (1997) described a subset of neurons whose burst metrics did not change during adaptation even though primary saccade amplitude towards $T_1$ changed appropriately during the McLaughlin task. These authors interpreted their results as being consistent with collicular output representing a gaze displacement command towards $T_1$, not the actual saccadic eye movement produced. In contrast, a more recent study by Takeichi and colleagues (2007) reported a subset of collicular neurons whose burst metrics changed systematically with saccade amplitude during adaptation. The latter result is consistent with the hypothesis that SC output specifies actual saccade amplitude during saccadic adaptation. The results of microstimulation studies have been equally ambiguous.

The amplitude of saccadic eye movements elicited by electrical stimulation in the deeper layers of the SC can be altered by presenting a visual target after movement onset that is either closer to or further
away from the initial fixation point compared to the stimulated movement endpoint (Fitzgibbon et al. 1986; Melis & van Gisbergen 1996); however, saccades towards a visual target presented at the location of the pre-adaptation stimulation endpoint fail to show the same magnitude of adaptation as the stimulated movements. In contrast to these early studies, Edelman & Goldberg (2002) observed a clear transfer of adaptation in the McLaughlin task to movements elicited by SC microstimulation. This was most apparent when the authors used lower current intensities than those used in the two previous studies to evoke saccades from the SC. In short, the results of these studies shed very little light on the mechanisms underlying saccadic adaptation.

During head-restrained saccadic adaptation, modification to saccade motor commands could occur in the local SC circuitry, in SC afferents, in the various regions of the oculomotor brainstem, and/or be specific to population output of the SC. The microstimulation experiment proposed in Chapter 4 is designed to test the hypothesis that a gaze command initiated in the SC of a head-unrestrained monkey can be modified by presenting a post-gaze shift visual error.

In summary, a number of behavioral questions about head-unrestrained gaze adaptation remain unanswered: 1) can large (> 15°) adjustments in gaze amplitude be elicited using the McLaughlin paradigm? 2) when the head is allowed to move, what components (eye
or head) of the gaze shift are adjusted during adaptation? 3) Are the characteristics (rate and magnitude) of head-restrained and head-unrestrained gaze adaptation similar? 4) Can gaze shifts initiated by microstimulation of the superior colliculus in a head-unrestrained monkey be altered by presentation of a visual target? These questions are the focus of the work presented in the following dissertation.
References:


Figure 1.1. Characteristics of primate gaze shifts produced by monkey S. A) Eye position as a function of time when the head is prevented from moving. B) Saccade amplitude-duration relationship when the head is prevented from moving. C) Gaze (black trace), eye (dark gray trace), and head (light gray trace) position as a function of time for a 45° rightward gaze shift. D) Gaze (green circles), saccade (red circles), head contribution (blue squares) amplitude for 35° rightward gaze shifts. See text for further details.
Chapter 2:

Human Head-Unrestrained Gaze Adaptation

2.1 Introduction

Saccades (high velocity, conjugate movements of the eyes) can redirect the line of sight such that the images of objects of interest fall near the fovea. These visual orienting movements, defined by a set of amplitude-velocity-duration relationships (Bahill, Clark, & Stark, 1975; Baloh, Sills, Kumley & Honrubia, 1975; VanGisbergen, Van Opstal, & Ottes, 1984), are accurate to within 5-10% of target displacement (Hyde, 1959; Becker, 1972; Becker & Fuchs, 1969; Henson, 1978,1979; Prablanc, Masse, and Echallier, 1978; Kowler & Blaser, 1995) and precise: the standard deviation of saccade endpoints is ~3-6% of target eccentricity (Kowler & Blaser, 1995). Maintenance of this degree of accuracy and precision must be accomplished in the face of growth and development, as well as possible damage and senescence of the sensorimotor control apparatus. Investigation of the mechanisms of sensorimotor adaptation responsible for adjustment of motor output given persistent changes in sensory inflow (Oestreich, Dembrow, George, & Zakon, 2006) within the context of saccadic eye movements has centered on the experimental introduction of visual errors at the end of saccades. For example, McLaughlin (1967) demonstrated that the
amplitude of a saccade to a visual target in a particular location can be gradually altered by repeatedly and surreptitiously shifting the location of the target. The resultant visual error (between the retinal image of the displaced target and the fovea) drives adaptation so that the amplitude of saccades become either smaller (“backward”) or larger (“forward”) than saccades made before adaptation (Wallman & Fuchs, 1998). The magnitude and rate of horizontal saccadic adaptation using the McLaughlin task has been characterized over a small range of visual errors (Hopp & Fuchs, 2004). The majority of experiments using this task attempt to elicit changes in saccade amplitude on the order of ~20-30% of the pre-adaptation movement amplitude (e.g. Straube, Robinson, & Fuchs, 1997; Deubel, Wolf, & Hauske, 1986). Since the preadaptation amplitude of saccades in these experiments is often between 8-15°, the 20-30% target shift amounts to approximately a 2-5° visual error at the end of the primary movement. In these experiments, adaptive mechanisms often fail to reduce this visual error to zero, and as a result saccade amplitudes are reduced or increased by ~2-4°. This type of saccadic adaptation has a roughly exponential time course with rate constants between 100-800 saccades in monkeys (Straube et al, 1997) and 30-60 saccades in humans (Albano, 1996; Deubel et al, 1986, Deubel, 1987; Frens & van Opstal, 1994). The rate and magnitude of saccadic adaptation is highly variable across subjects and across
experiments in the same subject (Fuchs, Reiner, & Pong, 1996; Straube et al, 1997; Robinson, Noto, & Bevans, 2003).

The role of the imposed visual error at the end of the primary saccade in driving saccadic adaptation was tested by Robinson et al. (2003). In their experiment, the amplitude of the initial saccade and the visual error at the end of this saccade were systematically varied. The visual errors that resulted in the largest changes in saccade amplitude were between 15-45% of the initial target eccentricity. Visual errors larger than 45% were only slightly less effective in inducing saccadic adaptation. Despite these observations, the largest primary movement amplitude used in this experiment was 18°. Few saccadic adaptation experiments have attempted to increase or decrease the amplitude of larger initial movements (however, see Phillips, Fuchs, Ling, Iwamoto, & Votaw, 1997). To date, regardless of whether the head is restrained or allowed to move, it has been assumed that large primary gaze shifts cannot be systematically adjusted in response to large visual errors.

When the head is free to move, gaze shifts are often accomplished by combinations of saccades and simultaneous movements of the head. The relationships between gaze, eye, and head amplitude, peak velocity, and duration are predictable when gaze amplitude (or target displacement) and the initial positions of the eyes
in the orbits are known (Volle & Guitton, 1993; Guitton & Volle, 1987; Delreux, Abeele, Lefevre, & Roucoux, 1991; Stahl, 1999; 2001; Freedman & Sparks, 1997; Freedman, 2005). Prior descriptions of head-unrestrained gaze adaptation have focused on the transfer of head-restrained saccadic adaptation to either head-only movements (Kroller, Pelisson, & Prablanc, 1996) or combined eye-head gaze shifts (Phillips et al., 1997). Kroller and colleagues (1996) did not observe transfer of saccadic adaptation to head only movements in humans. However, Phillips and colleagues observed the complete transfer of head-restrained, backward saccadic adaptation, induced using the McLaughlin task, to head-unrestrained gaze shifts in monkeys. Also, in one head-unrestrained subject, they were able to reduce gaze amplitude directly using this task. From these observations, Phillips and colleagues suggested that the gaze displacement command underlying both saccadic and combined eye-head gaze shifts had been adjusted by a visual error control mechanism. According to this hypothesis, a gaze displacement command, upstream of separate eye and head displacement commands, is altered during adaptation. This hypothesis predicts that the amplitude of a gaze shift will increase or decrease throughout the adaptation process independent of the relative amplitudes of the eyes and head used to shift the line of sight. In this case, the relative contributions of the eyes and head to a gaze shift are
determined downstream from the locus of adaptation. An alternative hypothesis states that either the eyes and/or head are altered independently from each other during the adaptation process. For example, if adaptation resulted in a $20^\circ$ reduction in gaze amplitude that was produced by reducing saccade amplitude by $15^\circ$ and a concomitant $5^\circ$ reduction in head contribution, these reductions in eye and head movements would persist in response to presentation of a target in the adapted location regardless of the initial conditions. These alternative hypotheses are dissociable when gaze shifts are initiated from a variety of initial eye positions.

The goals of the present study were to: 1) use the McLaughlin task to elicit large changes in gaze amplitude in head-unrestrained, human subjects; 2) describe the magnitude of forward and backward gaze adaptation; 3) quantify the relative contributions of the eyes and head to this adaptation, as well as 4) determine the amount of adaptation transfer between movements initiated with the eyes in different orbital positions. A preliminary account of this study has appeared elsewhere (Cecala & Freedman, 2005).
2.2 Material and Methods

Subjects

Ten neurologically normal human subjects (mean age 24.6± 2.4yr; 8 male and 2 female) served as subjects. With the exception of the first author (identified henceforth as subject A), subjects were naïve to the goals of the current investigation. Subjects participated in multiple data collection sessions that were separated by at least 2 days. Each data collection session is identified by a subject-specific letter and session number. For example, “H1” are data from the first adaptation experiment (regardless of adaptation direction) in which subject H participated, “H2” are data from the second adaptation experiment in which subject H participated, and so on.

All procedures were approved by the University of Rochester Institutional Review Board and were carried out in full accordance with the principles of the Declaration of Helsinki. The procedures were fully explained to the subjects, who gave written consent before the experiments and were compensated for their participation.

Visual Target Presentation

During all experiments subjects sat on a modified orthopedic chair in the center of 2.5m diameter, 0.5” plexiglas sphere (Capital
Plastics, Beltsville, MD). The sphere was placed inside a 2m cube, housing the Helmholtz coils used for magnetic field generation (CNC Engineering, Seattle, WA). Care was taken to align the cube and sphere centers. The inside of the sphere was painted 18% gray, and served as the surface upon which visual targets were presented. Targets consisted of a fixed array of 43 lasers (650 nm, Calpac). Lasers were focused on the surface of the sphere and each spot subtended 0.1°. Laser spot locations were determined using a Fick gimbal, and referenced to a central (0,0) location. This reference location was defined as the intersection of the sphere and a horizontal line passing through the geometric center of the sphere and parallel to the sides of the field coil frame.

Eye and Head Measurements

The magnetic field used to measure horizontal eye and head positions was generated by two pairs of coils in spatial and phase quadrature (Collewijn, 1977). Signals from the eye coil (Skalar Delft, The Netherlands) and matching head-mounted coil were linear within ~2% over 360° in the horizontal plane. Vertical eye and head positions were proportional to the sine of the angle of the coils and the straight ahead position. Horizontal and vertical, eye and head position signals were filtered and sampled at 1kHz. Velocities were calculated from position
signals using a parabolic differentiation (see Freedman, 2005 for description).

To insert the annular contact lens eye coils, a subject’s eye was anesthetized with proparacaine HCl (0.5%, Alcon Laboratories). To prevent irritation, eye coils were left in place for no longer than 40 minutes. The head coil was mounted on a lightweight head band securely fastened at the beginning of each experimental session. In addition to carrying the head coil, 3 diode lasers were secured to the top of the head band. The central laser of these three was aligned approximately in the midsagittal plane. The two other lasers pointed 30° to the left and right of this central laser. Head coil calibration was accomplished by asking subjects to align the central head-mounted laser spot with various static laser positions within the sphere; gains and offsets were adjusted appropriately. During experimental sessions the head-mounted lasers could be used to provide visual feedback of head position so that subjects could align their eyes and heads, or begin trials with the eyes deviated in the orbits either to the left or right of the head-centered position. This allowed the experimenter to control the initial position of the eyes at the onset of the gaze shift, which has been shown to systematically affect the relative eye and head amplitude associated with gaze shifts of particular amplitude and direction (Volle
Behavioral Tasks

Subjects performed 3 tasks that each began with the illumination of one of the 3 head-mounted lasers. This was followed by illumination of an initial fixation target (T0). Subjects were required to align the head-mounted laser spot with T0 and simultaneously fixate T0. T0 was typically located straight ahead of the subject (target location 0, 0). If the central head-mounted laser was lit, the eyes and head began aligned in the straight-ahead position. If one of the other lasers was illuminated, in order to align the head-mounted spot with T0, subjects needed to rotate their heads 30° to the right or left of straight-ahead while keeping line of sight directed at T0. Thus, initial positions of the eyes in the orbits could be zero (aligned with the head) or 30° to the left or right while the initial direction of gaze was constant. Subjects were required to look at and align the head-mounted laser spot on T0 for between 600 and 1600 ms (200 ms increments). If either the line of sight or head position deviated beyond a computer defined window (6° radius) trials were aborted.

Although the acceptance window was fairly large, alert subjects generally aligned the head-mounted laser and line of sight within ~2° of the illuminated target. If these conditions were met, the head-mounted
laser and T0 were extinguished and a target in a new location (T1) was simultaneously illuminated. To this point all trial types were identical. During “Step” trials (Fig. 2.1A), T1 remained illuminated, and subjects were required to fixate this new target and maintain fixation within a computer defined window for a variable interval (1500-2000ms). During “Probe” trials (Fig. 2.1B), T1 remained illuminated until the position of the line of sight exited the computer window centered on the location of the no longer visible T0. T1 was never re-illuminated during probe trials; no visual feedback was available on these trials. Probe trials were used to reveal the current state of the adaptation process without potentially confounding sensory inputs that could arise from the presence of visual targets during movements, and/or the visual error at the end of primary movements.

“Adaptation” trials (Fig. 2.1C) were similar to probe trials except that 20 ms after T1 was extinguished, a target (T2) in a new location was illuminated (i.e. the target was relocated from the T1 to the T2 location with a 20ms blank period inserted before T2 illumination). The new location could be further away from (forward adaptation) or closer to (backward adaptation) T0. Targets at 14 locations (Fig. 2.1D) were used for probe and step trials. On any particular Probe trial, the position of T1 was randomly selected from these possible locations. On every step, adaptation, and probe trial T0 was located at (0, 0). During forward
adaptation T1 could be located at (30, 0) or (-30, 0) and T2 could be located at (60,0) or (-60,0). During backward adaptation experiments, T1 could be located at (60, 0) or (-60,0), and T2 at (30,0) or (-30,0). The location of “adaptation targets” systematically alternated (left or right) when successive recording sessions were separated by 5 days or less, except for one forward experiment (M2) and two backward experiments (I2 and H3). For illustrative purposes, all targets and data are discussed as if gaze shifts were directed to the right.

Subjects were instructed to “fixate the peripheral target as rapidly and accurately as possible”. No specific instructions were given regarding how or whether they should move their heads. However, subjects were instructed to minimize movements of their shoulders and to maintain an upright posture during the session. No feedback was provided concerning their performance at any point either during or after the experimental session. Before adaptation trials were presented subjects performed probe and step trials to all 14 possible target locations. This pre-adaptation portion of the experimental session was followed by the “adaptation” phase. During this portion of the session, probe trials to all 14 possible locations continued to be presented and these were randomly interspersed with adaptation trials in either the forward or backward configuration. Adaptation and probe trials were
typically presented in a 3:1 ratio. Subjects performed between 77-187 adaptation trials per session (mean = 126.8±27).

Data Acquisition and Analysis

Horizontal and vertical gaze and head position signals were filtered to remove the magnetic field carrier frequencies and were digitized at 1kHz. All behavioral contingencies were accomplished in real-time with 1 ms resolution using custom software. Eye positions relative to the head were approximated by subtracting head from gaze position data. Data were analyzed off-line using Matlab (Natick, MA). Gaze beginning and end were defined using velocity criteria (60°/s onset; 35°/s offset); saccade amplitude was defined as the change in eye position that occurred between gaze onset and offset; head movement beginning and end were defined using 25°/s and 15°/s velocity criterion respectively. Movement amplitudes were defined as the change in position from the beginning to end of movements. Head contribution was defined as the change in head position that occurred during the gaze shift.

We compared the amplitudes of gaze, eye and head movements before and after adaptation. Means (±SD) were calculated using the last 5 probe trials to T1 prior to the introduction of adaptation trials (“pre-adaptation mean”) and these were quantitatively compared to the last 5
adaptation trials ("post-adaptation mean"). Probe trials during the adaptation phase are presented for qualitative comparison only (see Results section for details). When calculating mean differences between pre- and post-adaptation means, errors were propagated using the following formula: $\sigma_{\text{diff}} = \text{srt}(\sigma_{\text{pre}}^2 + \sigma_{\text{post}}^2)$, where $\sigma_{\text{pre}}$ represents the standard deviation of the pre-adaptation block and $\sigma_{\text{post}}$ the standard deviation of the post adaptation block. Unless otherwise noted, comparisons of means were made using a two-tailed student’s t-test, significance was determined using the criterion $p < 0.05$.

2.3 Results

We measured 11,150 gaze shifts made during step, probe, and adaptation trials collected from 10 subjects in a total of 40 experimental sessions. Eighteen of the 40 sessions were “forward adaptation” sessions; the remaining 22 were “backward adaptation” sessions. It was immediately clear that using the McLaughlin task resulted in adaptation of gaze amplitude in human subjects free to move their heads. Each of our subjects showed clear adaptation of gaze amplitude, however, adaptation did not occur to the same extent during every experimental session. A statistically significant change in primary gaze amplitude occurred during 16 of 18 forward adaptation and 19 of 22 backward adaptation sessions. It is unclear why some subjects adapted
during a particular session, but not another using the same stimuli. However, similar inter- and intra-subject variability have been reported during head-restrained, saccadic adaptation (e.g. monkey: Straube et al, 1997; human: Frens & van Opstal, 1994). Note also that during most experiments (exceptions are experiments A1, C1 and all “transfer” experiments) the onset of the each trial began with the random illumination of one of the three head lasers (see methods). Quantified data from a particular eye position (“Left”, “Centered”, or “Right”) presented below are from experiments in which there were a minimum of 5 pre-adaptation probe trials to the T1 used during adaptation trials and 5 post-adaptation trials from that eye position.

Eyes and Head Aligned – Forward Adaptation

The amplitude of gaze shifts made in response to presentation of T1 increased for each subject during the adaptation phase of forward adaptation experiments. In panels 2.2A-D gaze (green), eye (red), and head (black) positions are plotted as functions of time for typical gaze shifts made by subject A during forward adaptation (session A7). The initial target displacement (T1-T0) was 30° in each case and movements began after subjects aligned the eyes and head (accomplished by aligning the central head-mounted laser with T0). Average eye position at the onset of movements was 1.5±2.1°.
Figure 2.2A illustrates a gaze shift made during a pre-adaptation probe trial. The 28.5° gaze shift in this example was accomplished by combining a 25.0° saccadic eye movement with a head contribution of 3.5°. The head moved a total of 45.0° on this trial; most of this large head movement occurred after the line of sight was already directed toward T1. The vestibuloocular reflex allowed gaze to remain steady at this location during the ongoing head movement. In Fig. 2.2B, the first adaptation trial of the adaptation session is shown. The primary gaze shift in this example is similar to that shown in 2A. The 33.1° gaze shift was accomplished by a large saccade (28.0°) associated with a small head contribution (5.1°). However, the primary gaze shift was followed by two “corrective” gaze shifts which re-directed the line of sight so that the subject’s final gaze position was closer to T2 (T2-T0 = 60°).

