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# The characteristics and neuronal substrate of saccadic eye movement plasticity

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**Abstract**

Saccadic eye movements are shifts in the direction of gaze that rapidly and accurately aim the fovea at targets of interest. Saccades are so brief that visual feedback cannot guide them to their targets. Therefore, the saccadic motor command must be accurately specified in advance of the movement and continually modified to compensate for growth, injury, and aging, which otherwise would produce dysmetric saccades. When a persistent dysmetria occurs in subjects with muscle weakness or neural damage or is induced in normal primates by the surreptitious jumping of a target forward or backward as a saccade is made to acquire the target, saccadic amplitude changes to reduce the dysmetria. Adaptation of saccadic amplitude or direction occurs gradually and is retained in the dark, thus representing true motor plasticity. Saccadic adaptation is more rapid in humans than in monkeys, usually is incomplete in both species, and is slower and less robust for amplitude increases than decreases. Adaptation appears to be motor rather than sensory. In humans, adaptation of saccades that would seem to require more sensory-motor processing does not transfer to saccades that seem to require less, suggesting the existence of distributed adaptation loci. In monkeys, however, transfer from more simple to more complex saccades is robust, suggesting a common adaptation site. Neurophysiological data from both species indicate that the oculomotor cerebellum is crucial for saccadic adaptation. This review shows that the precise, voluntary behaviors known as saccadic eye movements provide an alternative to simple reflexes for the study of the neuronal basis of motor learning.


**Contents**



*Abbreviations:* LGN, lateral geniculate nucleus; BG, basal ganglia; NRTP, nucleus reticularis tegmenti pontis; OCM, oculomotor muscles; SC, superior colliculus; FEF, frontal eye field; LIP, lateral interparietal area; V1, primary visual cortex; CFN, caudal fastigial nucleus; OMV, oculomotor vermis; BBG, brainstem burst generator

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## 1. Introduction

In this review, we consider the characteristics and neuronal substrate of an example of motor learning in a voluntary behavior, the saccadic eye movement, which redirects gaze rapidly from one location to another. The saccade is an excellent movement by which to study motor adaptation because it can be manipulated behaviorally, its characteristics have been documented extensively, and its neuronal substrate may be better known than that of any other motor response. Because the saccade remains accurate despite the pressures of growth, injury and aging, the central nervous system must have a mechanism to adjust and maintain the amplitude and/or direction of saccades under changing behavioral conditions. This motor learning is called *saccadic adaptation*.

We divide our consideration of saccadic adaptation into three parts. First, we describe some of the different types of saccade and their possible neuronal substrates. This background information identifies the neuronal circuitry believed to subserve the various types of saccade and thus constrains the possible loci of adaptation. Second, we consider the characteristics of both natural and behavioral saccadic adaptation. Third, we discuss the behavioral and neurophysiological experiments that attempt to localize the site(s) of adaptation within the saccadic control system. Because the accuracy of saccades is most important in foveate animals and the behavioral manipulations that elicit saccades require diligent cooperation on the part of the subject, all of our knowledge to date has come from studies on primates, both humans and monkeys. Where experiments on the two primate species address similar topics, we will discuss them together.

## 2. Types of saccade

Primates use the fast, accurate saccade to look at objects of interest (targets) in their visual environment. Under natural conditions, most targets are stationary and we make a series of *scanning saccades* in rapid succession to peruse them. If a target suddenly appears in the visual field, a *targeting saccade* is made reactively towards it. If a target suddenly begins to move slowly, a *catch-up saccade* brings the target onto the fovea whereupon smooth-pursuit eye movements keep it there. Saccades are also made towards remembered locations (*memory-guided saccades*), and towards interesting sounds (*auditory saccades*).

In order to study the mechanisms of saccade generation, it is necessary to control precisely the location and timing of the target that elicits a saccade. In the laboratory, such control is achieved by instructing subjects, either verbally (human) or through a reward (monkey), to follow visual spots moving on a screen in front of them. By moving the targets in different ways, one can create the conditions necessary to evoke the various types of saccade that occur in real life.

The level of difficulty involved in the production of a particular type of saccade may give some indication of the amount of neural machinery that is involved in its generation. For ease of description, we parse saccades into two

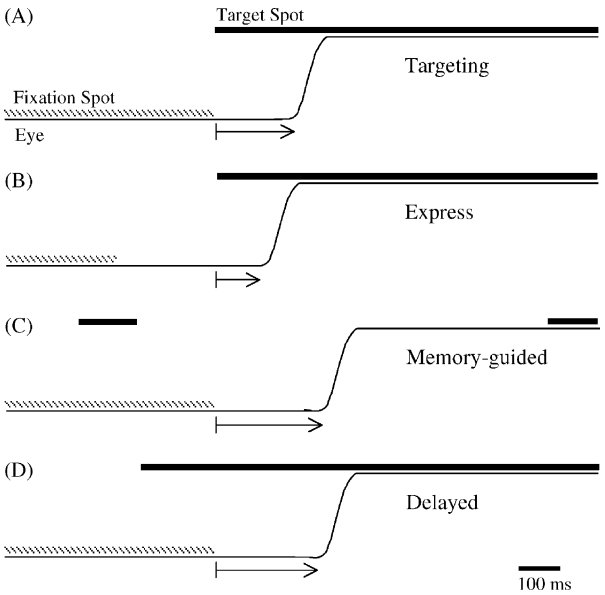


Fig. 1. Relative timing of target and fixation spots to elicit different types of horizontal saccade: (A) targeting; (B) express; (C) memory-guided; (D) delayed. Thin solid line, horizontal eye position; dashed line, location of fixation spot; thick solid line, location of target spot. Upward deflection of eye or target trajectory indicates rightward motion. Arrows denote saccadic latency with tail of arrow indicating the time the subject is instructed to make the saccade.

categories: *reactive* (Deubel, 1995b) and *higher-order*.[1] This categorization will provide a useful framework for our later discussion on the relative adaptation of the different types of saccade within each category. This dichotomy is based on the difficulty of the conditions that elicit the saccade and the saccadic latency, i.e., the time it takes to elicit a saccade in response to the instruction to make a saccade. For example, *targeting saccades* (Fig. 1A), which are considered to be reactive, have latencies of ∼180 ms in humans (Smit et al., 1987). They are elicited by presenting a target at the same time that the fixated target is extinguished and instructing the subject to look at the new target when it appears. These saccades probably involve, at most, a modest amount of cortical processing. Another type of reactive saccade is elicited by briefly extinguishing the fixated target prior to illuminating the peripheral target (Fig. 1B). Saccades elicited in this way can have extremely short latencies with peaks in their latency distribution at 100–135 ms in humans and 70–100 ms in monkeys (Fisher and Boch, 1983; Fischer and Ramsperger, 1984; Fischer et al., 1993). Because of their very short latencies, these *express saccades* are thought to involve minimal, if any, cortical processing (it takes visual signals at least 30–40 ms to leave the retina alone; Lee et al., 1994). In contrast to these two types of saccade that respond essentially reactively to the appearance of a target, the correct execution of other types of saccade requires more "deliberation". One such type of higher-order saccade is a *memory-guided saccade*. Memory-guided saccades are elicited by the brief presentation of a target whose location the subject must remember for some time before making a saccade to it (Fig. 1C). Such responses have latencies of well over 200 ms following the instruction to move. Presumably, additional steps are involved in their generation, e.g., remembering target position and delaying saccade initiation, and they likely involve more extensive cortical processing. Other higher-order saccades include *delayed saccades* (those made after a fixed delay to targets already present, Fig. 1D) and *scanning saccades* (those made sequentially between already-present stationary targets).

[1] Others have called 'reactive' saccades 'reflexive' (Pierrot-Deseilligny et al., 1991) or 'externally-guided' (Erkelens and Hulleman, 1993). Since these saccades do not involve simple reflexes like those found in the somatomotor system, but rather are generated voluntarily, we think 'reactive' is a better descriptor. 'Higher-order' saccades have been called 'volitional' (Deubel, 1995, 1999; Pierrot-Deseilligny et al., 1991) or 'internally-guided' (Erkelens and Hulleman, 1993). Since reactive saccades are also generated voluntarily, we prefer to use 'higher-order' to distinguish these more cognitive types of saccade.

## 3. Saccadic circuitry

Several neural structures and pathways have been implicated in the generation of saccades (Fig. 2; for comprehensive reviews, see Moschovakis et al., 1996; Scudder et al., 2002). The six extraocular muscles of each eye are innervated by motoneurons located in the III, IV, and VI cranial nuclei. To generate a horizontal saccade directed laterally, for example, motoneurons in the VI nucleus discharge a burst of spikes that begins a few milliseconds before the saccade starts and ends a few milliseconds before the saccade ends. To hold the eye in position these neurons discharge at a constant rate that increases with eye eccentricity. The transition of the firing rate from the burst to the final steady rate is gradual (a "slide"). The pulse-slide-step discharge pattern of motoneurons is produced by different premotor neurons in the nearby brainstem. The pulse signal, which seems to reflect eye velocity, comes from burst neurons in the paramedian pontine reticular formation. The step signal originates in neurons of the nucleus prepositus hyperglossi, which may integrate, in the mathematical sense, the burst of the burst neurons. The origin of the slide signal is currently unknown. These various local groups of neurons involved in the generation of the pulse-slide-step discharge pattern have been termed collectively the brainstem burst generator (BBG, Fig. 2).