In a later adaptation trial (Fig. 2.2C), the primary gaze shift (45.2°) was significantly larger than during pre-adaptation trials (2.2A). Note that the amplitude of the eye movement (28.4°) was similar to that seen during the movements in 2.2A and B. However, the head contribution increased substantially to 16.8°. This gaze shift was followed after a latency of more than 250ms, by a corrective movement. The primary gaze shift in the final adaptation trial of this session was 54.6° (2.2D). Saccade amplitude was 26.7° and the contribution of the head was 26.6°. Over the course of adaptation during this example session, eye
movement amplitude increased only slightly from 25.0° to 28.4°. The observed 26° increase in gaze amplitude resulted from a dramatic increase in head contribution (from 3.5° to 26.6°).

For experimental session A7, changes in primary gaze, eye, head contribution, and total head movement amplitudes are summarized in panels 2.2E-H. Arrows in E-H indicate amplitude measurements from the individual trials illustrated in panels 2.2A-D. As shown, gaze amplitude and head contribution increased gradually as more adaptation trials were performed (gray squares in panels 2.2E & 2G). Total head movement also increase throughout the adaptation session (2.2H). In contrast, the amplitude of eye movements was relatively unchanged throughout the session (compare pre-adaptation (black) and peri-adaptation (gray) trials in Fig. 2.2F). During probe trials to T1, interleaved during adaptation session A7, the amplitudes of gaze, eye and head movements were indistinguishable from those seen during adaptation trials (compare gray squares and black triangles in panels 2.2E-H). Recall that probe trials are identical to adaptation trials except that the T2 target is never illuminated; no visual error is presented after the primary gaze shift. During probe trials a visual stimulus identical to that presented before adaptation evokes an altered motor output, revealing the current state of the adaptation process without potentially confounding sensory inputs that could arise from the presence of visual
targets during movements, and/or the visual error at the end of primary movements.

Eyes and Head Aligned – Backward Adaptation

The amplitude of primary gaze shifts made towards T1 decreased for each subject during the adaptation phase of backward adaptation experiments. In panels 2.3A-D, gaze (green), eye (red), and head (black) positions are plotted as functions of time for typical gaze shifts made by subject H during backward adaptation (session H2). The initial target displacement (T1-T0) was 60° in each case and the average eye position at the onset of these movements was 1.5±0.6°.

Figure 2.3A illustrates a pre-adaptation trial in which primary gaze amplitude was 59.7°, saccade amplitude was 33.3°, and head contribution was 26.4°. The first adaptation trial (2.3B) was similar to pre-adaptation trials (gaze = 55.8°, eye = 29.3°, head contribution = 26.5°), the one notable difference being the two “corrective” saccades that followed the primary gaze shift by ~250ms. These secondary movements reduced the visual error introduced by shifting the target from the T1 to the T2 location (T2-T0 = 30°). Panels C and D illustrate trials part way through and at the end of the backward adaptation session. As shown, gaze amplitude significantly decreased over the course of this adaptation session. This gaze amplitude reduction was
mediated primarily by a reduction in head contribution; whereas eye amplitude was reduced only slightly over the course of adaptation.

For this adaptation session, changes in gaze, eye, head contribution and total head movement amplitude are summarized in panels 2.3E-H. In this example, gaze amplitude clearly declined as the subject was increasingly exposed to adaptation trials (2.3E). The decrease in gaze amplitude was mediated largely by a decrease in the head contribution (2.3G). Total head amplitude declined concomitantly (2.3H). As previously noted for forward adaptation, the subject’s behavior during probe trials (to the T1 target location) strongly resembled behavior during adaptation trials throughout the session (compare gray squares with black triangles in panels 2.3E-H).

The illustrated forward (Fig 2.2) and backward (Fig 2.3) adaptation sessions demonstrate the general tendency of subjects to alter gaze amplitude during adaptation by changing the head contribution to the gaze shift when the eyes began centered in the orbits. The histograms in figure 2.4 plot the differences in gaze, eye, head contribution and total head amplitude before and after adaptation, during all forward (A-D) and backward (E-H) sessions initiated with the eyes and head aligned. Positive values indicate an increase in amplitude and negative values indicate a decrease. As shown, gaze amplitude increased significantly in 16 of 18 forward adaptation experiments (2.4A). However, there was
variability within and across subjects; only one of our ten subjects failed to adapt significantly during these sessions (subject M). The average increase in gaze amplitude for all subjects (gray bar in 2.4A), including subject M, was 14.8±3.8° (range: 0 to 26.8°). Head contribution increased significantly in 11 sessions (range: -2.9 to 26.5°), while saccade amplitude increased significantly in only 5 sessions (range:-3.2 to 9.2°). Significant saccade amplitude increases associated with an increase in primary gaze amplitude tended to occur when gaze amplitude changed by less than 10° (D1, D4, E1, H1). On average, saccade amplitude did not change, whereas head contribution and total head movement increased significantly for the population (gray bars, 2.4B-D).

Gaze amplitude decreased significantly in 19 of 22 backward adaptation sessions (2.4E) and for the population (mean: -15.5±5.7; range: -2.6 to -23.9). A decline in gaze amplitude was associated with a significant decrease in head contribution in 15 sessions (2.4G). Total head movement also decreased significantly in 13 sessions and for the population (2.4H). There was a statistically significant decline in the saccadic component amplitude associated with the primary gaze shift in only 5 sessions (2.4F). Decreases in saccade amplitude occurred when gaze amplitude decreased by more than 15° (e.g. B1, B5, B6, H2, H3).
Eyes and Head Not Aligned

In the previous section, we described changes in gaze, eye, and head movements during forward and backward adaptation. At the beginning of these gaze shifts, the eyes and head were aligned. Data indicate that under these conditions, large changes in gaze amplitude induced during adaptation were not a result of dramatic changes in saccadic eye movement amplitude. Instead, changes in the degree to which the head contributed to gaze shifts accounted for most of the changes in gaze shift amplitude. One plausible hypothesis that can account for these data is that during head-unrestrained adaptation, the head command signal is altered. If this were the case, during forward adaptation, the visual error at the end of the primary gaze shift would lead to an increase in the amplitude of the head movement. As the amplitude of head movements and more importantly head contribution to the gaze shift increased over the course of many such trials, gaze amplitudes would also increase resulting in data similar to that described above. Alternatively, adaptive changes in gaze amplitude could result from visual-error-induced changes in the gaze shift command. If this were the case, gaze command changes would lead to increased (or decreased) gaze shift amplitude and the observed changes in head contribution would be a consequence of larger (or smaller) gaze shifts initiated with the eyes and head aligned. Put
another way, the relative contributions of the eyes and head to gaze shifts altered by adaptation would be predictable based only on knowledge of the (new) amplitude of the gaze shift and the initial positions of the eyes.

For completeness, we mention a third alternative: that the adaptation process alters only a saccade amplitude command. This hypothesis, however, can be rejected based on the observations described above: gaze amplitude changes occur with little or no changes in saccade amplitude.

The alternative hypotheses outlined above make differential predictions about the amplitudes of gaze, eye and head movements during adaptation under conditions in which the eyes and head are initially not aligned. For example, consider a backward adaptation experiment in which T1 is 60° to the right of the initial fixation location and T2 is 30° also to the right of the initial fixation target. If the eyes began deviated 30° to the left in the orbits one would expect 60° gaze shifts to have a relatively small head contribution (in order to be explicit in the following argument assume the head contribution under these conditions would be 10°). On the other hand, if the eyes began deviated in the orbits 30° to the right, the same 60° gaze shift would require a large head contribution (for example, 50°). During backward adaptation gaze amplitude would be expected to decline toward 30°. Because the
head contribution during movements made when the eyes begin deviated to the left is small (only 10°), the hypothesis that adaptation alters only the head movement command predicts that gaze amplitude will be reduced only slightly; it could be reduced only by the amount that the head initially contributed – 10°. In contrast, given the same visual stimuli, if the eyes began deviated 30° to the right, changes in head contribution could result in gaze amplitude changes up to 50°. In this example T2 is only 30° from T1, and we would predict at most a 30° change in gaze amplitude mediated by a 30° change in head contribution. The alternative hypothesis that adaptive changes result from changes in gaze command signals predicts that gaze amplitude will be reduced by approximately 30° during backward adaptation regardless of the positions of the eyes in the orbits. As a result when the eyes begin 30° to the left, gaze amplitude changes will result from minor changes in head contribution and larger changes in saccade amplitude, whereas, when the eyes begin deviated to the right, the changes in gaze amplitude will result largely from changes in head contribution. After adaptation, the relative amplitudes of the eyes and head are predicted to be appropriate for the altered amplitude of the gaze shift given the initial conditions of each movement. Again, to be specific, eye and head contributions after adaptation should be similar
to that observed during pre-adaptation control trials matched for gaze amplitude and initial eye position.

Using the 3 head-mounted lasers (see Methods) we were able to collect enough data to test the predictions of these alternatives in 6 of our 10 original subjects. The results of one forward adaptation session are illustrated in Fig. 2.5 (A-D). During this session, trials could be initiated with the eyes and head aligned or the eyes deviated in the orbits 30° to the left or to the right of center (on randomly interleaved trials). In panel 2.5A which plots the amplitude of gaze shifts as a function of trial number, squares represent movements initiated with the eyes deviated to the left (mean initial position = -27.9 ±0.7°), and triangles illustrate movements initiated with the eyes deviated to the right (mean initial position = 29.5 ±0.9°). Before adaptation trials were presented (black filled symbols) there were small differences in gaze shift amplitudes when comparing movements initiated from the drastically different initial eye positions; gaze shifts made when the eyes were nearly 30° to the right were systematically smaller (in the example ~7°) than those initiated with the eyes deviated to the left. Nonetheless, gaze amplitude increased consistently for both sets of movements during adaptation (gray symbols).

For comparison, this panel also presents mean (±SD) gaze shift amplitudes (black unfilled symbols) during pre-adaptation trials made
directly to the T2 target location. Before adaptation with the eyes initially deviated in the orbits to the right (triangles) or to the left (squares), the amplitudes of gaze shifts made in response to presentation of the T2 target were indistinguishable from the amplitudes of post-adaptation gaze shifts made in response to presentation of the T1 target.

When the eyes began deviated in the orbits to the left (Fig. 2.5B, black squares), saccade amplitude was approximately equal to gaze shift amplitude during pre-adaptation gaze shifts to T1. However, when the eyes were deviated to the right, saccade amplitudes during gaze shifts of similar amplitudes were quite small (2.5B, black triangles). In contrast, during pre-adaptation trials, when the eyes were deviated to the left, head contribution (2.5C) and total head movement amplitude (2.5D) were small whereas they were large when the eyes began deviated to the right (2.5C and D – black filled triangles). It is important to note that the relative contributions of the eyes and head after adaptation were quite similar to the relative contributions seen during amplitude matched gaze shifts made before adaptation. In 2.5B-D, for example, only small differences were observed in saccade amplitude, head contribution, and total head movement amplitudes made with the eyes deviated either to the right (unfilled triangles) of left (unfilled
squares) when gaze shift amplitudes were similar to post-adaptation movements.

An example of backward adaptation during gaze shifts initiated with the eyes in different orbital positions is illustrated in panels 2.5E-H. During backward adaptation, gaze shift amplitude declined systematically. This reduction in gaze amplitude was mediated primarily by a reduction in saccade amplitude when the eyes began deviated to the left, but was mediated primarily by a reduction in head contribution when the eyes began deviated to the right. Similar observations were made for all subjects who participated in data collection sessions in which the eyes and head were not initially aligned.

The hypothesis that adaptation occurs by alteration of a gaze command signal predicts that an increase in gaze amplitude during forward adaptation from the leftward eye position will result from primarily a change in saccade amplitude. Conversely, an increase in gaze amplitude when the gaze shift is initiated from the rightward eye position will result from an increase in head contribution. Figure 2.6 (A-D) illustrates the change in gaze, eye, head contribution, and total head movement amplitude during forward adaptation when gaze shifts were initiated with the eyes deviated to the left. Black bars in Fig. 2.6 represent means (±SD) from individual experiments and gray bars are population means. In each case the T1 target was 30° to the right of
fixation and the T2 target was 60° to the right of initial fixation (30°
more than the T1 location). As shown, with the eyes initially deviated
to the left in the orbits, gaze amplitude increased during all sessions.
During some sessions, amplitude increased by more than 20° (A1, A8,
A11, C5 and C7). However, there was inter- and intra-subject variability
and during other similar sessions gaze amplitude increased by less
than 10° (H4). Across sessions gaze amplitude increased by 17.7° (±
5.2). As shown in panel 2.7B, during gaze amplitude increases, when the
eyes began deviated to the left, saccade amplitude increased by 11.2°.
In contrast, the head contribution to gaze shifts (6C) increased only
slightly (6.3°). For comparison, Fig. 2.6 (E-H) plots the results of forward
adaptation when the eyes began deviated to the right. Under these
conditions, gaze shift amplitude increased by 16.6° (±4.4). This change
in gaze amplitude was not different than the increase observed when
the eyes began deviated to the left (t-test, p > 0.1). However, this change
in gaze amplitude was not mediated by a large increase in saccade
amplitude as seen with leftward deviation. As illustrated (2.6F), eye
movement amplitude was essentially unchanged during these forward
adaptation sessions. The large change in gaze amplitude was mediated
by a large increase (17.2°) in head contribution (2.6G).

During backward adaptation with the eyes initially deviated to the
left (Fig. 2.7A-D), gaze amplitude was reduced by 15.1° (±4.3). This
reduction was caused by a significant reduction (10.1°) in the saccadic component of gaze shifts (2.7B), and a small decrease (4.9°) in head contribution (2.7C). When the eyes began deviated to the right, backward adaptation resulted in an 18.6° reduction in gaze amplitude. However, this reduction was not the result of a reduction in the amplitude of the saccadic portion of the movement. On average, saccade amplitude changed 0.1°. The large change in gaze amplitude occurred because of a large decrease (18.7°) in head contribution (2.7G).

To summarize, during adaptation, changes in gaze shift amplitude were similar regardless of the initial positions of the eyes. However, these large changes in gaze amplitude were accomplished via large changes in head contribution when the eyes were deviated to the right (head deviated away from T1), and via changes in saccade amplitude when the eyes began deviated to the left (head deviated towards T1). Changes in head contribution and saccade amplitude depended not on the adaptation process directly, but instead on the position of the eyes in the orbits at the onset of gaze shifts.

Gaze Adaptation Transfer Experiments

Alahyane and Pellisson (2004) demonstrated that forward and backward adaptation can occur simultaneously by driving forward adaptation when the eyes are initially deviated upwards and backward
adaptation from downward eye positions. It is possible that data described above, illustrating that the amplitudes of eye and head movements were altered during adaptation in an initial-eye-position-dependent manner, could be due to a similar “context cue” effect. We tested this possibility by having a subset of our subjects (N=5) participate in gaze transfer experiments.

During the pre-adaptation phase, three head-mounted lasers were used to elicit control gaze shifts initiated from three different initial eye positions. Then adaptation was induced with the eyes in one particular position, for example, with the eyes deviated 30° to the left. After the subject performed ~75-100 trials under these conditions, gaze shifts were made with the eyes in different (non-adapted) initial positions. Note that the subject may have still been adapting to the intra-gaze target displacement at the time that the new initial eye positions were introduced. Therefore, after ~75-100 gaze shifts initiated from the novel eye positions, the original eye position was often reintroduced. Two examples of transfer experiments are shown in Figure 2.8 which plots gaze (A), eye (B), and head contribution (C) amplitudes as functions of trial number during pre-adaptation probe (closed squares) and adaptation (open squares) trials. During this forward adaptation transfer experiment (C7) the eyes could be deviated to the left (blue), to the right (red), or aligned with the head (green). Regardless of initial eye position,
the average pre-adaptation gaze amplitude was ~31° (filled symbols 2.8A). Different combinations of eye and head movements were used to accomplish these ~31° gaze shifts. As shown in 2.8B and C, when the eyes and head were aligned (green) head contributions were small (~10°), whereas when the eyes began deviated in the orbits to the right (in the direction of the ensuing gaze shifts), head contributions were large and accounted for nearly the entire gaze shift amplitude (saccade amplitudes were near 0° during these movements).

After ~100 pre-adaptation control trials, adaptation trials were introduced (vertical blue line in 2.8A-C), and during the first 75 adaptation trials the eyes were always deviated to the left at the beginning of gaze shifts (blue unfilled symbols). As shown, gaze amplitude gradually increased from 30.9° ±3.6 to 46.2° ±3.5 during adaptation. The gaze amplitude increase was mediated by a significant increase in saccade amplitude (30.0° ±2.8 to 37.5° ±1.5) and head contribution (0.8° ±1.0 to 8.8° ±3.2).

After these initial adaptation trials, adaptation trials continued with the eyes either deviated to the right (red unfilled squares) or centered in the orbits (green unfilled squares). As clearly illustrated in 2.8A, the amplitude of gaze shifts made from initial eye positions not used during adaptation, were similar in amplitude to those made near the end of the primary adaptation. Comparing the amplitude of the last 5
adaptation trials made from the initial eye position (in this case with the eyes deviated to the left) with the first 5 trials after introducing the two new initial eye positions revealed no significant change in gaze amplitude ($p > 0.05$ t-test). The degree of adaptation that developed with the eyes in one initial position transferred immediately and completely to gaze shifts initiated with the eyes in different orbital positions.

However, eye amplitude and head contribution to these gaze shifts were markedly different than those observed during similar amplitude gaze shifts at the end of the initial adaptation. At the end of the first 75 adaptation trials, saccade amplitudes were $\sim 40^\circ$ (unfilled blue squares: 2.8B). However, immediately after introduction of the novel initial eye positions, saccade amplitudes were markedly different. As shown, saccade amplitudes were near $0^\circ$ when the eyes were deviated to the right (2.8B red unfilled squares) and $\sim 20^\circ$ when the eyes and head were aligned (2.8B: green unfilled squares). During the initial period of adaptation, saccade amplitude increased $\sim 8^\circ$ (from $\sim 32^\circ$ to $\sim 40^\circ$). However, even on the first adaptation trials initiated with the eyes in different positions, eye movement amplitudes were very different. In addition, eye movements were not $\sim 8^\circ$ larger than control saccades made before adaptation from the same starting positions. Changes in the amplitude of eye movements observed during adaptation did not transfer to movements made with the eyes in new initial positions.
Similarly, the effects of adaptation on the contribution of the head did not transfer to movements initiated under different conditions.

Figure 2.8 (D-F) illustrates a similar example during backward adaptation (H3). Like the forward adaptation described above, gaze shifts made from eye positions not used during adaptation were approximately the same amplitudes as gaze shifts made at the end of adaptation. However, the eye and head components of these gaze shifts were not the same as those observed at the end of adaptation. Nor did the changes in eye or head contribution that occurred during adaptation, transfer to movements made under different initial conditions.

The following ratios were used to quantify the degree to which changes in gaze (G), eye (E), and head contribution (HC) observed during the initial adaptation transferred to movement made from novel eye positions:

\[
\text{Gaze ratio} = \frac{G_{IEP2}}{G_{IEP1}}
\]

\[
\text{Eye ratio} = \frac{E_{IEP2}}{E_{IEP1}}
\]

\[
\text{Head contribution ratio} = \frac{HC_{IEP2}}{HC_{IEP1}}
\]
Where $IEP_1$ is the eye position used during initial adaptation and $IEP_2$ indicates the novel eye positions introduced after initial adaptation. Average pre-transfer values were calculated from the last 5 adaptation trials before introducing new eye positions (data just prior to the green vertical line in figure 2.8). Post-transfer values were calculated from the first 5 adaptation trials after introduction of new positions (data just after the green vertical line in figure 2.8). Note that there could be more than one post transfer eye position. Table 2.1 contains the gaze, eye and head ratios for each of our 9 transfer experiments. These ratios were used to calculate the average values detailed below.

The hypothesis that adaptation occurs by alteration of a gaze command signal predicts that gaze amplitude before and after transfer should be the same regardless of initial eye position; in other words, the gaze ratio should be close to 1. The mean gaze ratio was $0.99 \pm 0.19$ when combining gaze ratios from all conditions (n=17). No statistically significant difference between forward and backward gaze ratios was observed ($p>0.05$). This suggests that the degree of adaptation that developed with the eyes in one initial position transferred nearly completely to gaze shifts initiated with the eyes in different orbital positions.

A second prediction of the gaze hypothesis is that the changes in eye and head movement amplitude observed during the initial
adaptation trials will not transfer to movements made from novel eye positions; rather the eye and head movement amplitudes will be appropriate for the gaze shifts of the adaptation-modified amplitude initiated from different eye positions. In 6 of 9 transfer experiments (the first 6 experiments listed in Table 2.1) initial adaptation trials were made when the eyes began deviated to the left (head deviated towards the target; e.g. Figure 2.8A-C). The mean eye ratios calculated from these experiments were 0.60±0.15 (when IEP$_2$ was with eyes and head aligned) and 0.02±0.21 (when IEP$_2$ was with the eyes deviated to the right). As expected, the saccadic eye movements associated with gaze shifts in the post-transfer phase from the centered and rightward eye positions were considerably smaller than those initiated from the leftward eye position in the post transfer phase. Conversely, the mean head contribution ratios were 4.3±2.7 (IEP$_2$: centered) and 12.4±14.5 (IEP$_2$: rightward) indicating that the head contribution was much larger when movements were made under these conditions.

In the remaining 3 experiments, initial adaptation trials were produced with the eyes and head aligned (e.g. Figure 2.8D-F). In these experiments, the eye and head contribution ratios calculated using the leftward eye position (n=3) were 0.04 ± 0.32 and 1.98 ± 0.7 respectively. In contrast, the eye and head contribution ratios calculated using the
rightward eye position (n=2) were 3.13 ± 0.6 and 0.40 ± 0.15. When adaptation was initially induced from the centered eye position, the saccade and head contribution in the post-transfer phase could be larger or smaller depending on the initial positions of the eyes in the orbits. In summary, although the transfer of gaze amplitude between pre- and post-transfer phases was almost 100%, the saccade and head contributions to gaze shifts were markedly different after gaze transfer and varied in an initial eye position dependent fashion.

2.4 Discussion

In animals that have retinal regions with high photoreceptor density (e.g. fovea), maintenance of gaze shift accuracy is critical for extracting high quality visual information from the environment. When the head is allowed to move, gaze shifts are often accomplished by coordinated movements of the eyes and head. Consequently, the adaptive mechanism that maintains gaze accuracy could affect the gaze command signal, or it could alter separately the independent signals driving the eyes and head. The goal of the present study was to describe changes in gaze, eye, and head movement amplitudes during a short-term adaptation task (McLaughlin, 1967) under conditions in which the alternative hypotheses make differential predictions.
Our data indicate that in human subjects with unrestrained heads:

1) large forward or backward target displacements during an ongoing gaze shift can gradually produce large changes in gaze amplitude, and that these changes persist during probe trials when targets are extinguished after gaze shift onset and not re-illuminated. The motor responses to visual stimuli presented in the adapted spatial location are altered during adaptation using the McLaughlin task when the head is free to move. 2) Data were inconsistent with changes to separate eye and/or head movement signals, but consistent with alterations of a gaze shift command. These observations are discussed in detail below.

The magnitude and time course of human saccade amplitude adaptation has been described extensively (for review see: Hopp & Fuchs, 2004). Typically initial target displacements ~10° have been used, and the target back-step (or forward-step) have been between 3-5° (30-50% of the primary movement; e.g. humans: Semmlow, Gauthier, & Vercher, 1987; monkeys: Straube et al, 1997). To our knowledge, the only example of saccade adaptation in which the primary gaze shift was 30° or more is a study in which Phillips and colleagues (1997), using rhesus monkeys as subjects, examined the transfer of head-restrained saccade adaptation to head-unrestrained gaze shifts. In their study, the initial target displacement during saccade adaptation was 50° and the target back-step was 20° (40%). On average, primary saccade amplitude
was reduced by 8.4° (range: 5.6-12.4°) or 18.3% (range: 12.8-27.0%).

Interestingly, the range of amplitude changes in the Phillips et al. study
was similar to values reported by Erkelens and Hullerman (1993), as well
as in other human (e.g. Miller, Anstis, & Templeton, 1981) and monkey
adaptation studies (e.g. Straube et al., 1997) in which the initial target
displacements were much smaller.

In the data presented here, the initial target displacement was
either 60° during backward adaptation or 30° during forward adaptation.
In both cases the target was moved 30° after the gaze shift was initiated.
As a result, during backward adaptation, in order to eliminate the visual
error at the end of the movement, gaze shift amplitudes would need to
be reduced by half. To eliminate visual error during forward adaptation,
movement amplitudes would need to be doubled. On average, our
subjects decreased gaze amplitude by ~12° (range: 6-27°) or 20%
(range: 10- 45%) of the primary movement in response to the 30° back-
step during backward adaptation experiments. During forward
adaptation, gaze amplitudes increased by ~15° (range: 0-26°) or ~50%
(range: 0-87%). Visual error was reduced by ~50% during backward and
by ~40% during forward adaptation. These changes in gaze amplitude
are of approximately the same magnitude as changes observed when
the head is prevented from moving and when target displacements are
much smaller. The ability to induce changes in movement amplitude
using the McLaughlin task appears to be similar regardless the
displacement of the targets, and independent of whether the head is
free to move or not.

Prior studies of saccadic adaptation have also shown that
primates can exhibit large variation in adaptation magnitude and rate for
nearly identical conditions (humans: Erkelens and Hullerman, 1993;
Albano and King, 1989; Frens and van Opstal, 1994; Fujita, Amagai,
Similar to head restrained saccade adaptation, the magnitude of gaze
adaptation in our subjects was highly variable both between (as noted
above) and within subjects. For example, in response to a 30° target
back-step, subject C decreased primary gaze amplitude between 13°
and 24° (see figures 2.5, 2.7, 2.8). Short-term adaptation under the
conditions used in these experiments produced consistent albeit
variable changes in gaze shift amplitude. On a day-to-day basis, the test
conditions were nearly identical. Despite efforts in this regard, given the
same visual stimuli, on some occasions gaze amplitudes changed
dramatically whereas during other sessions even with the same subject,
adaptation induced amplitude changes were much smaller. We have no
explanation for this variability, although it is similar to the inter- and
intra-subject variability observed when the head is restrained, and may
represent the variability of the adaptation process using the McLaughlin task.

The data in this report are consistent with the hypothesis that gaze adaptation induced using the McLaughlin task when the head is allowed to move alters the command to change the direction of the line of sight (i.e. a gaze shift command). This conclusion is based on the systematic changes in gaze amplitude observed during both forward and backward adaptation sessions, coupled with the observation that particular changes in gaze amplitude during individual sessions could be mediated solely by changes in head contribution, solely by changes in eye movement amplitude or changes in both eye and head components. The relative contributions of the eyes and head were appropriate in all cases for the amplitude of the executed gaze shift both before and after adaptation, and depended on the starting positions of the eyes in the orbits. Thus, after adaptation had reduced (or increased) gaze amplitude, eye and head components were qualitatively similar to matched amplitude gaze shifts initiated under the same conditions but produced before adaptation. Specific amplitude changes to the eye or head components of gaze shifts were not observed. In addition during the adaptation transfer experiments, after the initial adaptation trials performed from one particular initial eye position, changes in gaze shift amplitude transferred immediately to gaze shifts made from novel (non-
adapted) positions. In contrast neither the changes in eye or head movement amplitudes induced during the initial adaptation transferred to movements made when novel eye positions were introduced. These data are inconsistent with changes to eye- or head-specific commands, and indicate changes to a gaze command signal.

In the only previous investigation of head-unrestrained gaze adaptation, Phillips and colleagues (1997), using non-human primate subjects, describe the transfer of gaze amplitude changes induced when the head was prevented from moving to gaze shifts made after the head was released. In their report, reductions in saccade amplitude when the head was restrained transferred to head-unrestrained gaze shifts. Furthermore, the reduction in gaze amplitude (compared to pre-adaptation, head-unrestrained control movements to T1) resulted from changes in both eye and head movement amplitudes. As a result these authors concluded that the adaptation process did not alter saccade-specific signals, rather a gaze signal that drove both eye and head movements.

In a small number of cases (n = 2), these authors also report changes in gaze, eye and head movements produced during head-unrestrained gaze adaptation. The authors concluded that the most straight-forward explanation of these results was that adaptation induced changes to motor commands before gaze signals were
separated into eye and head specific commands. However, the alternative, that changes to eye and head specific signals could not be ruled out based on their results.

Due to the very large target displacements used in this study, it is tempting to assume that subjects were consciously aware of the target jump, whereas this explanation has largely been rejected (perhaps prematurely) when small target displacements and head restrained subjects are used. This presumed “awareness” of the target displacement could potentially influence the eye and head movements observed during these trials. We view this account with skepticism, particularly in its attempt to characterize head restrained saccadic adaptation using the McLaughlin task as a “true” adaptation, whereas in this view, head unrestrained adaptation using the same task is tainted by subjects’ conscious choices regarding the amplitude of their eye and head movements. There are several points to be raised in discussion of this issue. First, our conclusion that a gaze command signal is being modified by the altered visual stimuli presented during this task arises from considering the changes in gaze amplitude when the eyes begin in different orbital positions. Our data show that although the gaze shift amplitude has been altered regardless of initial eye position, the relative amplitudes of eye and head movements depend only on the amplitude of the gaze shift that is made, and the starting positions of the eyes in
the orbits. When gaze shifts of matched amplitude are made with the eyes in similar starting positions, but not in the context of adaptation, the relative amplitudes of the eyes and head are the same as observed during the adaptation process (Fig. 2.5). Second, randomly interleaved with adaptation trials are trials in which the T1 target is turned off when the gaze shift begins but the T2 target is not illuminated (Fig. 2.2 and 2.3). During these trials there is no displacement of the target during the ongoing gaze shift and therefore any potential “conscious awareness” of the target jump is eliminated. The relative amplitudes of eye and head movements on these trials are nearly identical to that seen during adaptation trials. If the subjects were aware of the target step it did not seem to have an impact on the relative amplitudes of the eye and head movements during adaptation. While it is not possible to rule out explanations for these results based on covert processes that the experiment was not designed to address, such hypotheses have little explanatory value, and apply equally to head unrestrained and head restrained adaptation data using the McLaughlin task. Importantly, the observation that changes in gaze shift amplitude are independent of the relative eye and head movement amplitudes support our conclusions that under the conditions of our experiment a gaze signal is being altered, and this conclusion does not depend upon assumptions
regarding the conscious awareness (or lack thereof) of the displacement of the target.

In summary, a large intra-gaze target displacement during human, head-unrestrained gaze shifts towards visual targets can produce large increases or decreases in primary gaze amplitude. Under these conditions, changes in gaze amplitude induced using the McLaughlin task were independent of the amplitudes of eye and/or head movements. This leads to the suggestion that the neural structures responsible for altering the motor output in response to a persistent visual error, are likely structures that encode the redirection of the line of sight (gaze); the superior colliculus seems like a good candidate for having some role in this process (Takeichi et al. 2007). The alternative, that adaptation under these conditions alters eye and/or head specific commands can be rejected based on these data.
References:


Figure 2.1A-C: Schematic diagrams of trial types used. In each panel, gaze position is represented by a thin black line and plotted as a function of time. Below this trace, targets are represented by thick bars indicating when within the trial each target was illuminated and extinguished. In all case, trials began with the illumination of a head-mounted laser (light gray bar) followed by presentation of T0. If behavioral contingencies were satisfied, the head-mounted laser and T0 target were extinguished and a second target (T1) was simultaneously illuminated at one of the spatial locations shown in panel D (black circles). A: The T1 target remained illuminated for the duration of the “target step” trials. B: During the “probe” trials, the T1 target was extinguished when the line of sight moved beyond a computer defined window (“position criterion”) surrounding T0. C: “Adaptation” trials were similar to probe trials until 20ms after the position criterion was satisfied, at which time T1 was turned off and a target at location T2 was illuminated. D: target locations used during adaptation and probe trials.
Figure 2.2 - Forward adaptation session (A7) with the eyes and head aligned. Panels A-D plot gaze (green), eye (red) and head (black) positions observed at specific times during the adaptation. Primary gaze (E), saccade (F), head contribution (G) and total head (H) movement amplitudes are plotted as functions of trial number. Pre-adaptation probe trials (black squares), probe trials during the adaptation phase (black triangles), and adaptation trials (grey squares) are superimposed for direct comparison. Labeled arrows indicate trials presented in panels A-D.
Figure 2.3 - Backward adaptation with the eyes and head aligned; experimental session (H2). Layout is identical to Fig. 2.2.
Figure 2.4 - Histograms summarizing adaptation-induced changes in amplitude during forward (A-D) and backward (E-H) adaptation with the eyes and head aligned. Each histogram bar indicates the mean (±SD) change in gaze (A, E), eye (B,F), head contribution (C,G) and total head movement amplitude (D, H) comparing the last 5 pre-adaptation trials with the last 5 adaptation trials in each session. Session/subject identifiers are listed on the abscissa. The group means (±SD) are indicated with the gray bar on the right of each panel. † indicates non-significant change in amplitude (p>0.05; two-tailed t-test); all other differences were statistically significant.
Figure 2.5 - Primary gaze (A,E), eye (B,F), head contribution (C,G) and total head amplitude (D,H) as a function of trial number for forward (C7) and backward (H2) adaptation sessions when the head and eyes were not aligned. Squares indicate data from gaze shifts made with the eyes initially deviated to the left. Triangles indicate movements made with the eyes initially deviated to the right. Black filled symbols are pre-adaptation trials; gray filled symbols are adaptation trials. Unfilled symbols show the mean (±SD) amplitudes during pre-adaptation trials made directly to the T2 target.
Forward Adaptation
Eyes and Head Not Aligned

"Leftward"

A
\( \Delta \text{Gaze Amp (deg)} \)

B
\( \Delta \text{Saccade Amp (deg)} \)

C
\( \Delta \text{Head Cont (deg)} \)

D
\( \Delta \text{Tot Head Amp (deg)} \)

"Rightward"

E

F

G

H

Subject Code

Subject Code

A1
A8
A11
C5
C7
E3
H1
H4
AVG
Figure 2.6 - Amplitude changes during forward adaptation when the eyes and head were not aligned. Histograms show the mean (±SD) difference between the last 5 adaptation trials and the last 5 pre-adaptation probe trials for gaze (A, E), saccade (B, F), head contribution (C, G), and total head amplitude (D, H). A-D: eyes initially deviated to the left; E-F: eyes initially deviated to the right. Gray bars indicate the group means (±SD). Subject/session codes indicated along the abscissa. † indicates non-significant change in amplitude (p>0.05; two-tailed t-test).
Figure 2.7- Amplitude changes during backward adaptation when the eyes and head were not aligned. Histograms show the mean (±SD) difference between the last 5 adaptation trials and the last 5 pre-adaptation probe trials for gaze (A, E), saccade (B, F), head contribution (C, G), and total head amplitude (D, H). A-D: eyes initially deviated to the left; E-F: eyes initially deviated to the right. Gray bars indicate the group means (±SD). Subject/session codes indicated along the abscissa. † indicates non-significant change in amplitude (p>0.05; two-tailed t-test).
Figure 2.8 - During forward (A-C; experiment C7) and backward (D-F; experiment H3) adaptation, changes in gaze (A, D), eye (B, E) and head contribution (C, F) amplitudes are plotted as functions of trial number. Filled symbols illustrated movement amplitudes directed to T1 target locations during pre-adaptation trials when the eyes began either aligned with the head (green), or deviated in the orbits to the right (red), or left (blue). After ~100 trials adaptation began (blue vertical lines); adaptation trials were initiated with the eyes in one particular position (deviated to the left: A-C; aligned with the head: D-F). After ~75 adaptation trials (unfilled symbols) under these conditions, adaptation continued with the eyes in new (non-adapted) initial positions (green vertical lines). After an additional 100 adaptation trials initiated from these new eye positions, the original initial eye position was re-introduced.
<table>
<thead>
<tr>
<th>Experiment</th>
<th>Condition</th>
<th>Eye Position</th>
<th>Gaze Ratio</th>
<th>Eye Ratio</th>
<th>Head Cont Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>B6 (Backward)</td>
<td>PreTrans</td>
<td>Left</td>
<td>0.82</td>
<td>0.68</td>
<td>9.49</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Center</td>
<td>0.87</td>
<td>0.22</td>
<td>41.69</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>0.84</td>
<td>0.15</td>
<td>4.31</td>
</tr>
<tr>
<td>C6 (Backward)</td>
<td>PreTrans</td>
<td>Left</td>
<td>0.89</td>
<td>0.48</td>
<td>2.32</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Center</td>
<td>0.84</td>
<td>0.15</td>
<td>4.31</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>0.84</td>
<td>0.15</td>
<td>4.31</td>
</tr>
<tr>
<td>C8 (Backward)</td>
<td>PreTrans</td>
<td>Left</td>
<td>0.79</td>
<td>0.45</td>
<td>2.47</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Center</td>
<td>0.77</td>
<td>0.13</td>
<td>5.27</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>0.77</td>
<td>0.13</td>
<td>5.27</td>
</tr>
<tr>
<td>G3 (Backward)</td>
<td>PreTrans</td>
<td>Left</td>
<td>1.26</td>
<td>0.52</td>
<td>5.05</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Center</td>
<td>1.20</td>
<td>0.09</td>
<td>6.84</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>1.20</td>
<td>0.09</td>
<td>6.84</td>
</tr>
<tr>
<td>C7 (Forward)</td>
<td>PreTrans</td>
<td>Left</td>
<td>1.02</td>
<td>0.57</td>
<td>2.80</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Center</td>
<td>1.02</td>
<td>0.57</td>
<td>2.80</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>0.97</td>
<td>-0.21</td>
<td>6.02</td>
</tr>
<tr>
<td>E3 (Forward)</td>
<td>PreTrans</td>
<td>Left</td>
<td>1.06</td>
<td>0.87</td>
<td>3.45</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Center</td>
<td>1.03</td>
<td>0.31</td>
<td>10.28</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>1.03</td>
<td>0.31</td>
<td>10.28</td>
</tr>
<tr>
<td>C9 (Backward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>0.83</td>
<td>-0.10</td>
<td>1.78</td>
</tr>
<tr>
<td>H3 (Backward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>1.44</td>
<td>2.72</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>1.44</td>
<td>2.72</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>0.86</td>
<td>-0.19</td>
<td>1.37</td>
</tr>
<tr>
<td>H4 (Forward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>1.12</td>
<td>3.53</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>1.06</td>
<td>0.41</td>
<td>2.80</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>1.06</td>
<td>0.41</td>
<td>2.80</td>
</tr>
</tbody>
</table>
Chapter 3: Monkey Head-Unrestrained Gaze Adaptation

3.1 Introduction

Adjustment of motor output in response to systematic movement errors is a critical function of the central nervous system. During visual orienting behaviors, this type of adaptation has been studied by introducing visual errors near the end of saccadic eye movements (McLaughlin, 1967; Deubel, 1987, 1991; Deubel et al, 1986; Miller et al, 1981; Noto et al, 1999; Robinson et al, 2003; Scudder et al, 1998; Semmlow et al, 1987; Straube et al, 1997). When the head is prevented from moving, a shift in target location triggered by the beginning of a saccade leads initially to a visual error at the end of the movement. As similar trials are repeated, the amplitude of the movements made to the first target location change (increasing or decreasing) so that the error at the end of the movement is reduced (McLaughlin, 1967; Deubel, 1987, 1991; Deubel et al, 1986; Miller et al, 1981; Noto et al, 1999; Robinson et al, 2003; Scudder et al, 1998; Semmlow et al, 1987; Straube et al, 1997). Changes in saccade amplitude follow a roughly exponential time course with ‘rate constants’ around 30-60 saccades in humans (Albano, 1996; Deubel, 1987; Deubel et al., 1986; Frens & van Opstal, 1994) and between 100-800 saccades in monkeys (Straube et al., 1997).
When the head is free to move and gaze shifts are accomplished by combining movements of the eyes and head, a persistent visual error at the end of a gaze shift could be caused by a variety of deficits. For instance, a systematic decline in the amplitude of saccadic eye movements could result in consistently hypometric gaze shifts. Similarly, a reduced head contribution (produced either by a reduction in head movement amplitudes or by altering the timing of eye and head movements) could lead to the same gaze dysmetria. The dysmetria caused by either hypometric saccades or reduced contribution of the head could be corrected by altering the command specifying the desired displacement of the line of sight. Consider, for example, a subject whose goal is to produce an accurate gaze shift to a visual target 30° to the right. However, the gaze shift is hypometric resulting in a large visual error at the end of the movement. Rather than issuing a command for a 30° change in gaze position, a 40° command could be generated. The hypometria of eye or head movements would reduce the requested 40° change in gaze position so that the actual movement was closer to the required 30°; the error at the end of gaze shifts to a target displaced 30° would be reduced. This mechanism relies on detecting gaze error at the end of a movement and modifying the gaze shift command signal to compensate for deficits in either the eye or head machinery. It is also possible to conceive of a mechanism that
determines that gaze hypometria resulted from a reduction in head movement or in saccade amplitudes. It would then be possible to modify head- or eye-specific command signals in order to compensate for the gaze hypometria. In this case, the gaze command signal would remain unaltered, but adaptive mechanisms would adjust the eye or head movements after these signals have been computed. From the subject’s point of view, the cause of the hypometria matters very little and either approach to correcting it will accomplish the overall goal: gaze shifts that bring the images of visual targets close to the fovea. However, understanding the mechanism employed by the nervous system to adapt to systematic movement errors is an important step in elucidating the neural control of visual orienting behaviors.