The burst generator receives input from at least three known sources (Fig. 2): the superior colliculus (SC), the oculomotor cerebellum via its caudal fastigial nucleus (CFN) and the frontal eye field (FEF). The SC, in turn, receives inputs from a variety of cortical and subcortical areas. The FEF projects to the SC both directly and also indirectly through the basal ganglia (BG). Higher-order cortical areas, such as the lateral interparietal area (LIP), project directly to the SC or relay their signals through the frontal lobe. Finally, the primary visual cortex (V1), and even the retina,

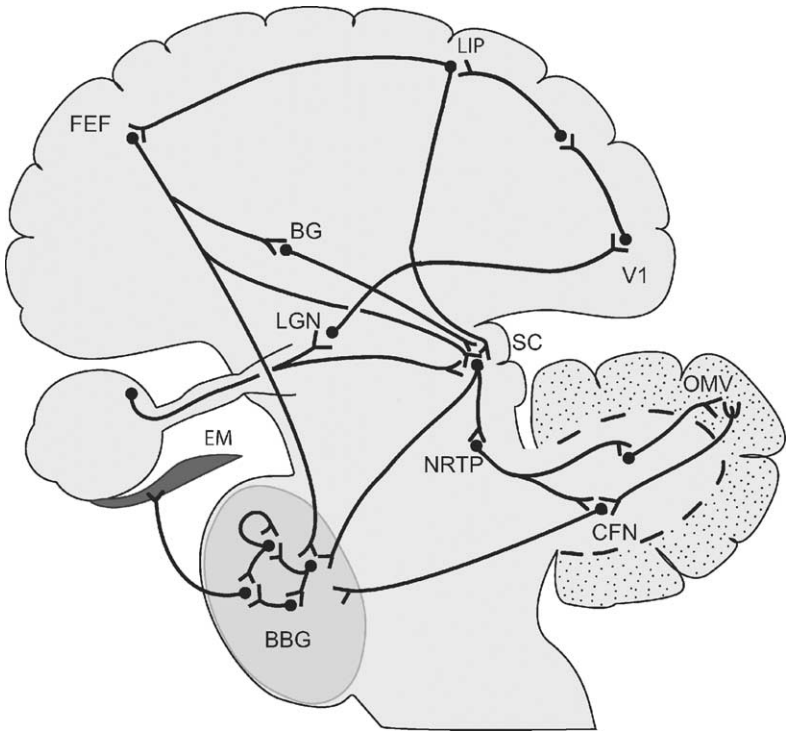


Fig. 2. Highly schematic circuit of the neuronal structures involved in saccade generation. Neuron-like elements are simply meant to indicate the forward flow of information and not actual synaptology; for clarity, reciprocal connections are not included. Visual information regarding target position enters the brain over the optic nerve and is distributed to the lateral geniculate nucleus and superficial layers of the superior colliculus (SC). Visual signals are processed through striate (V1) and extrastriate visual areas to produce descending signals via the frontal eye field (FEF) and lateral intraparietal area (LIP) to the SC. The FEF influences the brainstem burst generator (BBG) directly, indirectly through the SC, and more circuitously through the basal ganglia (BG) and SC. The oculomotor vermis (OMV) of the cerebellum and the caudal fastigial nucleus (CFN) receive strong projections from the nucleus reticularis tegmenti pontis (NRTP) and weaker ones from other pontine and brainstem nuclei (not shown). Both the CFN and intermediate and deep layers of SC provide direct inputs to the BBG, which in turn produces the appropriate contraction of extraocular muscles (EM) to generate a saccade.

can drive different layers of the SC directly. Extrastriate visual cortex projects to the FEF and LIP. The signal in the visual cortex comes largely from the lateral geniculate nucleus (LGN; to V1), which in turn receives a direct input from the retina. Thus, there are several different pathways by which the brainstem saccade generator can be accessed and through which saccade characteristics potentially can be modified on the basis of experience. However, all saccade pathways have the burst generator and early visual areas in common.

Based on the saccadic latency, the degree of difficulty and the results of some neurophysiological experiments, there have been speculations about the structures and pathways involved in generating the different types of saccade. For example, because of their short latencies, express saccades are thought to involve only early visual areas, the SC and the brainstem (Fischer and Weber, 1993). Indeed, monkeys with lesions of the FEF could still make express saccades (Schiller et al., 1987), whereas, after lesions of the SC they could not. However, monkeys with SC lesions could still produce longer-latency targeting saccades (Schiller et al., 1987). Similarly, human patients with lesions in the frontal lobe generate more express saccades than do control subjects, suggesting that the frontal lobe is unnecessary for express saccade performance (Braun et al., 1992). In contrast, evidence from human patients suggests that the frontal lobe *is* necessary for higher-order eye movements such as memory-guided, delayed, and predictive (those that anticipate target movement) saccades (for review, see Pierrot-Deseilligny et al., 1995). In addition, the FEF has been implicated in the control of memory-guided saccades in the monkey (Deng et al., 1985; Dias and Segraves, 1999).

## 4. Saccadic adaptation

The majority of saccadic eye movements are quite accurate to targets that appear within about $\pm 15^{\circ}$ of straight-ahead, and their metrics, i.e., amplitude, duration and peak velocity, are stereotyped (Becker, 1989). In the somatomotor system, movements are slow enough that visual feedback can help guide them if the movement becomes inaccurate. Saccades, however, are extremely brief (in humans a $10^{\circ}$ saccade lasts only about 40 ms; Becker, 1989), so visual feedback cannot be used to guide the saccadic trajectory. Indeed, vision is impaired during a saccade (Brooks and Fuchs, 1975; Riggs et al., 1982 and others). Consequently, in the absence of visual feedback

indicating its accuracy, a saccadic trajectory is thought to be programmed prior to its initiation. Nevertheless, the accuracy of targeting saccades in humans is maintained well beyond the age of 60 years, despite possible weakening of the extraocular muscles or natural neuronal aging in the saccadic circuitry (Warabi et al., 1984; Munoz et al., 1998). Therefore, a mechanism must exist that alters the efficacy of the saccadic command before a movement occurs. We will now address how this saccadic adaptation is induced, what its characteristics are, what experimental permutations affect the adaptation, and whether it is possible to localize the site(s) of the adapting loci in the saccadic pathways.

### 4.1. Conditions that cause adaptation of saccadic amplitude

#### 4.1.1. Natural induction

Naturally occurring adaptation of saccadic amplitude has been observed in both humans and monkeys. It was first observed in a patient with abducens palsy, in which the lateral rectus muscle that rotates the eye laterally had become weakened (Kommerell et al., 1976). During normal binocular viewing when the patient's paretic eye was dominant, the normal eye produced movements that were too big, or hypermetric. Since both eyes are thought to receive the same neural innervation during conjugate (the axes of the eyes, a line from the center of the cornea to the fovea, remain parallel) gaze shifts, the command necessary to bring the weak eye on target caused the good eye to make a saccade that was too large. When the paretic eye was patched, the hypermetric saccades of the normal eye had become normal in size, or normetric, when they were examined between 15 min and 3 days later. This reduction in the saccadic amplitude of the good eye was due to a decrease in the conjugate command to both eyes, which resulted in the saccades of the paretic eye becoming too small, or hypometric. Abel et al. (1978) confirmed this result by patching the good eye of a patient with a third nerve palsy and observing a gradual increase in saccadic amplitude towards normal in the weak eye and an increasing hypermetria of saccades in the good eye. When the patch was switched to cover the paretic eye, saccades of the good eye returned to normal and those of the weak eye again became hypometric.

Similar studies have been performed in monkeys that have undergone a resection of the tendons of the horizontal recti of one eye (Optican and Robinson, 1980; Snow et al., 1985). Again, patching of the weak eye resulted in hypometric saccades in that eye and normetric saccades in the normal eye. Subsequent switching of the patch to cover the normal eye caused a gradual increase in the amplitude of saccades until the weak eye produced normetric movements. Conjugate saccades in the normal eye were then hypermetric. In these experiments, changes in amplitude occurred within the first day of patching.

#### 4.1.2. Behavioral induction

Adaptation of saccadic amplitude also can be induced in normal subjects by shifting the target (an *adaptation step*) during a saccade so the saccade appears to be dysmetric. McLaughlin (1967), the first to use this behavioral paradigm, caused an amplitude reduction by having the adaptation step occur in a direction opposite that of the primary saccade (i.e., a back-step; see Fig. 3A, lower panel). When the eye landed, it had overshot the displaced target, thus making the saccade seem too large. A subsequent corrective saccade in the opposite direction was necessary to get the eye on target. After only a few repetitions of this adaptation paradigm, the amplitude of the initial saccade decreased until the eye eventually reached the displaced target location with a single saccade.