In an effort to distinguish between the alternatives outlined above (modification of a gaze shift command versus modification of separate eye and/or head specific signals) head unrestrained gaze adaptation was investigated in 3 rhesus monkeys (*Macaca mulatta*) whose gaze shifts began from a variety of orbital eye positions. The relative contribution of the eyes and head to a particular amplitude gaze shift depends on the orbital position of the eyes at gaze onset and gaze vector (Freedman & Sparks, 1997; Freedman, 2005). Typically, head-contribution is large when the eyes are deviated towards (head deviated away) and small when the eyes are deviated away (head deviated
towards) from a potential visual target. During gaze adaptation, the eye and head command only hypotheses predict that only one of these effectors is modified. In these instances, only the eye or head movement for gaze shifts from every eye position would be modified. However, an adaptive change to a gaze command would result in modifications to both eye and head movements and that the relative change in eye and head contribution during gaze adaptation would vary with starting eye position.

The data in this report illustrate that using the McLaughlin task in the head unrestrained monkey, gaze shift amplitudes change systematically and with an exponential time course. As gaze amplitudes are modified, the amplitudes of eye and head contributions change. However, relative contributions remain appropriate (i.e. similar to control trials) for gaze shifts matched for amplitude and starting positions of the eyes in the orbits. Finally, gaze adaptation was carried out with the eyes always in one starting position relative to the head. After the amplitude of gaze shifts was altered, movements were made with the eyes in different (unadapted) initial positions. Although the contributions of the eyes and head were very different when movements were started with the eyes in these novel positions, the amplitudes of gaze shifts remained at the adapted values; gaze adaptation transferred to movements made under unadapted initial conditions. These data are
consistent with the hypothesis that head-unrestrained gaze adaptation is mediated by changing gaze shift commands (Cecala & Freedman, 2008; Phillips et al, 1997).

The data in this paper extend our earlier study (Cecala and Freedman, 2008) in several ways. First, we demonstrate the effects of adaptation on gaze, eye and head movements in a non-human primate; a model system for future neurophysiological studies on the neural mechanisms of the adaptive process. In addition, in this report we compare head unrestrained adaptation with head restrained saccadic adaptation and report on the rates of adaptive changes when the head is free to move using large intra-gaze target displacements during the McLaughlin paradigm.

3.2 Material and Methods

Three female rhesus monkeys weighing 4.5-6.0 kg served as subjects. A scleral coil was implanted for monitoring gaze position (Judge et al. 1980) and, during the same aseptic surgery, a small head-restraint device was secured to the skull. After full recovery, subjects were trained to make gaze shifts to visual targets. All surgical and experimental procedures were approved by the University of Rochester Animal Care and Use Committee, and are in accordance with the National Institutes of Health Guide for the Care and Use of Animals.
During all training and experimental sessions, animals were seated in a primate chair designed to restrict movements of the hips and upper body while permitting unrestricted movements of the head. Data collection took place in one of two apparatus which used either a pair of movable lasers or an LED array as visual stimuli. When movable lasers were used as visual stimuli, the monkey was seated in the center of a 1.2m cube that housed 3 pairs of magnetic field coils (CNC engineering, Seattle, WA). The four vertical faces of the cube (front-back and left-right) contained two pairs of Helmholtz coils in spatial and phase quadrature (Collewijn, 1977). The current produced in the scleral and matching head coil were linear within ~2% over 360°. The top and bottom faces of the cube contained a third pair of Helmholtz coils that were used to measure the vertical angle of the scleral and head-mounted coils. Visual targets were presented by pointing green (532 nm) or red (650nm) laser diodes at the inside of a 1.5m diameter hemisphere (0.5” acrylic; Capital Plastics, Beltsville, MD). The center of the hemisphere’s vertical face was aligned with the geometric center of the field coil frame. Positioning of the green lasers was accomplished using two independent, 2-axis, motorized gimbals (custom designed using pairs of RGV 100 rotation stages; Newport Corp., Irvine CA, USA). Each pair of rotation stages, arranged in a Fick gimbal, could direct a laser spot at any location within the hemisphere with better than 0.01°
accuracy and precision rated at 0.0003°. The LED array was a flat panel array that subtended ±48° of visual angle horizontally and ±40° vertically (LEDs spaced every 2°). In other respects the two systems were similar (primate chair, coil system, etc.).

In both apparatus, a lightweight cam-lock device containing a coil similar to that implanted in the eye, was secured to the head. In addition, 3 laser diodes (red: 650nm) were mounted on the head. The center laser was aligned with the mid-sagittal plane of the subject, while the others were directed ~18° to the left or right of center. Each trial began with the presentation of a central target (T₀). Subjects were required to fixate T₀ while aligning the head-mounted laser spot at the same location. When the central head-mounted laser was illuminated this served to align the eyes and head at the initial fixation target. When either the left-pointing or right-pointing head-mounted lasers was lit, alignment of the head-mounted laser with the target (within a 3° computer defined window) required a rotation of the head (to the right or the left) while the direction of gaze was maintained. As a result, the positions of the eyes in the orbits at the beginning of each gaze shift varied as a function of which head-mounted laser was turned on.
*Trial Types*

All trials began as described above. Fixation of $T_0$ and alignment of the head-mounted laser had to be maintained for an interval that varied from 250 to 1250ms (100ms increments). At the end of this interval an additional target was illuminated. Head-alignment and fixation of the $T_0$ target had to be maintained during a delay period lasting between 250 and 1250ms (50ms increments). The location of the new target was selected randomly by computer from a set of potential targets ranging from -50° to 50°. Typically, during any particular session 8-10 target locations were used, and these always included the locations that were to be used for adaptation during the same session. At the end of the delay, the head-mounted laser and $T_0$ were turned off, cuing the subject to make a gaze shift to the still lit target. After the movement was completed, reward was delivered if the subject maintained fixation of the new location for 500ms within a computer defined window (5-7°) centered on the target location.

Adaptation trials differed from delayed gaze shift trials in two ways. First, the location of the gaze shift target remained the same for all adaptation trials on a given day (this target is referred to as the $T_1$ target throughout the text and in Fig. 3.1). The second important difference in adaptation trials was that after the gaze shift was initiated (when gaze position exceeded the computer-defined fixation window
centered on $T_0$) the $T_1$ target was turned off, and 20ms later another
target ($T_2$) was illuminated. During backward adaptation, the $T_2$ target
was located between $T_0$ and $T_1$; during forward adaptation the $T_2$ target
was further away from $T_0$ than was $T_1$. Example target locations for a
backward adaptation session are illustrated in Fig. 3.1F. Because the
amplitude of gaze shifts to the $T_1$ location are expected to become
smaller over the course of backward adaptation, the reward window size
was increased and centered on a location halfway between $T_1$ and $T_2$ so
that subjects continued to be rewarded despite making hypometric
movements. Note that if they made normometric movements subjects
would still be rewarded; there was no penalty for failing to change gaze
shift amplitudes. In order to assess gaze adaptation without the
potentially confounding effects of a visible target at $T_2$ during part of the
gaze shift, on randomly interleaved trials the $T_2$ target was not
illuminated (“probe” trials: Fig. 3.1B, F). When time permitted, recovery
from adaptation was facilitated by re-illuminating the target at the $T_1$
location (Fig. 3.1D, H).

Experimental sessions were carried out according to the
following pattern. Delayed gaze shift and probe trials to a variety of
targets were randomly interleaved. Movements to the $T_1$ and $T_2$ target
locations were included. After approximately 200 trials, adaptation trials
using $T_1$ and $T_2$ locations began; probe trials to the $T_1$ target and also to
8-10 other target locations continued to be presented during the adaptation period and were randomly interleaved with the adaptation trials. Probe trials made up approximately 30% of trials presented. Adaptation (and probe) trials continued to be presented for between 600 and 800 trials. At the end of this period of adaptation, only probe trials were presented (recall that there was no visual feedback about movement accuracy during probe trials). Following this period, recovery trials to $T_1$ were presented until the end of the session. With the exception of transfer experiments, each trial began by the random illumination of one of the three head mounted lasers throughout the duration of the experimental session.

During transfer experiments, all three head lasers were randomly intermixed during the pre- and post-probe epochs. However, at the beginning of the adaptation epoch (“initial adaptation epoch”) gaze shifts were initiated from a single eye position (e.g. “centered”). At the beginning of the “novel eye position epoch”, approximately half way through the adaptation session (300-400 trials), gaze shifts were initiated from only the remaining two eye positions (e.g. “leftward” and “rightward”). Note that towards the end of the adaptation epoch the original eye position (in this example case the centered eye position) was reintroduced in order to assess the magnitude of adaptation from this eye position at the end of the adaptation epoch. Adaptation
sessions were separated by at least one behavioral session in which the subject performed only delayed and/or probe trials.

Data Acquisition and Analysis

Custom behavioral control software running on a PC with an extended PCI bus (National Instruments; Austin TX, USA) controlled the switching on and off of the head-mounted lasers, movable lasers, and LEDs in real-time with 1ms resolution. Search coil signals were filtered to remove the coil carrier frequencies and stored for offline analysis using MATLAB (Natick, MA). Using velocity and acceleration criteria, gaze, eye, and head movements were identified, and their amplitudes calculated\(^1\). In addition, the contribution of the head to the accomplishment of each gaze shift (the amplitude of head movements that occurred during the gaze shift) was determined. The average amplitudes of movements made during probe trials to the T\(_1\) target before adaptation were compared with average amplitudes observed during the last 15 adaptation trials and/or with the first 15 probe trials collected after adaptation was complete. Note that during three experiments (P10, P11, P12) we were unable to collect enough trials during the post-probe epoch for

\(^1\) Gaze/eye onset was defined as the time at which velocity exceed 30° and 5000°/s/s acceleration. Gaze/eye offset was defined as the time at which velocity fell below 30° and 5000°/s/s. Head movement onset and offset were defined using 25°/s and 10°/s and 5000°/s/s and 200°/s/s acceleration/deceleration criteria respectively.
comparison. Unless otherwise noted, comparisons of means were made using a one way-ANOVA (Tukey-Kramer post hoc) in the MATLAB Statistical Toolbox, significance was determined using the criterion $p<0.05$.

Rates of adaptation were assessed by plotting movement amplitudes as functions of the number of completed adaptation trials (note that probe trials were randomly interleaved during adaptation; these trials were removed and excluded from adaptation rate calculations). Data were fit (least squares) with exponentials (Sigma Plot) and "trial constants" (analogous to rate constants) calculated.

3.3 Results

*Eyes and Head Aligned*

Primary gaze amplitude was altered in all 28 gaze adaptation experiments (17 backward, 11 forward) collected from three monkeys (P, Q, S). When the central head-mounted laser was illuminated, the eyes and head were aligned at the beginning of gaze shifts. During "backward" adaptation, the amplitude of gaze shifts made in response to presentation of $T_1$ decreased for each subject. In panels 3.2A-D, gaze (green), eye (red), and head (blue) positions are plotted as functions of time for typical gaze shifts made by subject Q during backward...
adaptation (session Q1). The initial target displacement ($T_1-T_0$) was 50° in each case and movements began after subjects aligned the eyes and head. Average initial eye position for these four representative trials was -0.3 ± 1.1°.

Figure 3.2A illustrates a gaze shift made towards $T_1$ during a probe trial before the introduction of adaptation trials. In Fig. 3.2A, and subsequent similar plots (Fig. 3.2B-D; Fig. 3.3A-D), position traces are aligned to gaze onset; for display purposes, 100 ms of data before movement onset are also shown. The 44.7° gaze shift (green) in this example was accomplished by combining a 35.1° saccadic eye movement (red) with a head contribution of 9.6°. The head moved a total of 36.7° on this trial (blue); most of this large head movement occurred after the line of sight was already directed toward $T_1$. During the continuing head movement, gaze position remained relatively constant; most likely a result of the vestibulo-ocular reflex. This subject’s primary gaze shift during the first adaptation trial (Fig. 3.2B) was similar in amplitude to that shown in Fig. 3.2A. The 45.1° gaze shift consisted of a large saccade (34.7°) associated with a small head contribution (10.4°). The primary gaze shift was followed by two “corrective” gaze shifts that re-directed the line of sight so that the subject’s final gaze position was closer to $T_2$ ($T_2-T_0 = 26°$).
In a later adaptation trial (Fig. 3.2C), the primary gaze shift (40.1°) was smaller than those seen during pre-adaptation probe trials (3.2A). Note that both the eye movement (33.6°) and head contribution (6.5°) amplitudes were smaller when compared to movements made before or at the beginning of adaptation (3.2A and 3.2B); the gaze shift in 3.2C was also followed by a small corrective saccade. During the last adaptation trial presented in this experimental session, gaze shift amplitude was 35.7° (2D); nearly 10° shorter than gaze shifts to T₁ before adaptation. In this example, saccade amplitude was 31.3° and the contribution of the head was 4.3°. Eye movement amplitudes changed from 35.1° to 31.3° and changes in head contribution from 9.6° to 4.3° during the course of adaptation.

All movements to T₁ made during this session (Q1) are shown in panels E-H. Gaze shift amplitude is plotted as a function of trial number in Fig. 3.2E. Triangles indicate trials during which T₁ was turned off when the gaze shift was initiated and no other targets were illuminated (“probe” trials). For all movements illustrated, the eyes and head initially were aligned (mean eye position at gaze shift onset = 0.1 ±1.1°). Before adaptation trials were presented (“pre-adaptation”) mean gaze shift amplitude was 46.6 ±1.8°. The trial indicated with the down-directed arrow (A) corresponds to the trial
shown in panel A. During these gaze shifts, saccadic eye movements (3.2F) made up ~83% of the change in gaze direction (saccade amplitudes were 38.7 ±1.7°); the head contributed (3.2G) the remaining 17% of gaze shift amplitude (7.8° ±1.0°). As shown in panels A-D, the head continued to move for several hundred milliseconds after the gaze shift ended and as a result the total amplitude of head movement (3.2H) was much larger than the head contribution to the gaze shift (32.1 ±2.1°).

Referring to the adaptation session illustrated in Fig. 3.2, after 350 control trials, adaptation trials were introduced (gray squares). These trials were identical to the ongoing “probe” trials except that after the movement is begun and T1 turned off, a second target (T2; in this example located between T1 and T0) is illuminated (fig. 3.1C). Recall that during the entire session, probe trials to targets other than the T1 target were randomly interleaved with adaptation trials as were probe trials to the T1 location. As adaptation trials were presented, the amplitude of gaze shifts to the T1 target gradually became smaller, as did gaze shifts during probe trials to the same location (black triangles). Arrows labeled B-D indicate individual trials shown in panels B-D. During the final 15 adaptation trials gaze shift amplitude was reduced from ~47° to 33.6° (± 2.8°). Saccade amplitude (F; 28.1 ± 2.8°), head contribution (G; 5.5 ± 0.7°) and total
head movement amplitude ($H; 20.2 \pm 4.2^\circ$) were also smaller after adaptation.

At this point adaptation trials were stopped. However, probe trials to the $T_1$ location continued (“probe only”). There is no visual feedback at the end of probe trials and movements to this target under these conditions continued to be much smaller compared to pre-adaptation probe trials. Subsequently, visual feedback was re-introduced (“recovery”) and gaze, eye and head movement amplitudes progressively increased.

During a different session (Q3: “forward adaptation”), $T_1$ was located 26° away from the fixation target ($T_0$), and $T_2$ was located 50° away. Figure 3.3 presents details of this session (layout the same as Fig. 3.2). Panels A-D illustrate gaze, eye and head positions plotted as functions of time for 4 movements at different points (indicated with arrows in panels E-H) during the adaptation. Figure 3.3A illustrates a pre-adaptation trial in which primary gaze amplitude was 27.6°, saccade amplitude was 24.5°, and head contribution was 3.1°. The first adaptation trial (3.3B) was similar to those made during pre-adaptation probe trials (gaze = 27.3°, eye = 24.6°, head contribution = 2.7°), the one notable difference being the large “corrective” movement that followed the primary gaze shift by ~300ms. Also shown are trials part way through (C) and at the end of the adaptation session (D). A clear
increase in gaze shift amplitude occurred during adaptation (Fig. 3.3E). Average gaze shift amplitude increased 13.1° over the course of adaptation. Eye movement amplitude increased by 8.7° (F), and head contribution increased by 4.4° (G). Although total head movement amplitude (H) also increased during adaptation trials compared to head movement amplitude before adaptation, variability was quite high during this session and the increase appeared to be stepwise rather than progressive.

The backward (Fig. 3.2) and forward (Fig 3.3) adaptation sessions illustrate the changes in gaze shift amplitudes observed during adaptation and indicate that these can be mediated by changes in both the amplitude of the saccadic portion of the gaze shift, and concomitant changes in the contribution of the head. Figure 3.4 summarizes the differences in gaze, eye, head contribution and total head movement amplitude during adaptation for all backward (A-D) and forward (E-H) sessions when gaze shifts began with the eyes and head aligned. Positive values indicate an increase and negative values indicate a decrease in movement amplitude. Black bars compare pre-adaptation amplitudes with amplitudes during the last 15 adaptation trials; gray bars compare movement amplitudes before adaptation with the first 15 probe trials during the “probe-only” period.
The mean change in gaze amplitude for all 17 backward adaptation sessions (3.4A) was -16.5 ± 3.1° (range: -9.7 to -22.3°). This decrease was mediated by significant decreases in head contribution (mean Δ = -6.8 ± 3.2°; range: -2.2 to -14.4°) and saccade amplitude (mean Δ = -9.7 ± 3.2°; range: -4.0 to -17.8°); decreases in gaze amplitude were accompanied by a decrease in total head movement amplitude (mean Δ = -11.9 ± 4.2°; range: -2.2 to -20.0°). Similar amplitude changes in gaze, saccade, head-contribution, and total head movement were observed when comparing pre- and post-adaptation probe trials to T₁ (gray bars; 3.4A-D).

During forward adaptation, gaze amplitude increased by 10.3 ± 3.0° (range: 6.9 to 15.1°). In the majority of cases, increases in gaze amplitude were mediated by significant increases in head contribution (mean Δ = 4.3 ± 2.4°; range: 0.6 to 8.3°), saccade amplitude (mean Δ = 6.1 ± 2.8°; range: 1.2 to 11.1°), and a large increase in total head amplitude (mean Δ = 21.5 ± 3.4°; range: 13.9 to 26.5°). Similar amplitude changes in gaze, saccade, and head-contribution were observed when comparing pre- and post-adaptation probe trials to T₁ (gray bars; 3.4E-H).
Eyes and Head Not Aligned

The results discussed thus far describe the changes in gaze, eye, and head movements during backward and forward, head-unrestrained gaze adaptation when the eyes and head were initially aligned. The results indicate that changes in gaze shift amplitude arise from changes in both eye and head components of head-unrestrained visual orienting movements. This suggests that the gaze amplitude changes observed during adaptation may be due to changes in the gaze displacement command. However, parametric changes in both eye and head components of gaze remain a plausible alternative that could account for these results. To attempt to address this latter possibility, gaze shifts were initiated with the eyes in different positions relative to the head. Figure 3.5 plots gaze, saccade, head contribution and total head amplitude data from gaze shifts initiated with the eyes directed to the left in the orbits (A-D; mean initial eye position = -14.9 ± 2.1°). During the same adaptation session (Q1), on randomly interleaved trials, gaze shifts were also initiated with the eyes deviated to the right in the orbits (E-H; mean initial eye position = 12.5 ± 1.0°). In each panel, data are plotted as a function of the actual trial number during the session. Recall that all data are plotted as if all gaze shifts were rightward. During this same adaptation session, additional trials initiated with the eyes and head aligned were also randomly presented (Fig. 3.2).
When the eyes began deviated to the left, the majority of the pre-adaptation gaze shifts (3.5A) to $T_1$ were accomplished by large saccadic eye movements (3.5B) accompanied by relatively small head movements (3.5D); the head contribution to these gaze shifts was $<5^\circ$ (3.5C). During adaptation, gaze amplitude decreased similarly during randomly interleaved adaptation (gray squares, 3.5A) and probe trials (black triangles, 3.5A) toward $T_1$. The decrease in gaze amplitude was largely a result of reduced saccade amplitudes. Note in panel 3.5C that head contribution (already quite small) declined very little during adaptation. There was, however, a clear reduction in the overall head movement amplitudes throughout the course of adaptation (3.5D). After adaptation, when only probe trials were presented, amplitudes of gaze, eye and head remained at the reduced, adapted levels.

In contrast, when the eyes began deviated to the right, gaze shifts in the pre-adaptation phase (3.5E) were accomplished by a smaller saccadic eye movement (3.5F) and larger head-contribution (3.5G) than those initiated with the eyes to the left. Total head movement (3.5H) was also significantly larger when the eyes began deviated to the right. During the adaptation phase, saccade, head-contribution, and total head amplitude each decreased significantly. Similar to the centered (Fig. 3.2) and leftward eye position data described above, these changes were maintained during an epoch after adaptation where the subject
performed only probe trials. Furthermore, the appropriate changes to eye and head movements from each of these eye positions were made during the recovery phase to produce primary gaze amplitudes that approached pre-adaptation amplitude values.

Figure 3.6 plots gaze, saccade, head contribution and total head amplitude data from gaze shifts initiated from the leftward (A-D; mean initial eye position = -13.0 ± 1.1°) and rightward (E-H; mean initial eye position = 14.1 ± 1.4°) eye positions as a function of actual trial number for a single forward adaptation experiment (Q3). These data are from the same experiment used to illustrate changes to these components from the centered eye position (Figure 3.3). Primary gaze shifts initiated from the leftward eye position were slightly (~3°) but not significantly, smaller than gaze shifts initiated from the rightward eye position. Nonetheless, gaze amplitude increased consistently for both sets of movements during the adaptation phase. Similar to the pre-adaptation gaze shifts made in the backward adaptation experiment (Q1; Fig 3.5), pre-adaptation gaze shifts to the T₁ target initiated from the leftward eye position were primarily the result of a saccadic eye movement (3.6B). The head did move during the pre-adaptation phase (3.6D) but contributed very little to these gaze shifts (3.6C). During the adaptation phase, changes in primary gaze amplitude (3.6A) were accomplished by changes in saccade amplitude (3.6B) and a very small, but significant
change in head-contribution (3.6C). In contrast, when gaze shifts began with the eyes deviated to the right, changes in gaze amplitude (3.6E) were accomplished by increases in both saccade (3.6F) and head contribution (3.6G).

For all experiments, the changes to gaze, saccade, head contribution, and total head amplitude that occurred when the eyes and head are not aligned during backward and forward adaptation experiments are illustrated in figures 3.7 and 3.8 respectively. The black bars in each of these figures represent the mean difference (±SD) between pre-adapt probes and adaptation trials; where as gray bars represent the mean difference (±SD) between pre-adaptation probes and post-probe means.

During backward adaptation when gaze shifts were initiated with the eyes deviated to the left in the orbits (Fig 3.7A-D), mean gaze and saccade amplitudes decreased significantly in every experiment regardless of the mean comparison (Pre-probe versus either adaptation or post-probe mean). Head contribution decreased significantly in 13 of 17 experiments during adaptation trials (black bars) and 12 of 16 experiments during adapt-probe trials (gray bars). Total head movement decreased significantly in 13 of 17 experiments during adaptation trials and 11 of 16 probe trials.
During backward adaptation when gaze shifts were initiated with the eyes deviated to the right in the orbits (Figure 3.7E-H), mean gaze and head contribution amplitude decrease significantly in every case regardless of the mean comparison. Post-adaptation mean saccade amplitude decreased significantly in 13 of 17 experiments and post-probe mean saccade amplitude decreased significantly in 12 of 16 experiments. Both post-adaptation mean head contribution and total head amplitude decreased significantly in every experiment.

Figure 3.8 (A-D) illustrates the changes in gaze, saccade, head contribution, and total head movement amplitude during forward adaptation when gaze shifts were initiated with the eyes deviated to the left. As shown, post-adaptation and post probe mean gaze and saccade amplitudes increased significantly in every experiment regardless of mean comparison. However, post-adaptation mean head contribution (C) increased significantly in only one experiment (Q3). Mean total head amplitude increased in 7 of 11 experiments during adaptation trials.

When the eyes began deviated to the right during forward adaptation experiments (Figure 3.8E-H), gaze amplitude (E), head contribution (G), and total head movement increased significantly during both adaptation (11/11) and probe trials (9/9). In half of the experiments, saccade amplitude increased during both adaptation and probe trials.
Head-Unrestrained Transfer Experiments

In our subjects, changes to eye and head movements depended upon the magnitude of gaze adaptation and the orbital positions of the eyes at gaze onset. However, it could be argued that initial eye position provided a sufficient context (Alahyane & Pelisson, 2004) so that different combinations of eye-head changes were specified during adaptation simultaneously from each starting position. The alternative assumes that a gaze displacement command is altered, and in this case initial eye position acts not as a context cue but instead determines the relative contributions of the eyes and head to a gaze shift of specific amplitude and direction. In the latter case, gaze amplitude adapted from a small range of eye positions should transfer to gaze shifts initiated from significantly different eye positions; whereas in the former, they should not.

Figure 3.9 illustrates data from an example backward adaptation transfer experiment (P5). In the pre-adaptation phase of all transfer experiments, subjects initiated gaze shifts from all three eye positions. As illustrated, monkey P produced accurate gaze shifts toward the T1 target located 50° to the right of T0 (Fig 9A – “pre-adaptation”). These gaze shifts were composed of different eye and head movements depending on initial eye position (3.9B-D). For instance, when the eyes
began centered in the orbits (green) 50° gaze shifts were composed of 35° saccadic eye movements and head contributions of 15°. However, head contribution was 30° and saccade amplitudes 20° when the eyes began deviated to the right (red). When deviated to the left (blue), eye movement amplitudes were 45° and head contributions were 5°.

In the example shown in Fig. 3.9, adaptation trials were initiated with the eyes in the same starting positions (deviated to the left in the orbits in this example). A significant decrease in gaze amplitude during this epoch occurred as a result of a large decrease in saccade amplitude and a very small decrease in head contribution and total head amplitude. At the beginning of the “novel eye position” epoch, gaze shifts were initiated from the remaining two initial eye positions; centered and rightward eye positions in this case. Two key observations can be made. First, gaze amplitude at the beginning of the “novel eye position” phase is the same as that at the end of the “initial adaptation position” phase (before transition = 32.2 ±1.9°; after transition = 31.9 ±2.7° (eyes right) and 32.6 ±2.5° (eyes centered)). In contrast, saccade amplitude was significantly smaller and head contribution (and total head movement) was significantly larger when initiated from the centered and rightward eye positions compared to the initially adapted leftward position. The change in gaze amplitude produced during adaptation with the eyes starting in one position, transferred
immediately and completely to gaze shifts made with the eyes in
different positions. Eye and head movement amplitudes were, however
very different under the different conditions.

Similar observations were made in each of our 13 transfer
experiments (8 backward; 5 forward). The metrics of gaze shifts before
and after transfer were assessed using the following ratios:

\[ \text{Gaze ratio} = \frac{G^{\text{IEP2}}}{G^{\text{IEP1}}}; \]
\[ \text{Eye ratio} = \frac{E^{\text{IEP2}}}{E^{\text{IEP1}}}; \]
\[ \text{Head Contribution ratio} = \frac{HC^{\text{IEP2}}}{HC^{\text{IEP1}}}; \]
\[ \text{Total Head Movement ratio} = \frac{TH^{\text{IEP2}}}{TH^{\text{IEP1}}}, \]

where IEP1 is the initial eye position from which all gaze shifts began
during the initial adaptation epoch and IEP2 indicates a novel eye
position introduced in the novel eye position epoch. Mean pre- and
post-transfer values were calculated using data from the 15 trials before
(data just before vertical black line in fig. 3.9) or after (data just after
vertical black line) transfer respectively. Table 3.1 contains the gaze,
eye, head contribution, and total head ratios and mean amplitudes (±SD)
from these epochs for all 13 of our transfer experiments. Although
there was some variation between experiments, the average gaze ratio
across all conditions was 1.02 ± 0.13. (n= 26). However, eye and head
movement amplitudes (both total head movement and head
contribution) in the post adaptation phase were different and varied in an initial eye dependent fashion.

**Rate of Gaze Adaptation**

For each adaptation experiment, we assessed the rate of gaze adaptation by fitting a plot of primary gaze amplitude versus adaptation trial number with either an exponential growth or decay function (see methods for details). The trial constant (analogous to a rate constant) and $R^2$ values from each experiment are listed in Table 3.2. Trial constants varied between and within animals during both forward and backward experiments. For example, during backward adaptation, trial constants ranged from 25 (P7) to 500 (S1) adaptation trials and trial constants for monkey S ranged from 100 to 500 adaptation trials. Similar ranges and variability can been noted for forward adaptation experiments. Average trial constants for backward and forward adaptation were 115.7 ± 117.0 and 236.9 ±139.1 respectively.

**“Adapted” versus “Normal” Gaze Shifts**

We compared the relative contributions of the eyes and head to gaze shifts produced before adaptation (pooled across data sessions) with those made during the last 15 adaptation trials of each data session. Fig. 3.10 plots mean (±SD) saccade (A-C) and head-contribution
(D-F) amplitude of control gaze shifts against those made during adaptation trials for each adaptation experiment. Data were separated into leftward (3.10A, D), centered (3.10B, E), and rightward (3.10C, F) eye positions. Note that mean gaze shift amplitude and initial eye position of control and “adapted” gaze shifts were not significantly different in any of these comparisons (p>0.05; Mann-Whitney U). During backward adaptation the relative amplitudes of the eyes and head were consistently different during adaptation trials versus control trials in subjects P and S (p<0.05; Mann-Whitney U), but not subject Q. When the eyes were centered or deviated rightward, gaze shifts during adaptation trials had larger head contribution and smaller saccade amplitudes than control movements (grey symbols, Fig. 3.10B, C, E, F). This was not observed for gaze shifts initiated from the leftward eye position in these animals. In contrast, there were no consistent changes in eye-head coordination during forward adaptation experiments in any of our subjects (black symbols, figure 3.10). Total head amplitude was consistently larger during forward adaptation and smaller during backward adaptation for gaze shifts initiated from all three eye positions by monkeys P & S; this trend was not observed for monkey Q (data not shown).
Comparison with Head-Restrained Adaptation

The general characteristics of head-unrestrained gaze adaptation described above are remarkably similar to head-restrained saccadic adaptation using smaller intra-saccade target displacements. However, it was not clear, a priori, that large target displacements during large amplitude head restrained saccades would produce the same large changes in amplitude. To address this issue, we collected a small number of head-restrained adaptation data from two monkeys (P & S) for comparison with head-unrestrained data. Figure 3.11 illustrates examples of head-restrained backward (A & B) and forward (C & D) gaze adaptation from each subject. During backward adaptation, $T_1$ was located 50° to the right of the initial fixation point ($T_0$), and $T_2$ was 26° to the right of fixation. Both subjects made slightly hypometric primary gaze shifts towards $T_1$ during probe trials (black triangles) in the pre-adaptation period (P: 48.1 ± 1.3°, n= 75; Q: 45.9 ± 1.3°, n= 62). Movement amplitudes systematically declined during adaptation such that the amplitudes of the last 15 adaptation (P: 32.2 ± 2.0°; Q: 28.4 ± 1.8°) and probe (P: 31.5 ± 1.3°; Q: 29.5 ± 1.6°) trials were significantly different than pre-adaptation probe trials. The last 15 adaptation and probe trials of the adaptation epoch were not significantly different from each other (p= 0.48). After adaptation, when only probe trials were presented, both subjects continued to produce movements that were significantly
shorter than pre-adaptation probes (P: 32.4 ± 1.6°, n = 60; Q: 30.4 ± 1.4°, n = 51; p<0.05), but indistinguishable from either the adaptation or probe trials at the end of the adaptation phase (p>0.05). As illustrated (Fig 3.11A & B), movement amplitudes returned toward pre-adaptation amplitudes during recovery. Note that the amplitudes of movements made during probe trials in the recovery period also returned toward pre-adaptation levels.

Both monkeys increased the size of their primary gaze shifts during forward adaptation (figure 3.11C & D). In these sessions, T₁ was displaced 26° and T₂ was displaced 50° to the right of the initial fixation point (T₀). Both subjects made fairly accurate movements towards T₁ during probe trials (black triangles) in the pre-adaptation phase (monkey P: 27.0 ± 0.7°, n = 92; Monkey Q: 23.2 ± 0.9°, n = 81). Gaze amplitude increased significantly during both adaptation and probe trials by the end of the adaptation epoch (p<0.05). Gaze shifts during the post-probe epoch were also significantly larger than those in the pre-adaptation epoch (p<0.05). Similar observations were made in each of our eight (4 backward, 4 forward) head-restrained, saccade amplitude adaptation experiments (Table 3.3).

In summary, when the head is restrained, large changes in movement amplitudes can occur when the intra-saccadic target step (T₂-T₁) is large (~25°). Furthermore, in accordance with previous accounts
of head-restrained saccadic adaptation (Miller et al, 1981; Deubel, 1991; Straube et al, 1997; Scudder et al, 1998; Noto et al, 1999; Bahcall & Kowler, 2000; Robinson et al, 2003), backward adaptation was larger in magnitude than forward adaptation in response to the same post-saccadic visual error.

**Head-Restrained to Head-Unrestrained Transfer**

Phillips and colleagues (1997) have shown that head-restrained saccadic adaptation transfers to head-unrestrained gaze shifts. We sought to replicate and expand their observations while testing the hypothesis that saccade amplitude adaptation results from a modification of a gaze shift command. The pre-adaptation epoch during each head-restrained to head-unrestrained transfer experiment consisted of two phases. At the beginning of the pre-adaptation epoch, monkey P produced head-unrestrained gaze shifts to a variety of T₁ targets (including the T₁ used during adaptation trials; ΔT₁-T₀ = 50°). After approximately 200-300 trials, the subject’s head was restrained using a vertical post and clamp such that gaze shifts could only be achieved using movements of the eyes. Between 100 -150 trials were presented using the same targets as used when the head was unrestrained. The adaptation epoch began with the introduction of intra-saccade back-step trials intermixed with probe trials while the head
remained restrained ($\Delta T_1-T_2 = 25^\circ$). At the end of the adaptation epoch (~400-500 trials), the monkey’s head was manually released by the experimenter while the subject sat in the dark. The post adaptation phase consisted of only probe trials in which the subject produced movements towards each of the $T_1$ targets presented in the pre-adaptation epoch. Note that head-unrestrained gaze shifts in the pre- and post-adaptation phases always began with the random illumination of one of the three head lasers.

The transfer of head-restrained saccade adaptation to head-unrestrained gaze shifts was quantified by comparing the change in head-restrained saccade amplitude to the change in head-unrestrained gaze amplitude. Comparisons were made for gaze shifts initiated from each of the different eye positions (left, center, right). The ratio of these values ("transfer ratio") is presented for each experiment and condition (Table 3.4). Again, note that data are presented as if all gaze shifts were rightward. As shown, the transfer from head-restrained saccades to head-unrestrained gaze shifts was incomplete and varied slightly for gaze shifts initiated from the different eye positions. However, note the following: 1) Head-unrestrained gaze shifts after head-restrained adaptation were significantly smaller than pre-adaptation gaze shifts regardless of the initial starting eye position (gaze ratio); 2) Changes in head-unrestrained gaze amplitude between pre- and post-adaptation
epochs were the result of changes to both eye (eye ratio) and head contribution (head-contribution ratio); 3) Total head movement was smaller during the post-adaptation epoch than pre regardless of starting eye position (total head ratio). The changes in head contribution and total head movement are not consistent with the hypothesis that only an eye movement command is modified during head-restrained saccadic adaptation. However, they are consistent with a change in a gaze command upstream of the separate eye and head signals.