In a variety of permutations, the McLaughlin paradigm has served as the cornerstone for research aimed at understanding saccadic adaptation in both man and monkey. The amplitude of saccades also has been increased by an intrasaccadic target jump in the same direction as the primary saccade (Miller et al., 1981; Deubel et al., 1986; Straube et al., 1997b; Noto et al., 1999; Scudder et al., 1998). In addition, the direction of saccades has been adapted by an intrasaccadic target jump perpendicular to the primary saccade (Deubel, 1987, 1991; Noto et al., 1999). Finally, a slide in post-saccadic eye position has been induced by exponential motion of a full-field stimulus at the end of a saccade (e.g., Optican and Miles, 1985; Deubel, 1991; Kapoula et al., 1987). In, this review, however, we will discuss only adaptation of saccadic amplitude and direction.

Although the McLaughlin behavioral paradigm is the one most widely used to induce saccadic adaptation, amplitude changes have also been produced by the wearing of specialized prisms (Henson, 1978) or anisotropic glasses (Lemij and Collewijn, 1991; Albano and Marrero, 1995; Erkelens et al., 1989; Oohira et al., 1991; Bush et al., 1994; Averbuch-Heller et al., 1999). We will consider such studies only briefly, because it is unclear whether the adaptation produced by such paradigms is the same as that produced by either muscle weakening or the McLaughlin paradigm. Furthermore, these paradigms have not been used in neurophysiological studies of saccadic adaptation.

### 4.2. General properties of saccadic amplitude adaptation

Because the majority of adaptation experiments have been performed using targeting saccades along the horizontal meridian, from now on we use the terms "saccadic adaptation" or "adaptation" alone to refer to adaptation of horizontal targeting saccades, unless otherwise noted.

#### 4.2.1. The course of adaptation

Fig. 3 shows typical courses of changes in saccadic amplitude during behavioral amplitude-reduction experiments for a monkey (Fig. 3A) and a human (Fig. 3B). The shape of the relation between saccadic amplitude and the num-

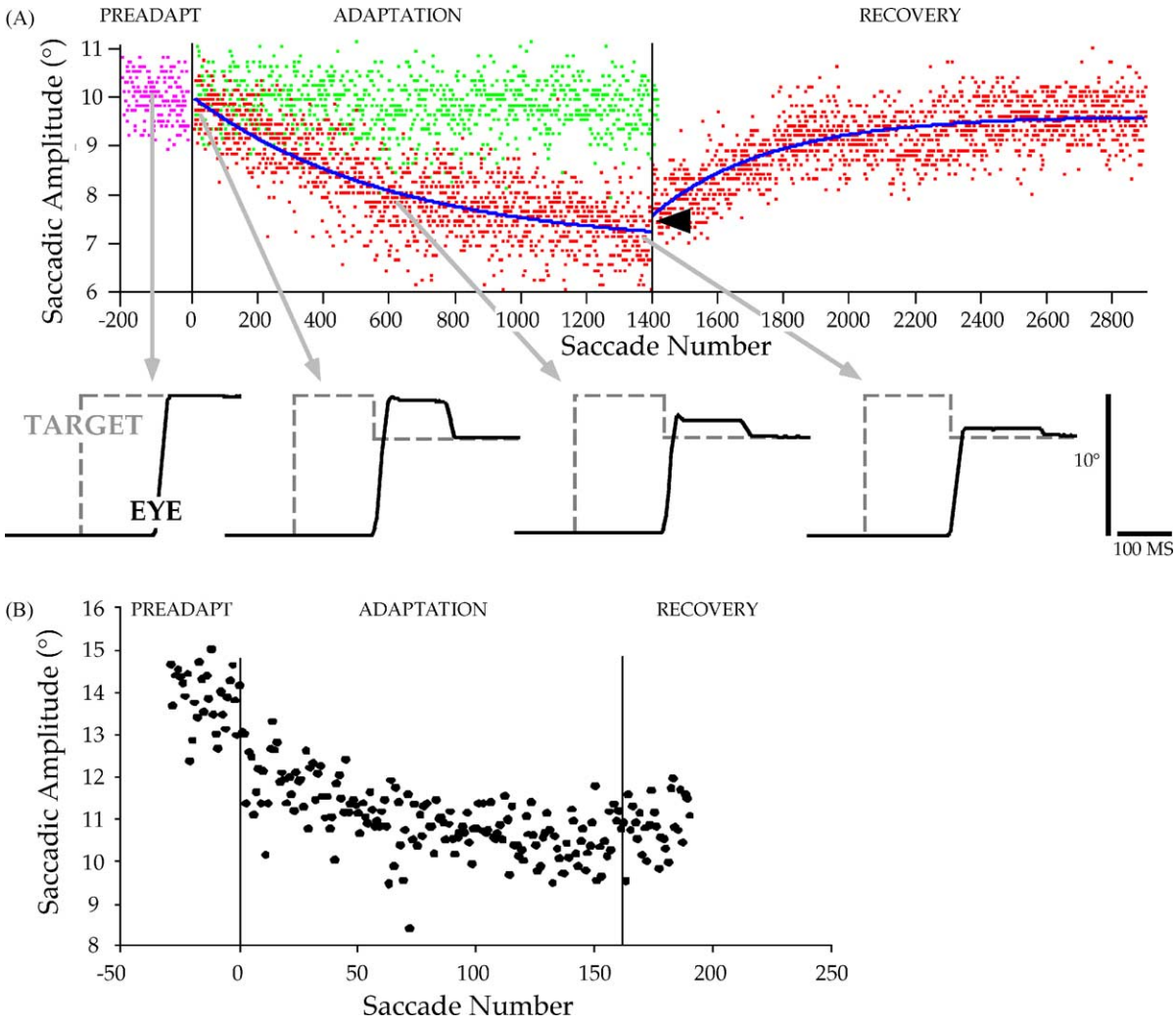


Fig. 3. Courses of representative saccadic amplitude adaptations for monkeys (A) and humans (B). Note the difference in abscissa scales! (A) *Top:* Adaptation and recovery of saccades made to 10° horizontal target steps with a 30% backward adaptation step. Saccadic amplitude is plotted as a function of the number of the trial in each direction. Magenta points, data from preadaptation trials. Red points, data from trials in the adapted direction. Green points, data from interleaved trials in the non-adapted direction. Adaptation and recovery data are fit by exponential function blue. Arrow indicates initial rapid recovery phase. *Bottom:* Representative examples of target (gray dashed lines) and eye (black lines) position for different trials during preadaptation and adaptation. (B) Adaptation and recovery of saccades made to 15° horizontal target steps with a 33% backward adaptation step. (Note that little change occurs during recovery because the target was extinguished deliberately during the saccade.)

ber of the saccade during adaptation is similar for monkeys and humans. The course of adaptation undergoes an initial, small rapid change (most noticeable in Fig. 3B), followed by a more gradual change, which asymptotes at a new steady-state level. The course of adaptation has most often been described by an exponential function (Deubel et al., 1986; Frens and van Opstal, 1994; Albano, 1996; Straube et al., 1997b; Scudder et al., 1998), although some authors have used a linear fit (Ditterich et al., 1999, 2000a). Although the general shapes of the course of behavioral adaptation are similar for monkey and man, there is a large difference in the rate of adaptation between the two species (note different abscissa scales in Fig. 3). For amplitude reduction (also called backward adaptation), the asymptote of the exponential fit is reached within 100 saccades in humans (rate constants ~30–60 saccades; Deubel et al., 1986; Deubel, 1987; Frens and van Opstal, 1994; Albano, 1996; Watanabe et al., 2003), whereas, monkeys require 1000 saccades to reach a steady state (rate constants range widely, ~100–800 saccades; Straube et al., 1997b). The reason for this dramatic difference between rate constants is currently unknown.

Do experimental conditions affect the speed of amplitude reductions during behavioral adaptation experiments? In both humans and monkeys, practice, i.e., repeated exposures to the adaptation paradigm in the same subject on different days apparently does not cause the amplitude reduction to be faster, larger, or more enduring (Fuchs et al., 1996; Straube et al., 1997b; Erkelens and Hulleman, 1993; Hopp and Fuchs, unpublished). Although practice does not seem to affect the course of adaptation, predictable target

locations cause adaptation to occur more rapidly, i.e., within a few saccades in humans (McLaughlin, 1967; Miller et al., 1981).

The course of adaptation for amplitude increases (also called forward adaptation) resembles that of amplitude reduction. However, most investigators have reported that rate constants for amplitude increases tend to be slower, 200–400 saccades in humans and ~1000 saccades in monkeys (Miller et al., 1981; Deubel et al., 1986; Deubel, 1987; Fitzgibbon et al., 1986; Straube et al., 1997b; Scudder et al., 1998; Kröller et al., 1999). Others (Albano and King, 1989; Albano, 1996) claim that the courses of forward and backward adaptation are similar and that the disparate rate constants observed by other investigators result from differences in the methods. In the Albano studies (Albano and King, 1989; Albano, 1996), the adaptation step moved the target to a location relative to the final position of the eye, whereas in the other studies, the adaptation step was relative to the original peripheral target location.

Finally, in humans, adaptation of saccade direction follows a course similar to that of amplitude reduction, with a rate constant of ~30–60 saccades. In monkeys, it is slightly faster than amplitude reduction, with a rate constant of ~200 saccades (Deubel, 1987).