3.4 Discussion

In rhesus monkeys, some changes in the line of sight (gaze) are accomplished by coordinated movements of the eyes and head. The ability to adjust the accuracy of gaze shifts in response to persistent visual errors is important for maintaining high acuity vision. One possible adaptive control mechanism adjusts gaze accuracy by modifying a gaze displacement command. Alternatively, changes in gaze accuracy could result from modifications to either of the separate signals used to move the eyes or head. Our results describe the changes in eye and head movements during a short-term gaze adaptation task under conditions in which these alternative hypotheses are dissociable (Cecala & Freedman, 2008).
Major findings

The results of our study of rhesus monkey gaze adaptation indicate that large changes in gaze amplitude can be elicited during backward and forward versions of the McLaughlin task regardless of whether the head is restrained or allowed to move. When our subjects’ heads were allowed to move, changes in gaze amplitude resulted from changes to both saccade amplitude and head contribution (Figs. 3.4, 3.7, & 3.8). Changes in gaze shift amplitude occurred systematically as a function of the number of adaptation trials presented to each subject. These changes in gaze shift amplitude were mirrored by changes in the amplitude of gaze shifts made during randomly interleaved “probe” trials. Note that during probe trials the T₁ target was turned off when the gaze shift was initiated, and the T₂ target was never illuminated. This reveals some underlying change in the sensorimotor apparatus linking a visual target in a particular spatial location to a movement of a particular amplitude; the movements associated with presentation of T₁ were altered. After adaptation when only probe trials were presented, the changes in gaze shift amplitudes that arose during adaptation persisted. Changes in gaze shift amplitudes were necessarily caused by changes in the eye and head movements that lead to changes in the direction of the line of sight. However, as gaze amplitudes were altered
during adaptation, the changes in eye and head movement amplitudes varied and were determined by the starting positions of the eyes in the orbits and by the amplitude of the ongoing gaze shift. The clearest demonstration of this point occurs during gaze transfer experiments in which changes in gaze amplitude during the initial adaptation phase resulted from specific changes in eye and head movements. However, when movements were initiated from eye positions not used during adaptation, gaze amplitudes were unaltered but the eye and head movements used to produce these gaze shifts were very different (Fig. 3.9; Table 3.1). These data suggest changes to a gaze command signal and are inconsistent with specific changes to separate eye and head movement commands.

**Previous Findings**

Two previous studies involving head-unrestrained primates have concluded that gaze adaptation results from modifying a gaze displacement command signal (Phillips et al., 1997; Cecala & Freedman, 2008). The study by Phillips and colleagues (1997) emphasized the transfer of head-restrained saccade amplitude adaptation to head-unrestrained gaze shifts produced by rhesus monkeys. Phillips et al. were successful in reducing 50° head-restrained saccades by back-stepping a target by 20°. When the head was subsequently allowed to
move, the induced changes in gaze amplitude persisted and were shown to be a result of changes in both eye and head movement amplitudes. The authors concluded that these changes were likely due to changes in a gaze-related command. However, they could not rule out the possibility that the observed changes in amplitude were a result of specific changes to separate eye and head movement commands. To rule out this alternative, movements must be initiated with the eyes and head in different positions.

Phillips and colleagues (1997) described an average of 81% transfer from head-restrained to head-unrestrained gaze shifts (n=8). It is not clear why our head-restrained to head-unrestrained gaze transfer values are less (average across all conditions = 58%). One possible explanation for our observation is the manual interaction between experimenter and subject when switching from head-restrained to head-unrestrained after the adaptation epoch; Phillips and colleagues released their subject’s head remotely thus not interrupting the subject’s performance (James O. Phillips, personal communication). However, the rest of our observations are consistent with those of Phillips and colleagues.

Using a paradigm similar to that used in the current report, we have shown that large changes in gaze amplitude can be elicited in head-unrestrained humans (Cecala & Freedman, 2008). In this study of
human gaze adaptation, pre-adaptation gaze shifts of ~30° (forward adaptation) and ~60° (backward adaptation) were adjusted using a 30° intra-gaze target displacement. On average, the 30° visual error was reduced by ~50% during backward, and by ~40% during forward adaptation. In the current study, monkey subjects adjusted gaze amplitude by amounts similar to human subjects when normalized to the 25° back- or forward-stepped target (backward mean: -16.5 ± 2.8° or 66%; forward mean: 9.2± 3.8° or 37%). Also, similar to the head-unrestrained transfer experiments in the current study, when gaze amplitude is altered from a small range of orbital eye positions in human subjects, the magnitude of gaze change transfers to other novel eye positions and the contribution of the eyes and head to gaze shifts in the novel eye position epoch are markedly different than those in the initial adaptation phase.

The rate of head-unrestrained gaze adaptation has never been quantified. Gaze adaptation (both head-restrained and head-unrestrained) in our subjects followed an exponential time course (Figs. 3.2, 3.3, 3.5, 3.6, 3.9, 3.11) like that noted in previous head-restrained saccadic adaptation studies (e.g. Straube et al, 1997). Thus, the ability to produce changes in gaze movement amplitude using the McLaughlin task appears to be similar regardless of the displacement of the targets,
and independent of whether the head is free to move (Cecala & Freedman, 2008).

**Differences in eye-head coordination**

Phillips and colleagues (1997) observed no differences in eye-head coordination when comparing equal amplitude gaze shifts before and after adaptation. In the current report, we compared the relative contribution of the eyes and head to gaze shifts made at the end of each adaptation epoch with those produced during control trials. When gaze shifts were matched for amplitude, initial eye position, and direction we consistently observed increases (forward adaptation) or decreases (backward adaptation) in total head amplitude in 2 of our 3 subjects (P & S). We also observed alterations in eye-head coordination in these monkeys during backward adaptation from particular eye positions (“centered” & “rightward”) where the head was most likely to contribute substantially to gaze shifts. Typically, saccade amplitude was smaller and head contribution was larger compared to matched control movements. However, as illustrated in the data from monkey Q, alterations to the normal eye-head coordination and total head movement need not accompany decreases in gaze amplitude during backward adaptation. Furthermore, consistent changes in eye-head
coordination were not observed during forward adaptation in any of our subjects.

It is not entirely clear that the differences in eye-head coordination observed in monkeys P and S are unique to the adaptive process. The spatial and temporal predictability of the target, and gaze shift amplitude, has been shown to influence the relative contribution of the eyes and head to gaze shifts (Moschner & Zangemeister, 1993; Zangemeister and Stark, 1982). We attempted to reduce our subjects’ ability to predict target location by intermixing probe trials in a variety of locations with adaptation trials during the adaptation epoch. However, during 75% of the trials our subjects produced movements towards the same $T_1$ location. We cannot rule out the possibility that the differences in eye-head coordination are a spurious result caused by a highly predictable target location.

**Physiological Implications**

Our data are consistent with the hypothesis that a gaze signal is modified prior to its separation into commands to move the eyes and head. Evidence gathered from microstimulation (Freedman & Sparks, 1996), inactivation (Walton et al, 2008), and single unit recording (Freedman & Sparks, 1997b) experiments in rhesus monkeys support a hypothesis that activity in the primate superior colliculus (SC) encodes
a gaze displacement command which is parsed downstream into commands to move the eyes and/or head. For example, suprathreshold stimulation of the deeper layers of the SC produces contraversive gaze shifts whose metrical relationships are comparable to visually guided gaze shifts matched for amplitude, direction, and initial eye position (Freedman & Sparks, 1996). Two alternative hypotheses describing collicular activity could account for the change in gaze output we observed during the McLaughlin paradigm. First, as gaze amplitudes change, the locus of SC motor activity could change systematically. In this case, the motor output of the SC specifies the motor output that is actually observed. Alternatively, the locus of SC motor activity could remain unchanged, thereby specifying a change in the line of sight towards the first visual target presented to the subject (T1). In the latter case, the collicular command must be altered “downstream” of the SC to account for the systematic change in gaze amplitude observed during adaptation.

To our knowledge, the SC has only been studied during head-restrained adaptation. Frens & van Opstal (1997) recorded single units from the deep layers of the SC during backward adaptation. These authors reported that ~60% of units recorded did not change activity throughout the adaptation epoch even though saccade amplitude decreased. These results, along with those of microstimulation
experiments (Meils & van Gisbergen, 1996; Edelman & Goldberg, 2000),
suggest a modification to collicular output occurs downstream from the
SC. In contrast, Takeichi and colleagues (2007) recently described
modifications to the movement fields of SC units that correlated with
changes in saccade amplitude, which they interpreted as the gaze
command being altered at the level of the SC (or its afferents) during
adaptation. Interestingly, when Takeichi and colleagues compared the
burst metrics of units recorded during backward adaptation in a fashion
similar to that used by Frens & van Opstal (1997), the majority (79%) of
cells “showed no change in the number of spikes at the desired
saccade size after adaptation”. Note that the somewhat mixed results
from these studies may be due to the relatively small target
displacements used to produce saccadic adaptation. The small changes
in saccade amplitude in response to these target steps may have
resulted in difficulty dissociating changes in SC neuronal burst metrics
from noise. The majority of evidence suggests that SC activity during
adaptation represents a desired displacement signal towards T₁ during
saccadic adaptation and that the SC command must be modified
downstream of the SC to account for changes in gaze amplitude.

The medio-posterior cerebellum has been implicated in the
adaptive control of saccadic eye movements (see Robinson & Fuchs,
2001 for recent review). The deeper layers of the SC are connected to
the medio-posterior cerebellum (caudal fastigial nucleus and oculomotor vermis (Ohtsuka & Noda 1990)) via nucleus reticularis tegmenti pontis (NRTP; Ohtsuka & Noda, 1990; May et al, 1990) and dorsal lateral pontine nucleus (Thier & Mock, 2005). Lesions to the medio-posterior cerebellum impair rapid saccade amplitude adaptation during the McLaughlin task (Barash et al, 1999; Takagi et al, 2000; Robinson et al, 2002); and the burst metrics of neurons in NRTP (Takeichi et al, 2005), caudal fastigial nucleus (Scudder & McGee, 2003; Inaba et al, 2003) and oculomotor vermis (Catz et al, 2005, Catz et al, 2008, Soetedjo & Fuchs, 2006) are altered along with saccade amplitude during head-restrained saccadic adaptation. Future studies are required to classify the types of motor command signals (gaze, eye, or head) represented at each level of this circuit prior to describing modifications to these signals during gaze adaptation using the McLaughlin task.

In summary, reliable changes in gaze amplitude can be elicited from the rhesus monkey using the McLaughlin (1967) task. These changes are the result of modifications to both eye and head movements which are dependent upon the magnitude of change in gaze amplitude and the positions of the eyes at gaze shift onset. This result, along with those of our transfer experiments, suggest that a gaze displacement command signal upstream of those used to drive
separately the eyes and the head is altered systematically during gaze adaptation.
References:


Figure 3.1 A-D: Schematic diagrams of trial types used. In each panel, gaze position is represented by a thin black line and plotted as a function of time. Below this trace, targets are represented by thick bars indicating when within the trial each target was illuminated and extinguished. In each case, trials began with the illumination of a head-mounted laser (light gray bar) followed by presentation of $T_0$. If behavioral contingencies were satisfied, the head-mounted laser and $T_0$ target were extinguished and a second target ($T_1$) was illuminated at one of the spatial locations shown in panel E (black circles). A: The $T_1$ target remained illuminated for the duration of the “delayed” trials. B: During “probe” trials, the $T_1$ target was extinguished when the line of sight moved beyond a computer defined window (“position criterion”) surrounding $T_0$. C: “Adaptation” trials were similar to probe trials until 20ms after the position criterion was satisfied, at which time $T_1$ was turned off and a target at location $T_2$ was illuminated. D: Recovery trials were identical to adaptation trials except that the $T_1$ target was re-illuminated and remained illuminated for the duration of the trial. E: target locations used during adaptation and probe trials. F, G, H: Example target and reward window locations during probe (F), adaptation (G), and recovery (H) trials during a backward adaptation experiment. See text for further details.
Figure 3.2 A-D: Gaze (green), eye (red), and head (blue) positions as functions of time during a backward adaptation session (Q1) in which the eyes were initially centered in the orbits (±5°). Each panel illustrates a gaze shift made at a different stage of the adaptation process. Position traces are aligned at gaze onset (“100ms”) in each plot. E-H: Gaze, saccade, head contribution and total head amplitudes of the primary gaze shifts made during pre-adaptation, adaptation, post-probe, and recovery segments of experiment Q1. Individual examples A-D are indicated with labeled arrows. Black triangles = probe trials; gray squares = adaptation trials; open diamonds = recovery trials
Figure 3.3 - Gaze (green), eye (red), and head (blue) positions as functions of time during a forward adaptation session (Q3) in which the eyes were initially centered in the orbits (±5°). Each panel illustrates a gaze shift made at a different stage of the adaptation process. Position traces are aligned at gaze onset ("100ms") in each plot. E-H: Gaze, saccade, head contribution and total head amplitudes of the primary gaze shifts made during pre-adaptation, adaptation, post-probe segments of experiment Q3. Individual examples A-D are indicated with labeled arrows. Black triangles = probe trials; gray squares = adaptation trials.
Figure 3.4 - Summary of the change in gaze (A, E), saccade (B, F), head contribution (C, G), and total head amplitude (D, H) for gaze shifts initiated from the centered eye position from 28 sessions (17 backward & 11 forward). The difference (±SD) between the pre-adaptation probe mean and the post-adaptation mean (black bars) or post-probe mean (gray bars) are illustrated. (*) denotes a change in movement amplitude between pre- and post means (t-test, p<0.05).
Figure 3.5 - Gaze, saccade, head contribution and total head amplitudes of the primary gaze shifts made during pre-adaptation, adaptation, post-probe, and recovery segments of backward adaptation experiment Q1.

A-D: Data from gaze shifts in which the eyes were deviated leftward (head deviated toward T1) in the orbits (mean IEP= -14.9 ±2.0°). E-H: Data from gaze shifts in which the eyes were deviated rightward (head deviated away from T1) in the orbits (mean IEP= 12.5±1.0°). Black triangles = probe trials; Gray squares = adaptation trials; open diamonds = recovery trials.
Figure 3.6 - Gaze, saccade, head contribution and total head amplitudes of the primary gaze shifts made during pre-adaptation, adaptation, post-probe segments of backward adaptation experiment Q3. A-D: Data from gaze shifts in which the eyes were deviated leftward (head deviated toward T1) in the orbits (mean IEP= -13.0 ±1.1°). E-H: Data from gaze shifts in which the eyes were deviated rightward (head deviated away from T1) in the orbits (mean IEP= 14.7±1.0°). Black triangles = probe trials; gray squares = adaptation trials.
Non-Aligned Backward Adaptation

A  Left Eye Position

B  Right Eye Position

C  Δ Saccade Amp (deg)

D  Δ Head Contribution

E  Δ Gaze Amplitude (deg)

F  Δ Saccade Amp (deg)

G  Δ Head Contribution

H  Δ Total Head Amp (deg)

Subject Codes: P P P P P P P Q Q Q S S S S S S

Subject Codes: P P P P P P P Q Q Q S S S S S S
Figure 3.7 - Summary of the change in gaze (A, E), saccade (B, F), head contribution (C, G), and total head amplitude (D, H) for gaze shifts initiated with the eyes and head not aligned during backward adaptation experiments. Data were extracted from same 28 sessions shown in figure 4. The difference (±SD) between the pre-adaptation probe mean and the post-adaptation mean (black bars) or post-probe mean (gray bars) are illustrated. (*) denotes a change in movement amplitude between pre- and post means (t-test, p<0.05).
Figure 3.8 - Summary of the change in gaze (A, E), saccade (B, F), head contribution (C, G), and total head amplitude (D, H) for gaze shifts initiated with the eyes and head not aligned during forward adaptation experiments. Data were extracted from same 11 sessions shown in figure 4E-H. The difference (±SD) between the pre-adaptation probe mean and the post-adaptation mean (black bars) or post-probe mean (gray bars) are illustrated. (*) denotes a change in movement amplitude between pre- and post means (t-test, p<0.05).
Transfer of Gaze Adaptation State to Novel Eye Positions

A

Gaze Amplitude (deg)

B

Saccade Amplitude (deg)

C

Head Contribution (deg)

D

Total Head Amplitude (deg)

Legend:
- Left Eye Position
- Right Eye Position
- Center Eye Position
- Probe
- Adapt Trial

Actual Trial Number
Figure 3.9 - Gaze Transfer Experiment (P4). Gaze shifts were initiated from all three eye positions in the pre-adaptation phase. During the initial adaptation phase gaze shifts were only initiated from the leftward eye position (blue). After ~300 trials novel eye positions (centered = green; rightward = red) were introduced. Note that the gaze amplitude at the end of the initial adaptation and the novel eye position phases are similar; however, the saccade, head contribution, and total head movements are not.
Figure 3.10 - Eye-head coordination during adapted versus control movements. Gaze shifts were matched for gaze amplitude and initial orbital eye position ("leftward", "centered", "rightward"). (A-C) Mean (±SD) control saccade plotted as a function of saccades during adapted movements. (D-F) Mean (±SD) control head-contribution plotted as a function of head-contribution during adapted movements. Data from monkey Q (▲), monkey S (●), and monkey P (■) are shown. Black symbols represent comparisons for forward adaptation experiments. Gray symbols represent comparisons for backward adaptation experiments. Open symbols represent statistically significant differences between adapted and control values (Mann-Whitney U, p<0.05).
Figure 3.11 - Large amplitude, head-restrained saccade adaptation.

Summary of primary saccades made during pre-adaptation, adaptation, post-probe, and recovery segments of backward (A, B) and forward (C,D) adaptation experiments from two monkeys (P, Q). Black triangles = probe trials; gray squares = adaptation trials; open diamonds = recovery trials.
<table>
<thead>
<tr>
<th>Experiment</th>
<th>Condition</th>
<th>Eye Position</th>
<th>Gaze Ratio (Amp)</th>
<th>Eye Ratio (Amp)</th>
<th>Head Cont Ratio (Amp)</th>
<th>Total Head Ratio (Amp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1 (Backward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(33.6±4.6)</td>
<td>(35.9±3.4)</td>
<td>(7.6±2.6)</td>
<td>(20.0±3.7)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>1.13 (37.8±2.5) *</td>
<td>1.3 (35.9±2.2) *</td>
<td>0.3 (11.9±0.5) *</td>
<td>0.51 (43.3±1.5) *</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>0.94 (31.7±4.2) *</td>
<td>0.52 (13.8±2.1) *</td>
<td>2.3 (16.0±4.0) *</td>
<td>0.39 (41.6±3.8) *</td>
</tr>
<tr>
<td>P3 (Backward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(21.5±3.6)</td>
<td>(26.9±2.4)</td>
<td>(5.9±1.1)</td>
<td>(18.4±2.6)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>1.07 (24.2±2.1)</td>
<td>1.27 (22.9±2.6) *</td>
<td>0.21 (13.3±0.5) *</td>
<td>0.16 (28.6±1.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>0.92 (20.4±2.6)</td>
<td>0.42 (13.4±2.1) *</td>
<td>2.03 (16.0±2.9)</td>
<td>2.25 (41.2±2.9) *</td>
</tr>
<tr>
<td>P4 (Backward)</td>
<td>PreTrans</td>
<td>Left</td>
<td>(22.2±1.9)</td>
<td>(30.8±2.1) *</td>
<td>(4.3±1.6)</td>
<td>(25.3±2.3)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Center</td>
<td>0.99 (31.5±2.7)</td>
<td>0.82 (25.2±2.9) *</td>
<td>4.97 (6.7±1.0) *</td>
<td>5.73 (23.0±2.8) *</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>1.01 (32.8±2.5)</td>
<td>0.51 (15.7±2.7) *</td>
<td>12.21 (18.9±2.5)</td>
<td>10.31 (41.4±2.6) *</td>
</tr>
<tr>
<td>P10 (Backward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(31.5±4.0)</td>
<td>(22.3±3.7)</td>
<td>(9.0±3.2)</td>
<td>(25.8±4.0)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>1.17 (33.7±1.5)</td>
<td>1.54 (34.4±1.6) *</td>
<td>0.42 (2.3±1.0) *</td>
<td>0.38 (5.9±1.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>1.01 (31.7±2.8)</td>
<td>0.50 (13.1±2.9) *</td>
<td>2.05 (19.5±3.0)</td>
<td>1.77 (41.7±3.8) *</td>
</tr>
<tr>
<td>P15 (Backward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(31.5±3.0)</td>
<td>(28.0±2.4)</td>
<td>(5.9±1.1)</td>
<td>(18.4±2.6)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>1.05 (23.2±5.6)</td>
<td>1.29 (26.3±2.2) *</td>
<td>0.29 (1.6±0.9) *</td>
<td>0.19 (3.9±2.5) *</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>1.07 (25.6±5.2)</td>
<td>0.83 (14.9±3.0) *</td>
<td>2.58 (14.7±3.4) *</td>
<td>1.59 (39.8±2.9) *</td>
</tr>
<tr>
<td>P16 (Backward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(28.5±4.0)</td>
<td>(23.2±2.9)</td>
<td>(6.3±1.8)</td>
<td>(22.9±2.8)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>1.08 (21.6±4.3)</td>
<td>1.31 (30.4±4.0) *</td>
<td>0.25 (1.5±0.7) *</td>
<td>0.24 (5.5±3.3) *</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Right</td>
<td>1.09 (32.8±4.6)</td>
<td>0.84 (14.9±2.2) *</td>
<td>2.78 (17.5±4.6)</td>
<td>1.88 (42.6±4.1) *</td>
</tr>
<tr>
<td>Q2 (Backward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(29.2±2.1)</td>
<td>(35.8±2.9)</td>
<td>(3.4±1.0)</td>
<td>(18.7±2.6)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>1.01 (31.7±2.2)</td>
<td>1.19 (30.7±2.2) *</td>
<td>0.32 (1.1±0.3) *</td>
<td>0.21 (3.9±1.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>1.12 (32.8±2.3) *</td>
<td>0.96 (24.5±1.4)</td>
<td>2.41 (8.2±1.2)</td>
<td>1.78 (33.0±1.9)</td>
</tr>
<tr>
<td>S2 (Backward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(28.5±1.3)</td>
<td>(26.9±1.6)</td>
<td>(11.2±2.2)</td>
<td>(20.3±2.6)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>0.99 (37.0±1.6)</td>
<td>1.13 (20.4±2.1) *</td>
<td>0.67 (7.5±1.1)</td>
<td>0.61 (17.4±1.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>0.89 (30.0±4.2)</td>
<td>0.57 (15.3±2.1) *</td>
<td>1.35 (15.2±2.9)</td>
<td>1.37 (35.6±2.0)</td>
</tr>
<tr>
<td>P11 (Forward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(33.9±2.6)</td>
<td>(31.5±3.1)</td>
<td>(1.4±0.8)</td>
<td>(20.7±3.3)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>0.61 (27.0±1.1) *</td>
<td>0.0 (27.0±1.1)</td>
<td>0.0 (1.0±0.1)</td>
<td>0.0 (4.0±1.0) *</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>1.14 (37.0±2.3)</td>
<td>0.94 (30.5±0.7)</td>
<td>9.77 (17.8±2.0)</td>
<td>1.52 (30.5±1.9)</td>
</tr>
<tr>
<td>P12 (Forward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(31.5±3.4)</td>
<td>(26.3±2.2)</td>
<td>(5.5±2.9)</td>
<td>(35.3±2.7)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>0.86 (26.7±0.7)</td>
<td>1.01 (26.5±0.7) *</td>
<td>0.06 (0.5±0.2) *</td>
<td>0.34 (12.6±7.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>1.25 (40.0±3.4) *</td>
<td>0.69 (18.2±1.4) *</td>
<td>3.08 (21.8±3.7)</td>
<td>1.41 (49.0±3.4)</td>
</tr>
<tr>
<td>P14 (Forward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(36.7±2.3)</td>
<td>(31.1±3.3)</td>
<td>(7.1±4.5)</td>
<td>(32.9±3.3)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>0.75 (28.9±5.4)</td>
<td>0.92 (28.5±3.1)</td>
<td>0.05 (0.3±0.3)</td>
<td>0.15 (4.4±3.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>1.19 (42.3±2.4)</td>
<td>0.67 (20.8±2.6)</td>
<td>3.30 (21.4±3.2)</td>
<td>1.53 (60.2±2.9)</td>
</tr>
<tr>
<td>Q4 (Forward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(28.5±1.5)</td>
<td>(29.3±1.3)</td>
<td>(2.2±0.8)</td>
<td>(35.9±2.8)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>0.95 (27.0±0.9)</td>
<td>0.96 (26.8±0.8)</td>
<td>0.08 (1.2±0.9)</td>
<td>0.62 (34.5±1.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>1.13 (22.2±1.4)</td>
<td>1.00 (27.0±1.1)</td>
<td>2.01 (4.3±0.8)</td>
<td>1.32 (31.5±2.0)</td>
</tr>
<tr>
<td>S5 (Forward)</td>
<td>PreTrans</td>
<td>Center</td>
<td>(33.0±1.5)</td>
<td>(23.0±2.2)</td>
<td>(6.1±3.1)</td>
<td>(43.4±1.8)</td>
</tr>
<tr>
<td></td>
<td>PostTrans</td>
<td>Left</td>
<td>0.84 (27.8±1.3)</td>
<td>1.11 (26.4±2.8)</td>
<td>0.15 (13.4±0.8)</td>
<td>0.47 (27.3±2.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>1.07 (35.5±1.7)</td>
<td>0.89 (16.4±2.5)</td>
<td>2.11 (19.1±2.5)</td>
<td>1.4 (60.7±2.4)</td>
</tr>
</tbody>
</table>
## Table 3.2: Gaze Adaptation Trial Constants

<table>
<thead>
<tr>
<th>Backward Experiments</th>
<th>Trial Constant</th>
<th>R²</th>
<th>Forward Experiments</th>
<th>Trial Constant</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>63.3</td>
<td>0.98</td>
<td>P6</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>P2</td>
<td>277.8</td>
<td>0.88</td>
<td>P6</td>
<td>200</td>
<td>0.88</td>
</tr>
<tr>
<td>P3</td>
<td>502.2</td>
<td>0.98</td>
<td>P9</td>
<td>64.1</td>
<td>0.96</td>
</tr>
<tr>
<td>P4</td>
<td>153.8</td>
<td>0.99</td>
<td>P11</td>
<td>80.9</td>
<td>0.98</td>
</tr>
<tr>
<td>P7</td>
<td>25</td>
<td>0.97</td>
<td>P12</td>
<td>333.3</td>
<td>0.97</td>
</tr>
<tr>
<td>P8</td>
<td>76.9</td>
<td>0.99</td>
<td>P14</td>
<td>114.9</td>
<td>0.97</td>
</tr>
<tr>
<td>P10</td>
<td>70.4</td>
<td>0.99</td>
<td>Q3</td>
<td>217.4</td>
<td>0.98</td>
</tr>
<tr>
<td>P13</td>
<td>79.4</td>
<td>0.99</td>
<td>Q4</td>
<td>322.6</td>
<td>0.99</td>
</tr>
<tr>
<td>P15</td>
<td>83.6</td>
<td>0.98</td>
<td>S2</td>
<td>196.1</td>
<td>0.98</td>
</tr>
<tr>
<td>P16</td>
<td>28.8</td>
<td>0.98</td>
<td>S5</td>
<td>526.3</td>
<td>0.99</td>
</tr>
<tr>
<td>Q1</td>
<td>47.4</td>
<td>0.99</td>
<td>S7</td>
<td>303</td>
<td>0.98</td>
</tr>
<tr>
<td>Q2</td>
<td>53.7</td>
<td>0.99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q5</td>
<td>62.6</td>
<td>0.99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1</td>
<td>500</td>
<td>0.99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S3</td>
<td>125</td>
<td>0.99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S6</td>
<td>100</td>
<td>0.99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S8</td>
<td>169.5</td>
<td>0.99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>115.7 ± 117.0</td>
<td>0.99 ± 0.006</td>
<td>Mean ± SD</td>
<td>236.9 ± 139.1</td>
<td>0.98 ± 0.009</td>
</tr>
<tr>
<td>Experiment</td>
<td>Δ Gaze Amp (Adapt-Pre)</td>
<td>Δ Gaze Amp (Probe-Pre)</td>
<td>Δ Gaze Amp (PostProbe-Pre)</td>
<td>Rate</td>
<td>R²</td>
</tr>
<tr>
<td>------------</td>
<td>----------------------</td>
<td>-----------------------</td>
<td>---------------------------</td>
<td>------</td>
<td>----</td>
</tr>
<tr>
<td><strong>Backward Adaptation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR-P1</td>
<td>-16.6 ± 1.8</td>
<td>-15.9 ± 2.4</td>
<td>-15.7 ± 2.0</td>
<td>322.6</td>
<td>0.99</td>
</tr>
<tr>
<td>HR-P4</td>
<td>-12.6 ± 1.5</td>
<td>-12.3 ± 2.2</td>
<td>-12.0 ± 1.7</td>
<td>161.3</td>
<td>0.99</td>
</tr>
<tr>
<td>HR-Q2</td>
<td>-16.4 ± 2.0</td>
<td>-17.4 ± 2.2</td>
<td>-15.5 ± 3.1</td>
<td>217.4</td>
<td>0.99</td>
</tr>
<tr>
<td>HR-Q4</td>
<td>-17.7 ± 2.4</td>
<td>-16.6 ± 2.0</td>
<td>-15.1 ± 1.8</td>
<td>133.3</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>Mean (±SD)</strong></td>
<td>-15.8 ± 2.2</td>
<td>-15.6 ± 2.3</td>
<td>-14.6 ± 1.7</td>
<td>208.7 ± 83.6</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>Forward Adaptation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR-P2</td>
<td>6.3 ± 1.4</td>
<td>5.9 ± 1.7</td>
<td>5.8 ± 1.8</td>
<td>833.3</td>
<td>0.99</td>
</tr>
<tr>
<td>HR-P3</td>
<td>7.2 ± 1.4</td>
<td>6.6 ± 1.2</td>
<td>5.6 ± 1.2</td>
<td>370.4</td>
<td>0.99</td>
</tr>
<tr>
<td>HR-Q1</td>
<td>8.9 ± 2.5</td>
<td>8.6 ± 1.3</td>
<td>8.5 ± 1.6</td>
<td>344.8</td>
<td>0.99</td>
</tr>
<tr>
<td>HR-Q3</td>
<td>7.1 ± 1.8</td>
<td>5.8 ± 3.1</td>
<td>5.8 ± 1.6</td>
<td>140.8</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>Mean (±SD)</strong></td>
<td>7.3 ± 1.1</td>
<td>6.7 ± 1.3</td>
<td>6.4 ± 1.4</td>
<td>422.3 ± 292.6</td>
<td>0.99</td>
</tr>
</tbody>
</table>
Table 3.4. Changes to Gaze, Saccade, Head Contribution, and Total Head Amplitude during Head-Restrained to Head-Unrestrained Transfer Experiments

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Eye Position</th>
<th>Transfer Ratio</th>
<th>Gaze Ratio (Δamp)</th>
<th>Eye Ratio (Δamp)</th>
<th>Head Cont Ratio (Δamp)</th>
<th>Total Head Ratio (Δamp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA19AUG08</td>
<td>Left Center</td>
<td>0.77</td>
<td>0.76 (-11.6)*</td>
<td>0.83 (-5.8)*</td>
<td>0.34 (-5.8)*</td>
<td>0.55 (-11.6)*</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>0.76</td>
<td>0.78 (-10.9)*</td>
<td>0.87 (-4.1)*</td>
<td>0.34 (-6.8)*</td>
<td>0.60 (-6.8)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.88</td>
<td>0.82 (-9.7)*</td>
<td>0.92 (-1.8)*</td>
<td>0.75 (-8.1)*</td>
<td>0.84 (-10.0)*</td>
</tr>
<tr>
<td>PA29AUG08</td>
<td>Left Center</td>
<td>0.57</td>
<td>0.85 (-7.3)*</td>
<td>0.92 (-4.8)*</td>
<td>0.72 (-4.8)*</td>
<td>0.92 (-7.3)*</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>0.55</td>
<td>0.89 (-7.1)*</td>
<td>0.93 (-2.5)*</td>
<td>0.72 (-4.8)*</td>
<td>0.92 (-8.6)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.56</td>
<td>0.91 (-4.9)*</td>
<td>0.95 (-4.5)*</td>
<td>0.77 (-6.0)*</td>
<td>0.90 (-6.0)*</td>
</tr>
<tr>
<td>PA29AUG09</td>
<td>Left Center</td>
<td>0.68</td>
<td>0.81 (-8.8)*</td>
<td>0.84 (-6.5)*</td>
<td>0.57 (-2.3)*</td>
<td>0.87 (-6.5)*</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>0.57</td>
<td>0.85 (-7.5)*</td>
<td>0.90 (-3.4)*</td>
<td>0.72 (-4.5)*</td>
<td>0.77 (-6.0)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.57</td>
<td>0.86 (-7.5)*</td>
<td>0.88 (-3.2)*</td>
<td>0.84 (-4.5)*</td>
<td>0.61 (-7.3)*</td>
</tr>
<tr>
<td>PA02SEP06</td>
<td>Left Center</td>
<td>0.57</td>
<td>0.85 (-7.0)*</td>
<td>0.87 (-5.4)*</td>
<td>0.65 (-1.6)*</td>
<td>0.67 (-5.8)*</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>0.37</td>
<td>0.91 (-4.4)*</td>
<td>0.50 (-3.4)*</td>
<td>0.93 (-1.9)</td>
<td>0.87 (-5.6)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.48</td>
<td>0.91 (-5.7)*</td>
<td>0.60 (-2.9)*</td>
<td>0.90 (-2.9)</td>
<td>0.67 (-7.4)*</td>
</tr>
</tbody>
</table>

Transfer Ratio = \( \frac{\text{Head-Unrestrained Gaze Amp}}{\text{Head-Restrained Gaze Amp}} \)

Head-unrestrained Comparisons (pre vs. post probes; average of all gaze shifts during these epochs)

- Gaze Ratio = \( \frac{\text{Post-Adapt Gaze Amp}}{\text{Pre-Adapt Gaze Amp}} \)
- Eye Ratio = \( \frac{\text{Post-Adapt Eye Amp}}{\text{Pre-Adapt Eye Amp}} \)
- Head Cont Ratio = \( \frac{\text{Post-Adapt Head Contribution Amp}}{\text{Pre-Adapt Head Contribution Amp}} \)
- Total Head Ratio = \( \frac{\text{Post-Adapt Total Head Amp}}{\text{Pre-Adapt Total Head Amp}} \)

* indicates significantly different pre-versus post-adaptation amplitudes (two-tailed t-test)
Chapter 4:
Superior Colliculus Stimulation and Conclusion

4.1 Introduction

Maintaining the accuracy and precision of gaze shifts in response to dynamic internal and external environmental changes is necessary for the efficient extraction of visual information from the surrounding environment. The adaptive control of gaze shifts has been investigated primarily by introducing visual errors following gaze shifts (McLaughlin, 1967; for review see Hopp & Fuchs, 2004). In the two previous chapters I have shown that: 1) head-unrestrained primates alter gaze amplitude in response to large, residual visual errors (>20°); 2) gaze amplitude changes are the result of alterations to both eye and head movement amplitudes; 3) modifications to eye and head movements are dependent upon the position of the eyes at gaze onset; and 4) changes to gaze amplitude at one initial eye position transferred to gaze shifts initiated from other eye positions. These results support a hypothesis that states that a gaze command is modified during head-unrestrained adaptation using the McLaughlin task, not individual eye or head related commands.

As reviewed in the Introduction (Chapter 1), it is clear that the superior colliculus is involved in the generation of gaze movements;
however, previous attempts to describe the contribution of this structure to gaze adaptation using microstimulation (Meilis & vanGisbergen, 1996; Edelman & Goldberg, 2000) and single unit recording (Frens & van Opstal, 1997; Takeichi et al, 2007) in head-restrained subjects have produced ambiguous results. The experiment described below was designed to test the hypothesis that a gaze command initiated by microstimulation in the deeper layers of the SC (Freedman et al, 1996) can be modified by introducing a visual error after the elicited movement in a head-unrestrained monkey.

4.2 Methods

Data was collected from a female rhesus monkey (P) weighing 5.7 kg. A scleral coil was implanted for monitoring gaze position (Judge et al. 1980) and a small head-restraint device was secured to the skull during an aseptic surgery. In a separate surgery, after Monkey P was trained to orient the line of sight to visual targets as described in chapter 3, a stainless steel cylinder which served as the receptacle for a hydraulic microdrive (Kopf) was secured to the skull. The cylinder was placed above a 15mm diameter craniotomy, centered on the midline at stereotaxic anterior-posterior position zero. All surgical and experimental procedures were approved by the University of Rochester
Animal Care and Use Committee, and are in accordance with the National Institutes of Health Guide for the Care and Use of Animals.

During each experimental session, a lightweight cam-lock device containing a coil similar to that implanted in the eye and 3 laser diodes (red: 650nm) were secured to the head. The center laser was aligned with the mid-sagittal plane of the subject, while the others were directed ~18° to the left or right of center. Each trial began with the presentation of a central target (T₀). The monkey was required to fixate T₀ while aligning the head-mounted laser spot at the same location (Fig. 4.1). When the central head-mounted laser was illuminated this served as a signal to align the eyes and head at the initial fixation target. When either the left-pointing or right-pointing head-mounted laser was lit, alignment of the head-mounted laser with the target (within a 4° computer defined window) required a rotation of the head (to the right or the left) while the direction of gaze was maintained. As a result, the positions of the eyes in the orbits at the beginning of each gaze shift varied as a function of which head-mounted laser was turned on. Fixation of T₀ and alignment of the head-mounted laser had to be maintained for a “fixation” interval that varied from 250 to 750ms (100ms increments).
Trial Types

During “delay trials”, at the end of the fixation interval an additional target was illuminated (4.1A). Head-alignment and fixation of the $T_0$ target had to be maintained during an additional “delay period” lasting between 250 and 750ms (50ms increments). At the end of the delay, the head-mounted laser and $T_0$ were turned off, cuing the subject to make a gaze shift to the still lit target. After the movement was completed, reward was delivered if the subject maintained fixation of the new location for 500ms within a computer defined window (5-7°) centered on the target location.

“Probe Trials” (4.1B) were identical to delayed gaze shift trials except that $T_1$ was extinguished and never re-illuminated after gaze position left the computer defined window surrounding $T_0$ (“position criterion”). Subjects were rewarded for maintaining gaze position within the computer defined window (5-7°) centered on the target location for 500ms.

During both “gap-stim” and “stim-adaptation” trials, stimulation train onset occurred 50ms after the simultaneous offset of $T_0$ and the head laser. During gap-stim trials, an eccentric target ($T_1$) was illuminated at a random location 1000ms after stimulation train offset. Subjects were rewarded for orienting towards and fixating this target for 500ms. During stim-adaptation trials, a peripheral target ($T_2$) was
illuminated after gaze position exited a computer defined window surrounding $T_0$. $T_2$ remained illuminated for the remainder of the trial and was at the same position with respect to the initial fixation point on every stim-adaptation trial. Subjects were rewarded for maintaining gaze position within a computer defined window centered between the stimulation endpoint determined in the pre-adaptation phase (determined online by the experimenter) and $T_2$ and whose diameter extended 2-3° beyond the stimulation endpoint produced during gap trials and $T_2$.