Because robust behavioral adaptation occurs within ~100 saccades in man and 1000 saccades in monkeys, it takes only a few minutes in man and about 0.5 h in monkeys. In contrast, adaptation following muscular damage originally was thought to take several days in humans (Kommerell et al., 1976; Abel et al., 1978) and one day in monkeys (Optican and Robinson, 1980). However, testing in these latter subjects began some time after adaptation had started so the rate constants were only rough approximations.

*4.2.1.1. Differences in rate constants in the two adaptation paradigms.* The dramatic difference between the rate constants of behavioral adaptation and adaptation due to damage of the eye muscles or their innervation suggested that two different adaptation mechanisms were at work. More recently, however, Scudder et al. (1998) have determined that the difference in the courses of the adaptations are the result of methodological differences (Scudder et al., 1998). During behavioral adaptation, only a small number of target amplitudes have been used and thus subjects performed many identical trials. In contrast, during experiments involving muscular damage, subjects made spontaneous saccades to a number of locations in the natural visual environment and each location represented a different "target" eccentricity and/or direction (Miller et al., 1981). Because adaptation of saccades to target steps of each amplitude and direction requires a certain number of repeated saccadic dysmetrias, it follows that the course of adaptation is slowed by the addition of more target amplitudes (Miller et al., 1981; Albano and King, 1989). Also, when back-step trials were mixed with those in which the target did not undergo an adaptation step, the amount of adaptation depended on the percentage of back-stepping trials (Noto and Robinson, 2001). If monkeys with muscle resections view a restricted number of target steps, the course of adaptation is similar to that produced by behavioral adaptation in normal monkeys viewing the same steps (Scudder et al., 1998). Consequently, similar neuronal mechanisms probably are engaged in the paretic muscle and behavioral paradigms at least in monkeys.

*4.2.2. Recovery from adaptation*

As might be expected, when adapted subjects are required to follow targets that no longer undergo an adaptation step, the adapted saccades initially are inaccurate and saccadic amplitudes gradually return to their pre-adaptation values (Fig. 3A, recovery). Some authors conclude that in monkeys this recovery process has the same course as that of the original adaptation (Straube et al., 1997b), whereas, others suggest that in humans the course of recovery is different (McLaughlin, 1967; Deubel et al., 1986). Deubel et al. (1986) found that recovery after amplitude-decreasing adaptation had a longer course of adaptation than the original adaptation and concluded that the recovery was simply a forward adaptation, which generally has a longer course of adaptation. The recovery can be greatly retarded if the target is turned off during the saccade to eliminate a post-saccadic error signal (Semmlow et al., 1987; Seeberger et al., 2002).

At the onset of recovery, there is an initial, small, rapid change in saccadic amplitude in the direction of the more gradual return to a steady-state level (Fig. 3A, arrow; Frens and van Opstal, 1994; Straube et al., 1997b; Scudder et al., 1998). This rapid change may represent a fast component of the adaptation process. A similar initial jump in saccadic amplitude in the same direction as the adaptation sometimes also occurs at the beginning of adaptation (Straube et al., 1997b; Scudder et al., 1998), and its size is related to the number of targets presented (Scudder et al., 1998).

*4.2.3. Magnitude of adaptation*

For both humans and monkeys, the amount of adaptation achieved is less than the amount demanded by the size of the adaptation step, whether the step is forward or backward (Miller et al., 1981; Semmlow et al., 1987; Straube et al., 1997b; Scudder et al., 1998; Robinson et al., 2003; but see Deubel et al., 1986). However, the size of the adaptation step does seem to affect the amount of adaptation achieved, and the effect in humans is different from that in monkeys. In humans, backward adaptation steps of 25–50% of the initial target step caused proportional percentages of amplitude reduction (Miller et al., 1981). In monkeys, however, the average percentage reduction to a demanded 50% back-step was slightly less than the percentage reduction to a demanded 30% back-step (Straube et al., 1997b). Furthermore, the rate constant was longer for the 50% back-step (827 saccades versus 368 saccades for the 30% back-step), suggesting that the adaptive mechanism is more efficient at correcting small errors (Straube et al., 1997b).

To further examine how the amount of dysmetria affects adaptation in the monkey, Robinson et al. (2003) caused the target to step backwards by a fixed amount relative to the approximate position of the eye at the end of the saccade, thereby keeping saccadic error constant. In this adaptation paradigm, saccadic amplitude decreased to an asymptote despite the presence of a persistent visual error. The amount of amplitude reduction remained relatively constant at ∼36% for all fixed errors between 10 and 50% of the target amplitude; for larger fixed errors, the percentage of amplitude reduction decreased substantially (Robinson et al., 2003). The rate constants obtained in these experiments seem longer (average 894 saccades) than those obtained for adaptation steps that are fixed in size relative to the target. However, the authors argue that the rate constants in the two conditions are similar, perhaps because both are highly variable.

Why do neither amplitude decreases nor amplitude increases compensate completely for the intrasaccadic target displacement, i.e., why does the adaptation not go to completion? One possibility is that the adaptation process has at least two components, a relatively rapid phase and a slower phase, and that only the relatively rapid phase occurs during the course of adaptation in most behavioral experiments (Miller et al., 1981; Scudder et al., 1998; Robinson et al., 2003). Perhaps a rapid visual mechanism corrects only a portion of the retinal error, after which it hands further corrections off to a slower mechanism that uses another unknown error signal (Miller et al., 1981). It also is possible that too few adaptation trials were performed in most experiments and with more trials, adaptation, at least for backward steps (Deubel, 1986), would have gone to completion.

#### 4.2.4. Reasons for differences in forward and backward adaptation

Why is the adaptation process associated with amplitude increases different from that associated with amplitude decreases? It is clear that forward adaptation is more difficult to achieve than backward adaptation, as evidenced by its longer course and more modest amplitude changes (Miller et al., 1981; Deubel, 1991; Straube et al., 1997b; Scudder et al., 1998; Noto et al., 1999; Bahcall and Kowler, 2000; Robinson et al., 2003). Perhaps, this is because the saccadic system is designed to be hypometric; indeed, human saccades to targets >15° from straight-ahead fall ∼10% short of the target (Becker, 1989). The maintenance of a hypometric state is advantageous because corrective saccades following a hypometric saccade have shorter latencies than those following a hypermetric saccade, allowing the target to be acquired sooner. If the saccadic system wants to maintain a hypometric state, reason suggests that it would be easier to decrease than to increase saccadic amplitude (McLaughlin, 1967; Henson, 1978; Miller et al., 1981; Deubel, 1991). Indeed, if the saccadic system prefers to undershoot the target, an amplitude-reduction mechanism presumably is already in place so this mechanism could be easily appropriated to deal with pathological overshooting (Straube et al., 1997b). This notion is supported by experiments in which specialized prisms were used to adjust the perceived location of the target at the end of a saccade, such that the saccade appeared to be too large, although they did not change the perceived location of the peripheral target before the saccade was generated (Henson, 1978). Amplitude adaptation occurred and caused the majority of saccades to be hypometric, as they were normally, without prisms. Thus, Henson (1978) concluded that the saccadic system adjusted itself towards a hypometric state.

Semmlow et al. (1987) argued that amplitude increases and decreases employ different behavioral adaptation processes. Based on a correlation analysis between the end position of the saccade and its amplitude, they suggested that amplitude increases involve a remapping of the desired end position of saccades, whereas amplitude decreases are best described by an overall reduction in gain (saccade amplitude/target amplitude) of the saccadic system.

#### 4.2.5. Reproducibility of adaptation

The amount of adaptation achieved in any given experiment is highly variable, both between subjects and within a single subject. For example, in response to a 50% target back-step, human subjects decreased their saccade amplitudes by anywhere between 10% and 42% (Erkelens and Hulleman, 1993). In response to a ∼33% back-step, other subjects (3/10) did not adapt at all (Frens and van Opstal, 1994). Also, the same subject can exhibit a large variation in adaptation on different days for nearly identical conditions whether she is a human (Albano and King, 1989; Erkelens and Hulleman, 1993; Frens and van Opstal, 1994; Fujita et al., 2002; Hopp and Fuchs, unpublished) or a monkey (Fuchs et al., 1996; Straube et al., 1997b). For example, a single monkey showed an almost two-fold difference in the amount of amplitude change on two different days (Straube et al., 1997b).

#### 4.2.6. Effect of adaptation on saccade metrics

Although behavioral adaptation usually produces a clear change in the amplitude (or direction) of saccades, there is disagreement as to whether the characteristics, or metrics, of the saccades themselves also are affected. Targeting saccades in alert motivated subjects are relatively stereotyped and can be described by their duration, which increases linearly with saccadic amplitude, and their peak velocity, which increases linearly for low amplitudes and then undergoes a soft saturation for saccades above ∼15° (Becker, 1989). Abrams et al. (1992) argued that after an amplitude reduction, human saccades have longer durations and smaller accelerations; however, they did not compare saccades of similar magnitudes before and after the adaptation. Erkelens and Hulleman (1993) claimed that the amplitudes of human saccades after an amplitude reduction are more variable; however, only one of their two subjects demonstrated this result. Straube and Deubel (1995) described an increase in duration and a decrease in peak velocity

in amplitude-increasing experiments with humans, and no change in saccadic metrics in amplitude-reduction experiments. Finally, others have claimed that the metrics of human saccades are not affected by adaptation (Albano and King, 1989; Frens and van Opstal, 1994), but data in these studies are either limited or anecdotal.

In monkeys, the changes in saccade metrics are idiosyncratic from animal to animal (Straube et al., 1997b). Larger saccades clearly became slower in one of four animals (see also Fitzgibbon et al., 1986; Frens and van Opstal, 1997), whereas in the other animals the change was modest. However, some of the slowing can be attributed to fatigue or inattention (Straube et al., 1997a). When an animal with a paretic eye underwent long-term adaptation while viewing through that eye, saccadic duration and peak velocity increased, whereas when the animal viewed with the good eye, the opposite occurred (Scudder and McGee, 2003). Short-term adaptation (that occurring during a recording session) produced similar, but more variable, changes in saccade metrics. Adaptation caused no consistent change in saccadic latency (Straube et al., 1997b).

In our view, it currently is unclear whether adaptation affects the metrics of saccades. Straube et al. (1997b) compared the duration versus amplitude and peak velocity versus amplitude relationships of saccades before and after behavioral adaptation. Unfortunately, the results were not consistent across monkeys: some animals showed differences in the metrics whereas others did not. Similarly, adaptation in response to weakened eye muscles caused variable effects on saccade metrics, especially during the short-term adaptation that occurred during a recording session (Scudder and McGee, 2003). A similar study has not been performed in humans. The ideal experiment would be to compare saccades of identical amplitudes before and after adaptation.

#### 4.2.7. Adaptation is not parametric

McLaughlin (1967) claimed that saccadic adaptation is parametric. We do not know what McLaughlin meant by "parametric". However, in this review we consider a parametric change in the context of control systems, where a parameter is usually a constant multiplier or a gain. By our definition, if the gain of the saccadic system (eye amplitude/target amplitude) were altered, then *all* saccades would be influenced by the same multiplier, i.e., a 20% change in the gain of one saccadic amplitude would result in a 20% change in the gain of all saccadic amplitudes. However, McLaughlin did not test whether adaptation was "parametric" by our definition as he adapted and tested saccades to target steps of only one size.

It was soon shown that adaptation of saccades was not strictly parametric by our definition because adaptation of saccades to target steps in one direction produced no change in the amplitudes of saccades to target steps in the opposite direction. This directional specificity occurred in both subjects with a paretic eye (Abel et al., 1978) and normal subjects undergoing behavioral adaptation (Weisfeld, 1972; Miller et al., 1981; Deubel et al., 1986; Deubel, 1987; Semmlow et al., 1987; Moidell and Bedell, 1988; Frens and van Opstal, 1994; Albano, 1996; Straube et al., 1997a,b). However, for saccades produced in the same direction, Deubel et al. (1986) did conclude that amplitude adaptation in humans *was* parametric. After reduction of the amplitude of saccades to target steps of one size in one direction, they claimed that the amplitudes of saccades to target steps in the same direction but with slightly larger and smaller amplitudes (differing by 4°) showed similar percentage decreases.

In all other studies with humans and monkeys, however, adaptation of saccades to target steps of one size did not generalize completely to saccades elicited by target steps of other sizes in the same direction, although the pattern of transfer differed somewhat across studies (Miller et al., 1981; Semmlow et al., 1987; Frens and van Opstal, 1994; Albano, 1996; Straube et al., 1997a,b; Noto et al., 1999). After amplitude adaptations of horizontal saccades, transfer to horizontal saccades elicited by target steps larger than that adapted was greater than to saccades elicited by smaller target steps. The greater transfer to larger than smaller saccades occurred for both amplitude increases and decreases in humans (Semmlow et al., 1987) and monkeys (Noto et al., 1999). For example, in monkeys, following an adaptation of saccades made to 15° targets, greater than 82% of the adaptation transferred to saccades made to 25° targets, but only ~30% of the adaptation transferred to saccades made to 5° targets (Noto et al., 1999). In contrast, Miller et al. (1981) found the opposite transfer pattern following an amplitude decrease in humans, but for amplitude increases the transfer also was greater to saccades elicited by larger target steps than to saccades elicited by smaller ones.

Therefore, although the details differ, most studies indicate that adaptation transfer is always <100% to saccades in response to target steps that were not used in the adaptation paradigm. Furthermore, the amount of transfer decreases the more the amplitude of the tested saccade deviates from that of the adapted saccade (see Fig. 3 in Noto et al., 1999; and Fig. 7 in Semmlow et al., 1989). This observation also explains the results reported by Deubel et al. (1986); because they tested only saccades to target steps with amplitudes within 4° of the target amplitude used during the adaptation, a substantial amount of the adaptation would be expected to transfer. Furthermore, at least two of their subjects, showed what seems to be qualitatively less adaptation of saccades made to target steps that were slightly larger or smaller than the adapted amplitude.

In both humans (Miller et al., 1981; Semmlow et al., 1987) and monkeys (Watanabe et al., 2000), it is possible to increase the size of saccades to targets of one amplitude while simultaneously decreasing the size of saccades to targets of different amplitudes in the same direction. Semmlow et al. (1987) suggested that the amount of adaptation of saccades made to target steps with amplitudes intermediate to the adapted amplitudes reflects a linear sum of the amount of adaptation that would be produced at the

intermediate amplitude by each adapted amplitude alone. On the other hand, Watanabe et al. (2000) claimed that in monkeys a linear summation does not account for the amount of adaptation. It is unclear, however, whether the latter study considered the effect that adaptation of saccades to the one target amplitude, in isolation, had on the other.

Based on all the evidence, adaptation of saccadic amplitude is not parametric in the sense that a single multiplicative factor accounts for the effect of adaptation on saccades of all sizes. Therefore, it is more accurate to talk of saccadic *amplitude* adaptation than saccadic *gain* adaptation. The notion of selective adaptation should come as no surprise because similar selectivity for the adapting condition is seen in other oculomotor responses. For example, if magnifying lenses force an increase in the gain of the vestibular ocular reflex at 0.5 Hz, less gain increase is demonstrable at other, nearby frequencies (Lisberger et al., 1983).

*4.2.7.1. Adaptation fields.* Based on their study of horizontal saccades, Frens and van Opstal (1997) suggested that the decreasing influence of an adapted saccade on the amplitudes of saccades made to larger or smaller target steps was reminiscent of the movement fields of some units in the SC (Fig. 4; Sparks et al., 1976). Neurons in the SC discharge most vigorously for a saccade of a preferred vector and increasingly less well for saccadic amplitudes that deviate more and more from the preferred vector. Some SC neuron movement fields are symmetrical about the preferred vector, whereas for others the discharge rate falls off quickly for amplitudes smaller than the preferred direction and more slowly for amplitudes larger than the preferred direction. By analogy with such SC "motor fields", Frens and van Opstal (1997) named the spatial property of saccadic adaptation an "adaptation field." In fact, like the movement fields of SC units, adaptation fields also are two-dimensional (Fig. 4; Deubel, 1987, 1989; Noto et al., 1999). As stated previously (Section 4.2.7), after adaptation of horizontal saccades to target steps of one size, horizontal saccades made to target steps of other sizes were adapted but to a lesser extent. Furthermore, saccades made to oblique targets with the same horizontal component (Noto et al., 1999) or with the same magnitude as the adapted horizontal target amplitude (Deubel, 1987, 1989) also were adapted, but again to a lesser extent. As the test target steps became less horizontal (more oblique), the amount of adaptation decreased. Thus, after amplitude adaptation of saccades to one target amplitude and direction, saccades to target steps of either different amplitudes or different directions show less adaptation, such that the two-dimensional adaptation field resembles a mound centered on the adapted vector (Fig. 4). In addition, there is some evidence that adaptation also occurs for vergence saccades, in which case adaptation fields may be three-dimensional (Chaturvedi and van Gisbergen, 1997).

Adaptation of saccadic direction also can be characterized by an adaptation field in both humans (Deubel, 1987, 1991) and monkeys (Deubel, 1987, 1991; Noto et al., 1999). After

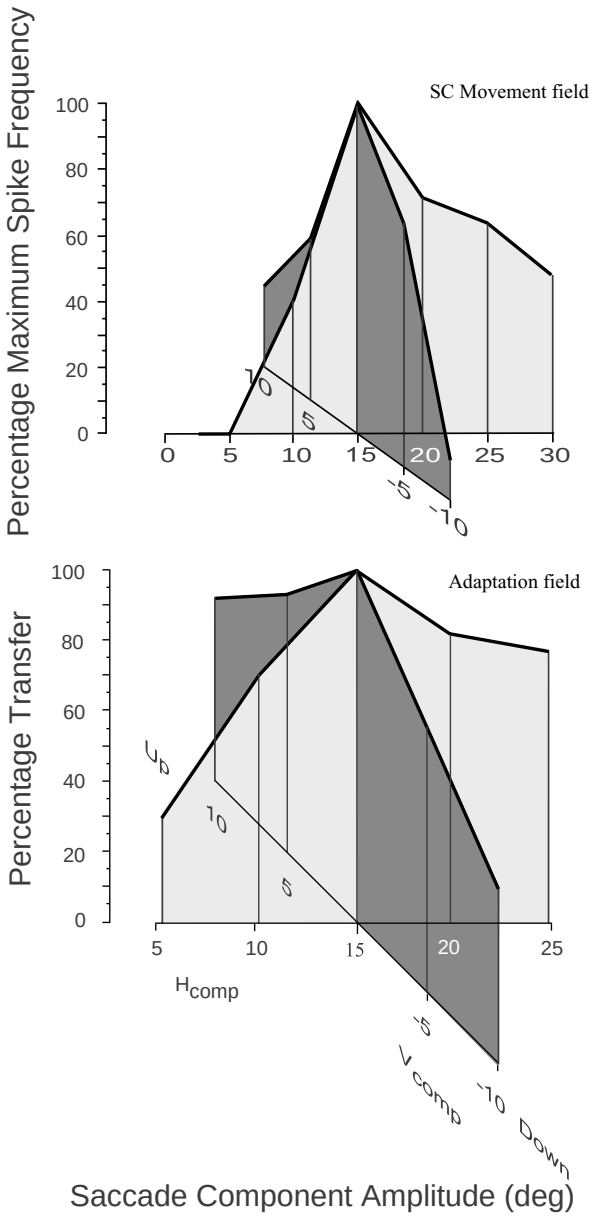


Fig. 4. Comparison of the two-dimensional shapes of a movement field for a SC burst neuron and an adaptation field in a monkey. For the SC neuron, activity was recorded for horizontal saccades of six different sizes and oblique saccades with a 15° horizontal component and four different vertical components. The neural response is plotted as the percentage of the firing rate associated with the unit's optimal vector, i.e., 15° horizontal. For the adaptation field, saccades to a 15° horizontal target step underwent an amplitude reduction (30%) and the transfer was determined to horizontal saccades elicited by four other horizontal target steps and to oblique saccades elicited by targets with the same horizontal component but four different vertical components. The transfer is plotted as a percentage of the adaptation produced at the adapted (15°) saccadic amplitude. (Figure developed from Noto et al., 1999, and reproduced with permission of the American Physiological Society.)

the direction of saccades to horizontal targets of one size was altered by a vertical adaptation step, saccades made to horizontal target steps with larger and smaller amplitudes also exhibited changes of direction, but to a lesser extent. Similarly, saccades made to oblique target steps that had

either the same horizontal component (Noto et al., 1999) or the same amplitude as the adapted target step (Deubel, 1987, 1991) also showed changes in direction. As with amplitude adaptation, the adaptation field for directional adaptation is not symmetric along the horizontal meridian; a larger change in direction occurred for saccades elicited by larger target steps than for saccades to smaller target steps (Fig. 11 in Noto et al., 1999). The amount of transfer seems to be more symmetric for saccades made to oblique target steps, such that saccades made to target steps with upward components experienced changes in direction similar to that of saccades made to target steps with downward components.

In summary, behavioral adaptation can cause both increases and decreases in saccadic amplitude as well as changes in saccadic direction, although it is unclear whether they can be adapted independently. Current data suggest that amplitude adaptation does not alter direction. In the directional adaptation experiments published to date, however, amplitude also had to change because the adaptation step was orthogonal to the target step (Deubel, 1987; Noto et al., 1999). For adaptations of either saccadic amplitude or direction, the course of adaptation usually has been fit with an exponential function. For the same demanded change, amplitude increases are smaller and require more trials than amplitude decreases in both humans and monkeys. Also, the magnitude of the adaptation does not reach the demanded amount for either increases or decreases. Furthermore, both amplitude and direction adaptation exhibit adaptation fields in which the most adaptation occurs for saccades elicited by the adapting target step and decreases as the test target steps deviate more from the amplitude and direction of the target vector used during the adaptation. The existence of adaptation fields is further evidence that saccadic adaptation is not parametric. Finally, adaptation is highly variable from one testing session to another and from subject to subject. Because the induction of amplitude reductions is more reliable and robust, essentially all of the remaining characteristics of saccadic adaptation, which we will discuss now, have been revealed with this paradigm.

### 4.3. What drives amplitude adaptation?

For adaptation to occur, a signal is required to indicate saccadic accuracy. This signal could be provided by either the retinal error remaining after the dysmetric initial saccade or the size of the subsequent corrective saccade made to finally foveate the target (see Fig. 3A, lower panel). Apparently, corrective saccades are not necessary for adaptation to occur. In monkeys and humans, robust amplitude reductions occur even if the number of corrective saccades is reduced by stepping the target backwards only briefly during an adaptation step and then returning it to its original displacement (Wallman and Fuchs, 1998). With this paradigm, only ∼1.2% of adaptation trials had corrective saccades. Although robust, the amount of adaptation was only ∼50% of that achieved when the back-stepped target remained in position. Also, the initial rate of the adaptation was reduced.

It is possible that re-illuminating the target at its initial displacement caused a visual conflict that deterred the adaptation process. In this scenario, the adaptation step served as a signal to decrease saccadic amplitude, whereas the target's subsequent return to the initial displacement indicated that no amplitude change was necessary. As we shall see later, the effect of an adaptation step decreases with increasing delays from the primary saccade (Bahcall and Kowler, 2000; Shafer et al., 2000; Fujita et al., 2002). Therefore, the slightly delayed return of the target to its initial displacement, which may serve as a forward adaptation step, would be less effective, resulting in a smaller net reduction in amplitude. To eliminate the possibility of conflicting visual errors, Noto and Robinson (2001) subjected monkeys to only a brief backward adaptation step and then extinguished the target, a procedure that nearly eliminated corrective saccades yet produced adaptation comparable to that achieved with a simple back-step.

Bahcall and Kowler (2000) also suggested that corrective saccades are unnecessary for the adaptation process in humans. If the target used during the adaptation is an open circle rather than a small spot, the number of corrective saccades generated is quite low (<16% of trials), yet the amount of adaptation achieved with the circle target is similar to that achieved with a spot target.

Thus, the weight of the available evidence indicates that corrective saccades, or signals associated with them, are not the source of the error signal for behavioral reduction of saccadic amplitude. Rather, it is more likely that the visual error, which exists when the primary saccade lands, drives adaptation.

#### 4.3.1. Temporal constraints on the visual error signal that drives adaptation

The timing of the visual error affects the amount of adaptation achieved. When the adaptation step is illuminated for only a fixed duration, the amount of adaptation achieved increases as the duration increases up to ∼80–100 ms (Shafer et al., 2000). For durations beyond ∼100 ms, the amount of adaptation remains relatively constant. If the target is extinguished during the saccade and a delay up to ∼100 ms is introduced between the end of the saccade and the adaptation step, the amount of adaptation is comparable to that achieved without a delay. However, as delays increase beyond 100 ms, the amount of adaptation decreases gradually in both humans (Bahcall and Kowler, 2000; Fujita et al., 2002) and monkeys (Shafer et al., 2000). However, significant amplitude reductions can still be achieved after adaptation step delays of ∼600–700 ms in both humans (Fujita et al., 2002) and monkeys (Shafer et al., 2000). Thus, the visual error driving adaptation is most effective if it occurs within 80–100 ms after the saccade ends.

#### 4.3.2. Adaptation is not specific to the specific visual characteristics of the target

Does adaptation depend on the visual features of the target? Bahcall and Kowler (2000) reported that the shape of the adapting target did not influence amplitude reduction in their human subjects. Adaptation produced by a spot target was similar in both its magnitude and rate to adaptation produced using a circle target. In addition, when a forward adaptation step occurred during saccades to square targets and a backward adaptation step occurred during saccades to circle targets, adaptation did not occur in either direction. The authors concluded that the backward adaptation caused by a target of one shape cancelled the forward adaptation produced by the other. Similarly, the color of the adaptation stimulus is not important in humans because when saccades to targets shaped like green crosses underwent amplitude reduction, saccades to red circles also exhibited adaptation to the same degree and at a similar rate (Deubel, 1995a). Although the role of the features of the target has not been explored fully, the available data suggest that the human adaptation process is invariant with respect to specific characteristics of the adapting target. Indeed, the adaptation process probably affects all targeting saccades about equally, whatever the characteristics of the target that elicits them.

#### 4.3.3. Adaptation does not depend on the visual background

Not only are the specific features of the target unimportant in the adaptation process, but there is some indication that the background upon which it moves is also inconsequential. In humans, the amount of adaptation induced without a background present transfers completely to saccades made to spot targets moving over a background, despite the possibility that the background itself could be used as a reference to localize the target in space (Deubel, 1995a). In both monkeys and humans, a spot target that moves across a stationary background, whether a random dot pattern, a combination of squares and circles, or a color photo, induces robust adaptation if the spot target alone undergoes an adaptation step (Deubel, 1995a; Ditterich et al., 1999; Robinson et al., 2000). Furthermore, in humans, adaptation to a spot target with or without a background present is statistically the same (Ditterich et al., 1999). In monkeys, however, the amount of adaptation with a background present is usually less than that produced by a spot target on a black background (Robinson et al., 2000). If the background shifts with the target, either in the same direction (shown for both monkeys and humans) or opposite direction (shown for humans only), the amplitude reduction is the same as when the background is stationary (Ditterich et al., 1999; Robinson et al., 2000). If instead of an intrasaccadic shift of the target spot, there is an intrasaccadic shift of the background, monkeys undergo very little adaptation, and in some cases the adaptation occurs in the wrong direction (e.g., an increase in amplitude occurs when the background is stepped backward; Robinson et al., 2000). An amplitude increase might be explained if the monkey perceived a backward shift of the background as a forward shift of the target. Collectively, these observations suggest that the presence of a background has very little, if any effect on the adaptation of saccadic amplitude to a target within the background.

However, there are situations in which the presence of a background *does* influence saccadic adaptation. When saccades were made not to salient targets on a background but to patterns within a background, shifting the entire background during the saccade reduced saccadic amplitude in humans (Deubel, 1991; Ditterich et al., 1999). Although no obvious target was present, subtle patterns within the background might have served as a visual target signal to drive adaptation. These experiments may be more representative of how the adaptation mechanism operates in the natural visual environment where there are many potential targets. In monkeys, saccadic amplitude was reduced significantly when the target eliciting the saccade was extinguished at the same time that the background underwent an intrasaccadic back-step (Robinson et al., 2000). In many experiments, the amplitude reduction was comparable to that obtained when a target without a background was extinguished briefly (for either 250 or 1000 ms) during a saccade and then re-illuminated at the back-stepped location.

In conclusion, these experiments indicate that as long as the adapting target is clearly visible on a background, the background does not influence adaptation. Only if the background is moved in the absence of a specific saccadic target can it produce adaptation.

### 4.4. Interaction of adaptation and attention

The minimal effect of the background might be the result of attention being focused on the target and not on the background. While tracking a target, the subject attends to the target and may actively suppress attention to other stimuli (e.g., the background). Ditterich et al. (2000b) attempted to control the area of the focus of attention by using either a spot target or a 4.8° diameter circle. Either target was presented on top of a background. They argued that the spot target focused attention narrowly on the target, but the circle target focused attention diffusely across the circle and thus included the encircled background. During experiments in which the background shifted in the same direction as the adaptation step of the spot target, the rate of adaptation was significantly different from zero. In contrast, when the background shifted in a direction opposite that of the adaptation step of the spot target, the rate of adaptation was not significantly different from zero. However, the *difference* between the rates of adaptation in the two conditions *was not* statistically significant, so the authors concluded that the background did *not* affect the rate of adaptation. However, because the rate of adaptation was not significant when the background moved opposite to the target, but *was* significant when the background moved with the target we might argue that the background *did* have an effect. Like the spot target experiment, when the background moved in the same direction as the adaptation step of the

circle target, the rate of adaptation was significantly different from zero. When the adaptation step of the circle target and background moved in opposite directions, the rate of adaptation was not significantly different from zero. However, unlike the spot target experiment, there *was* a significant difference in the amount of adaptation between these two conditions. Thus, the authors suggest that when the circle target is used, the background *does* have an effect on the rate of adaptation. Therefore, they concluded that the background influences the rate of adaptation only when it is attended to.

Although attention seems to influence whether a background affects adaptation, the focus of attention itself does not seem to shift with saccadic adaptation. In the experiments of Ditterich et al. (2000a), just before a subject made a saccade to a spot target, two other targets, a discrimination target and a distractor, were presented briefly at various locations to the left or right of the spot target. At the end of the saccade, the subject had to describe the physical characteristics of the discrimination target. If a correct response was given, the location of the discrimination target relative to the saccade target was taken to be the location of the focus of attention. After adaptation, the average measured location of the focus of attention remained unchanged relative to the saccade target, suggesting that attention had not been adapted. The authors proposed two possibilities for this lack of a shift in the focus of attention with adaptation. First, it is possible that the signals for attention and those for saccades are processed separately. Second, attention and saccades could be processed together, but the adaptation takes place downstream of this processing and influences only saccades. We would suggest a third possibility that adaptation simply reflects an early remapping of the visual world, in which case attention and saccades would be affected equally. In this scenario, a 20% adaptation would cause 10° targets to appear at 8°, resulting in an adapted 8° saccade. If the same adapted visual representation were used by the attention mechanism, the locus of attention would remain unchanged relative to the adapted target, as it did in the Ditterich et al. (2000a) experiments.

McFadden et al. (2002) determined that the focus of attention itself could be adapted. They used a modification of the 'shooting line illusion' (Hikosaka et al., 1993). To elicit this illusion, the subject fixated a constantly illuminated central point while another target (the cue) was illuminated in the periphery. Shortly thereafter, a line appeared across the cue position. If the focus of attention had shifted to the cue location when the line appeared, the subject reported that the line was drawn outward from the cued point, in either direction. If the focus of attention was not at the cued location when the line appeared, the subject reported that the line appeared all at once. McFadden et al. (2002) adapted the focus of attention by shifting the cue at the estimated time the focus of attention shifted from the fixation target to the cued location. This time was determined for each subject. They found that attention could indeed be adapted, and that this adaptation was gradual, specific for the adapted direction, and could be shifted both forward and backward. The course of adaptation of attention was shorter and the amount of adaptation was less than that normally seen with adaptation of saccadic amplitude. In five of seven subjects, saccadic amplitude also showed a modest change and the sign of the change, i.e., an increase or decrease, was the same as that for the attention adaptation. These data suggest that that adaptation of attention transfers to saccades.

Several issues must be clarified in these very difficult experiments (McFadden et al., 2002). First, in half of the experiments, the amount of adaptation of attention waxed and waned, rather than increasing monotonically with the number of the trial. Therefore, the amount of adaptation depended on when the adaptation paradigm was stopped. Second, the interpretation of the data depend on an accurate estimate of the time the focus of attention shifts for individual subjects. Unfortunately, there was no way for the authors to be sure this estimate was accurate or what its variance was. Therefore, it is possible that on some trials the focus of attention shifted prior to the shift of the cue for the line illusion. If this were the case, a subject may have noticed the shift in the cue location and could have strategically altered her focus of attention during the experiment. Thus, the 'adaptation' of attention observed during these experiments may be different than the type of adaptation we have been describing for saccades. Finally, regarding the saccadic adaptation pursuant to attention adaptation, we would like to know its magnitude and whether it was statistically significant.

In summary, adaptation seems to be driven by the visual error experienced at the end of a dysmetric saccade. This error is most effective during the 80–100 ms after the primary saccade lands. The specific visual characteristics of the target do not seem to provide contextual cues for adaptation (see Section 4.8 for specific experiments on the effects of context on adaptation). Generally, the background over which the adapting spot target moves has no effect on adaptation but can influence adaptation under some circumstances if it is within the subject's focus of attention. Finally, the evidence as to whether adaptation affects attention is inconclusive, although it appears that attention itself can experience adaptation.

### 4.5. Does adaptation affect visual perception?

The two studies that considered the effect of adaptation on visual perception have led to different conclusions. When subjects whose saccadic amplitude was adapted were asked to locate a test target relative to a flashed saccade target, they mislocated the target in the same direction as the adaptation, whether the adaptation caused amplitude increases or decreases (Bahcall and Kowler, 1999). Since subjects properly localized the test target relative to the saccade target prior to adaptation, they also would do so after adaptation if the adaptation were taken into account. In that case, the test target would have appeared relatively further away from the saccade target after a backwards adaptation and relatively

closer to the saccade target after a forward adaptation. Because targets were mislocated, the authors suggested that the perceptual system uses signals that represent the original target displacement rather than the size of the actual saccade. Although they conclude that perception is not affected by adaptation, their findings also could be explained if adaptation occurred before the perceptual decision was made, e.g., if adaptation had caused a remapping of the neuronal visual map of target location upon which the perception had been based.

However, adaptation did affect a different visual perception. After horizontal saccades had undergone a direction adaptation to acquire an upward component, the threshold for detecting upward motion of a visual target increased and that for detecting downward motion decreased (Mack et al., 1978). The opposite threshold changes occurred after saccades were adapted to have a downward component. The authors suggest that these changes in motion perception are a result of the adapted changes in the saccadic direction.

It is possible that the results of Mack et al. (1978) and Bahcall and Kowler (1999) are different because the two types of perceptions use different neurological structures, one influenced by the adaptation and the other not. Another possibility is that adaptation *did* influence perception in both experiments because the Bahcall and Kowler (1999) results could be explained if adaptation had caused a remapping of the neuronal visual map, as suggested previously.

### 4.6. Is the adaptation process strategic or a true neuronal plasticity?

A variety of observations support the notion that the adaptation of saccadic amplitude is not strategic. First, most human subjects are unaware of an intrasaccadic adaptation step and therefore could not use it to alter their behavior voluntarily. For example, Deubel et al. (1986) reported that the rates of detection of an intrasaccadic target step were small (10–25%). Although Frens and van Opstal (1994) noted that subjects experienced with the adaptation paradigm could recognize the adaptation step whereas naïve subjects could not, their experienced and naïve subjects nevertheless exhibited the same amounts of adaptation. Similarly, some experienced subjects in our laboratory can detect an adaptation step; however, they claim they do not consciously alter their behavior nor is there any evidence that they do (Hopp and Fuchs, unpublished). Second, it is unlikely that adaptation is strategic because there is some residual adaptation several hours after completion of an experiment (Semmlow et al., 1987; Straube et al., 1997b; Noto et al., 1999). Third, some authors found that the course of adaptation and the recovery from adaptation are similar (Straube et al., 1997b). If adaptation were strategic, recovery might be faster. Fourth, adaptation of saccades produced by adaptation steps using targets of one color transfers to saccades generated toward a target of another color (Deubel, 1995a), suggesting that strategic control of adaptation on the basis of color is unlikely. Fifth, the use of strategy might be reflected as a change in the saccadic latency or reaction time. For example, the latency might decrease if anticipation were occurring or increase if an overt cognitive strategy, such as canceling an initial saccade, were employed. However, the latency of saccades did not change during the adaptation of targeting saccades in either humans (Albano and King, 1989) or monkeys (Straube et al., 1997b). Although none of this evidence alone is conclusive, taken together it suggests that adaptation cannot be controlled voluntarily.

As mentioned above, many investigators have observed anecdotally that amplitude adaptation can persist the day after an experiment, thus suggesting that there is a true neuronal reorganization in the brain. The perseverance of adaptation was tested objectively by adapting monkeys and placing them in the dark for 20 h (Straube et al., 1997b) or in normal illumination for 16–24 h (Noto et al., 1999). The animals placed in the dark received no visual input about the accuracy of their saccades. In these four monkeys, the amount of adaptation retained after an amplitude reduction for target sizes of 10 and 15° ranged between ∼6 and 100%, but three of four retained 66–100% of the adaptation (Straube et al., 1997b). Adapted saccades to 5° target steps consistently showed the least retention. Animals placed in normal illumination after adaptation, retained 45–71% of amplitude reductions, 13–17% of amplitude increases, and 18–25% of directional adaptations (Noto et al., 1999). The reduced amount of retention in the light probably occurs because these animals receive some feedback that their saccades are inaccurate as they view ‘targets’ in their natural visual environment. If the adaptation were strategic, we would not expect robust retention during recovery either in the dark or under normal illumination. The retention of adaptation beyond ∼24 h has not yet been examined.

### 4.7. Effect of eye position on adaptation

The majority of studies indicate that adaptation of saccades to targets of a given vector is not affected by either their starting or ending eye positions (Frens and van Opstal, 1994; Deubel, 1995a; Albano, 1996; Noto et al., 1999). For example, if rightward horizontal saccades to 10° target steps in the left visual field are adapted, rightward horizontal saccades to 10° target steps in the right visual field show similar amplitude changes.

These data conflict with those of Shelhamer and Clendaniel (2002b), who found that saccades in the left visual field could be reduced in amplitude, while saccades to similar target steps in the right visual field could be increased in amplitude. The difference between these data and those of the previous studies could be reconciled if the system default is to generalize adaptation to all parts of the saccadic operating range, as seen in the previous studies (Frens and van Opstal, 1994; Deubel, 1995a; Albano, 1996; Noto et al., 1999). However, when conditions demand independent control, e.g., when forward and backward

adaptation steps are presented to different parts of the visual world, the adaptation can also be specific to the parts of visual space where the differential adaptation is demanded. Unfortunately, in the experiment by Shelhamer and Clendaniel (2002b), the target positions were highly predictable, so that the subjects may have adjusted the amplitudes of their saccades strategically when they switched between the two halves of the visual field.

### 4.8. Context specific adaptation

In humans, saccadic adaptation can indeed depend on certain contextual cues (Shelhamer and Clendaniel, 2002a,b). For example, saccadic amplitudes can be increased when the head is tilted 45° clockwise and decreased when the head is tilted 45° counterclockwise (Shelhamer and Clendaniel, 2002a,b). During tilts in both directions, saccades were made horizontal relative to the head, and both contexts used the same size target steps. The authors also claim that differential adaptation (increases versus decreases) of horizontal saccades relative to the head was produced in other contexts, which included gaze directed either left or right of the midline, gaze directed either up or down, and subjects positioned either upright or supine (Shelhamer and Clendaniel, 2002b).

There are several concerns with the results of these two studies on contextual adaptation. First, the target locations were very predictable so that subjects may have used an overt strategy to alter their saccades in different contexts. Second, each subject was tested only once, which could produce misleading results because of the high degree of variability in adaptation experiments from day to day. Third, the experiments were not repeated with the conditions reversed, such that amplitude increases in one context in the first experiment became amplitude decreases in the same context in the second. This would have ruled out the possibility that the adaptation in a given context can occur with only one type of adaptation, either forward or backward. Finally, not all conditions showed a robust difference between the contexts, nor were there always significant saccadic amplitude changes under both contexts in the same experiment.

Despite these caveats, these studies showed that adaptation *did not simply generalize* between contexts, in which case we would have expected to see an amplitude change (either increase or decrease) in the same direction for both contexts. However, when adaptation steps are presented in only *one* context, the adaptation *does* generalize (Frens and van Opstal, 1994; Deubel, 1995b; Albano, 1996; Noto et al., 1999; Shelhamer and Clendaniel, 2002b). Therefore, context clearly can have some effect. Again, it seems that adaptation usually generalizes but, if demanded, context specificity can occur.

Depth has also been used as a context (Chaturvedi and van Gisbergen, 1997). The amplitudes of saccades made toward the subject can be decreased while the amplitudes of saccades made away from the subject are increased.

### 4.9. Does adaptation occur conjugately for both eyes?

Experiments by Albano and Marrero (1995) indicate that adaptation occurs conjugately in humans (but see Averbuch-Heller et al., 1999). These experimenters required subjects to wear stereo-goggles, which presented the visual scene to each eye separately. Although an adaptation step was presented to one eye only while the other eye viewed a normal target step, both eyes gradually adjusted their saccadic amplitudes in the direction appropriate for the eye receiving the error (either amplitude increases or decreases). Furthermore, the amount of adaptation was similar for both eyes. Albano and Marrero (1995) did not compare the adaptation produced when only one or when both eyes experienced an adaptation step. In addition, when subjects experienced adaptation steps in one eye with the other eye patched, robust adaptation occurred in saccades made by the patched eye although it received no visual information that saccades were in error. It is unclear whether the amount of adaptation of saccades made by the patched eye was similar to that of saccades made by the viewing eye, since recordings were made only in the patched eye; however, any adaptation at all in the non-seeing eye indicates that adaptation is, at least in part, conjugate.

Other studies performed with the use of anisometric spectacles, which cause the two eyes to see the same target at different retinal locations, would argue that adaptation can act on the two eyes independently since, after viewing through such spectacles, subjects make disconjugate saccades (Erkelens et al., 1989; Lemij and Collewijn, 1991; Oohira et al., 1991). However, Bush et al. (1994) reported that when subjects wore such spectacles, their eye movements became disconjugate immediately (the other studies examined the eye movements a minimum of 1 h after the spectacles were placed on the subject). Based on this latter observation, such a change in conjugacy is not “adaptation” as we have been describing it thus far, i.e., one that represents a gradual neural rearrangement. Instead, this rapid change in conjugacy reflects the system’s ability to send the appropriate eye movement commands to each eye individually, if necessary. With the anisometric spectacles, the eyes “see” the target in different spatial locations, so monocular motor commands are necessary to acquire the target.

In the monkey, adaptation is thought to occur conjugately (Optican and Robinson, 1980; Snow et al., 1985). As described previously, when movement of one eye was impaired and a patch was placed over the good eye, *both* eyes increased the amplitudes of their saccades until the hypometric weak eye became more normetric. However, adaptation can also occur disconjugately (Snow et al., 1985). When a monkey viewed with both its weak and normal eye simultaneously, both eyes adjusted their saccadic amplitudes toward normal: the weak eye increased its amplitude and the normal eye adjusted its amplitude as necessary. We think that the evidence in the monkey suggests that true adaptation can occur disconjugately, if necessary, but the system defaults to

conjugate adaptation if it does not receive information that separate control of the two eyes is needed.

## 5. Where in the saccadic circuitry does adaptation take place?

### 5.1. Motor versus sensory

Adaptation of either the amplitude or direction of saccades could be largely a motor event that occurs after sensory signals about target location have been converted into a motor command. Alternatively, adaptation could affect the neuronal representation of the visual field. For example, a 10° target step in a 20% amplitude-reduction experiment would appear to be located at an 8° eccentricity. In this scenario, an 8° saccade accurately reflects the remapped visual world caused by a sensory adaptation.

There have been several approaches to answer the question of whether adaptation is a motor or sensory event. One approach has been to adapt saccades of one direction and amplitude and examine saccades of the same vector but elicited by target steps at retinal locations not used during the adaptation. In our laboratory, we decreased the amplitudes of saccades to 10° target steps along the horizontal meridian and then tested saccades of the same vector made to targets in a "virgin territory" by jumping a target first 10° vertically and then 10° horizontally (Wallman and Fuchs, 1998). The target was extinguished as the first (vertical) saccade occurred. Thus, at no time did a target appear at the 10° horizontal position on the retina. Across all monkeys and both target directions, there was ∼92% transfer from the adapted saccades to the horizontal saccades made in the virgin territory, suggesting that adaptation is a motor event. However, such transfer would also occur if adaptation had caused a visual