$T_1$ locations used during delayed, probe, and gap-stim trials were selected from a set of potential targets ranging from $-50^\circ$ to $50^\circ$. Typically, during any particular session 6-10 target locations were used, and this target set included the $T_2$ target used during “adaptation trials” in the same session and a $T_1$ at the approximate stimulation gaze endpoint location.

Experimental sessions were carried out according to the following pattern. Delayed gaze shift, probe, and gap-stim were randomly interleaved during the pre-adaptation epoch. After 175-250 pre-adaptation trials, stim-adaptation trials began and were interleaved with probe trials. Probe trials made up approximately 30% of trials presented in the adaptation epoch. Stim-adaptation (and probe) trials were then presented for 500-800 trials. At the end of this adaptation
epoch, only probe and gap-stim trials were presented. Recall that there was no visual feedback during probe trials and that the $T_2$ was presented at a random location, 1000ms after stimulation offset. These characteristics should retard or completely prevent recovery of adaptation during the post-adaptation epoch (Wallman & Fuchs, 1998).

**Electrical Stimulation**

Electrical stimulation was delivered using a Grass S88 stimulator and stimulus isolation unit (GrassPSIU6). After encountering visual activity in the superficial layers of the superior colliculus (SC), we advanced an electrode slowly while monitoring multiunit activity in the delayed gaze shift task. The electrode tip passed through the superficial layers to a depth $\geq 750\mu m$ (range: $750\mu m - 1750 \mu m$) beyond the location at which we first encountered visual activity to a location where saccade related discharge dominated the temporally separate visual response. Stimulation threshold was defined as the current that elicited gaze shifts on $>75\%$ of stimulation trains with duration and frequency equal to 200ms and 500Hz respectively. Using 1.5x threshold current, duration was increased to a length just shorter than that which elicited a staircase of gaze shifts. Current level (range: 20 to 50µA), duration (range: 150 to 250 ms) and frequency (500Hz) of the stimulation train were fixed within a particular experimental session.
4.3 Preliminary Results and Discussion

Figure 4.2 plots gaze (A), eye (B), and head-contribution (C) data from an example forward adaptation experiment (PA07AUG08). In this experiment, the average evoked primary leftward gaze, eye, and head contribution amplitudes during gap-stim trials in the pre-adaptation epoch were $-25.1 \pm 1.2^\circ$, $-24.8 \pm 1.2^\circ$, and $-0.3 \pm 0.1^\circ$ ($n = 28$) respectively. After ~175 pre-adaptation trials, stim-adaptation trials were introduced. Gaze shift amplitude gradually increased to $-31.7 \pm 1.1^\circ$ (average of last 15 stim-adaptation trials) by the end of the stim-adaptation epoch. The change in gaze amplitude between these epochs was the result of a significant change in eye amplitude ($-24.8^\circ \rightarrow -31.2^\circ$; $p < 0.05$, two-tailed, t-test), whereas head-contribution was unchanged ($-0.3^\circ \rightarrow -0.4^\circ$; $p = 0.13$, two-tailed, t-test). Gaze ($-29.6 \pm 1.1^\circ$) and eye ($-29.1 \pm 1.1^\circ$) amplitude elicited during gap-stim trials ($n = 12$) in the post-probe epoch were also significantly larger that those evoked in the pre-adaptation epoch.

In order to test the hypothesis that a gaze command is being altered in the experiment described above, visual errors must be presented after stimulation evoked gaze shifts that include a large head contribution from at least one of the three initial eye positions. Each of the preliminary stimulation sites ($n = 4$) were at locations too
rostral in the collicular motor map to produce gaze shifts with significant head contributions from the orbital eye positions used in this study. Future experiments must include large gaze shifts evoked from more caudal sites in the collicular motor map or gaze shifts initiated from more eccentric eye positions.

4.3.1 Alternative Loci for adaptation

The following text discusses alternative neural substrates underlying the adaptive control of horizontal, head-unrestrained primate gaze shifts. This is by no means an exhaustive list of structures that may partake in this process. Rather, each of the structures discussed below was chosen because clear predictions concerning their role in gaze adaptation may be generated based on data accumulated from anatomical, behavioral, and physiological experiments including those data generated in chapters 2 and 3 of the current thesis.

4.3.2 Brainstem Control of Primate Eye and Head Movements

If the neural activity in the deep layers of the superior colliculus (SC) codes for gaze shifts to $T_1$ throughout the McLaughlin task (see introduction), any change in gaze amplitude must be the result of changes to motor commands closer to the motor neurons found in the brainstem cranial nerve nuclei and cervical spinal cord associated with
the eyes or head. In this case, an adaptive mechanism would be in place to modulate pre-motor neuron activity in brainstem nuclei where gaze, eye, or head command signals are located.

A great deal is known about the brainstem regions involved in the generation of horizontal saccadic eye movements when the head does not move. Several types of neurons that show horizontal saccade-related activity are found in the paramedian zone of the pontine reticular formation (PPRF) and medulla (Moschovakis et al., 1996; Scudder et al., 2002). Long-lead burst neurons (LLBNs), excitatory burst neurons (EBNs), and inhibitory burst neurons (IBNs) generate high-frequency bursts of activity before ipsilateral saccades (Keller, 1974; Hepp & Henn, 1983; Scudder et al., 1988). The bursts of LLBNs are not as tightly coupled to saccade onset as the burst of EBNs and IBNs. EBNs make excitatory, monosynaptic connections (Strassman et al., 1986) with neurons in the ipsilateral abducens (VI) and provide the main source of excitatory drive for the saccade-related pulse of motor neuron activity that is used to overcome the viscosity of the oculomotor plant and drive the eye to a new orbital location. In contrast, IBNs make monosynaptic, inhibitory connections with motor neurons (which innervate antagonistic muscles) in the contralateral brainstem (cat: Shinoda et al., 2008). The amplitude, duration and velocity of saccades are correlated with the number of spikes generated, burst duration and peak firing rate
of the burst of activity, respectively for both EBNs (Keller, 1983; Hepp & Henn, 1983) and IBNs (Scudder et al, 1988). Therefore, an “eye-only” adaptive control mechanism could adjust eye amplitude during gaze adaptation simply by altering the burst metrics of EBNs and/or IBNs. There has been some recent evidence that the relationship between the number of spikes and saccade amplitude in IBNs is modulated during head-restrained saccadic adaptation (Kojima et al, 2008).

Comparatively little is known about the regions of the brainstem involved in the generation of horizontal head movements. Stimulation in the rostral portion of nucleus reticularis gigantocellularis (NRG) produces horizontal head movements ipsilateral to the site of stimulation (Quessy and Freedman, 2004, Cowie & Robinson, 1994). Freedman and Quessy (2004) have shown that stimulation frequency and duration can influence the metrics (latency, amplitude, peak velocity, and duration) of evoked head movements. Therefore, a “head-only” adaptive control mechanism might control head amplitude by modulating the rate, duration, and/or onset latency of neuronal activity in the NRG. Control of any of these variables could influence the head contribution to a gaze shift and thereby alter gaze amplitude (Freedman and Quessy, 2004).

A hypothesis stating that an adaptive controller modifies the gaze command upstream of the locus where it is parsed into separate eye
and head commands would predict modifications to the burst metrics in both the oculomotor and cephalomotor brainstem. This hypothesis would be supported by showing that any changes in burst metrics that occur during adaptation are also dependent upon orbital eye position at gaze onset. The result suggests that a common input to these brainstem regions may have been modified. The oculo- and cephalomotor brainstem share a common input from the midline cerebellum.

4.3.3 Cerebellar involvement in Primate Gaze Control

The medial deep cerebellar nuclei (the fastigial nuclei) are intimately connected to a variety of brainstem structures involved in the generation of eye and/or head movements (Batton et al, 1977, Noda et al, 1990; Homma et al, 1995; Yamada and Noda, 1987). The caudal portion of each fastigial nucleus (cFN) receives disynaptic, excitatory input from the contralateral superior colliculus (SC) via mossy fiber projections originating in the nucleus reticularis tegmenti pontis (NRTP). The purkinje cells overlying the cFN (lobules VI-VII) also receive motor commands from the SC relayed through NRTP (via granule cells). Outputs from the cFN cross the midline and contact cells in the pontine and medulary reticular formation involved in the generation of saccades (e.g. NRTP, excitatory and inhibitory burst neurons in the PPRF). The results of microstimulation (Noda et al, 1991), inactivation (Goffart et al,
2004; Quinet & Goffart, 2005, 2007; Robinson et al, 1993; Vilis & Hore, 1981), and single unit recordings (Fuchs et al, 1993; Ohtsuka & Noda, 1990, 1991, 1992) in the cFN of head restrained and head-unrestrained monkeys support a hypotheses stating that the cFN is involved in the control of saccadic eye movements relative to the head.

The rostral portion of the fastigial nucleus (rFN) also receives inputs from brain regions involved in the control of eye and/or head movements. The rFN receives input from the vestibular nuclei, anterior vermis (lobules I-V), and nodulus (lobule X). However, in contrast to the cFN, the rFN projects primarily to nucleus reticularis gigantocellularis (NRG) and other reticular formation regions known to be involved in the control of head movements (see Isa and Sasaki, 2002 for review). A great deal of attention has been paid to the rFN's participation in the control of reflexive eye movements (Bryan and Angelaki, 2009; Büttner et al. 1991; Gardner and Fuchs 1975; Shaikh 2004; Shaikh et al. 2005; Siebold et al. 1997, 1999; Zhou et al. 2001); however, the rFN's role in the control of head (or gaze) movements during voluntary gaze shifts remains elusive.

In general, lesions to the cerebellum result in an impaired ability to adjust motor output given changes in sensory input (Thach et al, 1992; Barlow, 2002). In the context of gaze adaptation, lesions to either the cFN or the oculomotor vermis (lobules VI-VII) impair the ability of
subjects to correct for persistent visual errors after saccades (Optican & Robinson, 1980; Robinson et al, 2002; Takagi et al, 1998). These results, combined with neuronal recording studies which note modifications to cFN burst metrics correlated with a change in saccade amplitude (e.g. Scudder & McGee, 2003), suggest that the midline cerebellum participates in saccade amplitude adaptation. The physiological and anatomical results summarized above place the rFN and cFN in an optimal position to influence head and eye movements either independently ("eye-only" or "head-only" change) or in a coordinated fashion to alter gaze amplitude during head-unrestrained gaze adaptation. Transient inactivation experiments could be used to test the hypothesis that an intact cFN and/or rFN is required for head-unrestrained gaze adaptation.
References:


Figure 4.1 A-D: Schematic diagrams of trial types used. In each panel, gaze position is represented by a thin black line and is plotted as a function of time. Below this trace, targets are represented by thick bars indicating when each target was illuminated and extinguished. Stimulation onset and offset are represented similarly. In each case, trials began with the illumination of a head-mounted laser (light gray bar) followed by presentation of T₀. If behavioral contingencies were satisfied, either a second target (T₁) was illuminated (A, B) or a stimulation train was delivered to the deep layers of the superior colliculus (C, D). A: The T₁ target remained illuminated for the duration of the “delayed” trials. B: During “probe” trials, the T₁ target was extinguished when the line of sight moved beyond a computer defined window (“position criterion”) surrounding T₀. C: During “gap-stim” trials a stimulation train was delivered 50ms after the head laser and T₀ were extinguished. A peripheral target (T₁) was illuminated 1000ms after stimulation train offset (not shown); D: “Stim-adaptation” trials were similar to gap-stim trials except that a target at location T₂ was illuminated 20ms after the position criterion was satisfied. See text for further details.
Figure 4.2 Forward Adaptation Experiment. Gaze (A), saccade (B), head contribution (C) the primary gaze shifts made during pre-adaptation, adaptation, post-probe segments of experiment PA07AUG08. Black symbols = pre-adapt gap-stim trials; gray squares = stim-adaptation trials; open symbols = post-adaptation gap-stim trials. Stimulation parameters: current = 20µA; frequency = 500 Hz; duration = 150ms. See text for further details.
Chapter 5: General Synthesis

While writing the previous chapters I have, almost habitually, been drinking coffee from a cup placed to the right of my computer monitor. Whenever my cravings for caffeine became intolerable I looked at this cup, reached for it, picked up the cup, and brought it to my mouth. This series sensorimotor events occurred hundreds of times throughout the writing of this document with the same, optimal result; a sip of coffee in my mouth, not on my shirt. But what happens if the sensory stimulus, in this case, the location of the coffee cup on my retina, no longer represents the veridical location of the coffee cup on my desk? Will I ever be able to plan an accurate movement with this faulty information? Thomas Thach and colleagues asked this question in a slightly different context (tennis ball throwing), but their results are relevant for this discussion. In their experiment, human subjects were asked to throw tennis balls as accurately as possible towards a target on the wall. Most subjects performed this task quite well. However, after subjects were asked to don prisms that shifted the perceived target location to the right of its actual wall location they initially threw the tennis balls towards the perceived visual location; i.e. to the right of the actual location of the target on the wall. Subjects received visual feedback that they had committed this error. Over the next several throws subjects gradually regained their ability to throw accurately to
the target. In short, they were able to reduce their throwing errors by adjusting their motor output (throwing movement) in response to persistent changes in sensory input (visual image shift caused by wearing prisms). This behavior has been observed in a variety of motor modalities and has been dubbed “sensorimotor adaptation”.

Although sensorimotor adaptation has been studied in primates making reaching or throwing movements, the complexity of this “simple” behavior has made it difficult to identify which sensory signals or motor commands are altered during adaptation. After all, these movements involve multiple effectors (eyes, head, arm), tens of muscle groups acting across multiple joints, and multiple sensory feedback mechanisms (vision, position sense, etc.) that could be used to inform the nervous system that it has committed an error. Recognizing these facts, I chose to investigate the mechanisms underlying sensorimotor adaptation in a slightly less complicated motor event common to both reaching and throwing behaviors; the movement the eyes and head to change the line of sight (gaze) in order to capture the visual target of interest.

Historically, most studies of gaze adaptation describe changes in the amplitude of rapid eye movements (saccades) when the head does not move. In the late 1960’s Jon McLaughlin developed a task that surreptitiously introduces small visual errors (<5°) at the end of
saccades. Similar to the reaching and throwing examples described above, primates can alter the size of saccades by gradually reducing these persistent visual errors. For the last 40+ years the “McLaughlin Task” has been used to study behavioral characteristics and neurophysiological mechanisms underlying saccade amplitude adaptation. However, it was not clear at the conception of the current thesis that primates could compensate for large (>20°), persistent visual errors during rapid gaze shifts when the head was free to move, a more ethologically “natural” behavior. Furthermore, it was not clear which motor commands (eye, head, or gaze displacement) would be altered during head-unrestrained gaze adaptation.

The results of my human and monkey behavioral studies (see chapters 2 & 3 for details) are consistent with the hypothesis that a gaze command is modified before it is separated into commands to move the eyes and the head during large amplitude gaze adaptation in the McLaughlin task. Furthermore, the results of the microstimulation study described in chapter 4, as well as unpublished results from mentor’s laboratory (Quessy & Freedman, 2008), are consistent with the hypothesis that this gaze command is not modified at the level of the superior colliculus (see Introduction and chapter 4 for background). Although these results draw the field of systems neuroscience closer to
understanding the signals modified during gaze adaptation there are
many more questions to be addressed:

*Where does the gaze command modified during the McLaughlin Task?*

The results of the current thesis suggest that a gaze command is
modified before it is decomposed into separate eye and head
commands. Although it is known that a gaze command may be issued
from the superior colliculus (see chapter 1 for background), the
brainstem location where this decomposition takes place is unknown at
this time. Locations in the brainstem that receive monosynaptic input
from the superior colliculus and project directly to brainstem regions
known to be involved in generating only eye or head movements are
likely candidates for this decomposition. However, even if the cell type
in the brainstem that is involved in the decomposition of gaze into
separate eye and head motor commands is identified, and modifications
in burst metrics of these cells are strongly correlated with changes in
gaze amplitude during the McLaughlin task, this cell type’s burst
metrics are most likely modulated by other brain regions known to play
a role in sensorimotor adaptation. For example, damage to the
cerebellum results in an inability to correct for visual errors in a variety
of motor modalities (e.g. reaching, eye movements, walking), which
makes this structure a likely candidate for modulating brainstem
structure(s) involved in generating gaze shifts. However, the anatomical and physiological substrates by which the cerebellum would modify a gaze command are not known at this time primarily because so few studies have described cerebellar activity under conditions where eye, head, and gaze commands are dissociable.

Is the modified gaze command used by other motor systems?

It is not immediately obvious that modification of a gaze command during the McLaughlin task would produce changes in the output of other motor systems (e.g. reaching). This question could be easily addressed by looking for transfer of gaze amplitude modifications seen during the McLaughlin task to reaching movements towards the same target location(s). If transfer does occur, it suggests a general signal, which actually may be an internal representation of the external environment, is modified during gaze adaptation. If transfer does not occur, it suggests that the modification of the gaze amplitude in the McLaughlin task is a change unique to the gaze control system and that other motor control systems must have experience about changes in the external world in order to modify their output. These potential outcomes are equally likely given our current understanding of gaze and reaching motor systems.
Are there circumstances under which an eye or head motor command should be modified independently from a gaze command?

There might be circumstances where a modification of either eye or head commands independently would be appropriate. For instance, take the case where the right lateral rectus muscle, which is used to abduct the right eye, is weakened. At the time of initial insult, a subject’s ability to produce accurate movements to targets in their right visual field is impaired; rightward, rapid eye movements produced with the right eye with the will fall short of their intended target. However, with more experience, it has been shown that primates can gradually increase the size of saccades such that the intended visual target will fall on the receptor rich region of the retina (the fovea). It would be interesting to record from gaze related neurons in the brainstem in a subject whose lateral rectus (or an equivalent head muscle) has been damaged. Do the burst metrics of this cell change along with changing saccade amplitude? Is this change in burst metrics similar to that observed during the McLaughlin task? If the burst metrics of this gaze related cell type do not change along with eye amplitude after muscle weakening, this suggests that the gaze command is unaltered prior to its decomposition during this form of adaptation. This result would be consistent with a hypothesis that adjustments are made to only the eye (or head) motor commands in this context.
Is the McLaughlin task really a useful task to study sensorimotor adaptation?

When the head is restrained, the gross behavioral characteristics (magnitude and rate) of saccade amplitude adaptation during the McLaughlin task and muscle weakening are comparable. This observation has prompted most authors to suggest that the neural substrates underlying adaptation in these two contexts to be equivalent. What happens if the neural substrates underlying gaze adaptation during the McLaughlin task and muscle weakening are found to be different? What does this say about the usefulness of the McLaughlin task in exploring the characteristics of gaze adaptation?

In my opinion, a distinction would need to be made between gaze adaptation to bodily changes ("internal"; muscle weakening) and environmental changes ("external"; target jump during the McLaughlin task) in the systems neuroscience lexicon. Even if the stimulus driving adaptation (visual error following the gaze shift) is the same, differences in neural substrates between the two tasks suggest that the adaptive mechanism(s) have knowledge of the cause of the error (external versus internal). Second, the purpose for gaze amplitude changes in response to externally generated visual errors is unknown at this time. The ethological significance of this particular adaptive mechanism may be to take into account the statistics of the external environment when planning movements of the line of sight with the end goal of obtaining
useful environmental information. For example, anticipating the prey movements given particular visual cues. This particular concept needs to be explored in greater detail in future studies of primate gaze adaptation.

References: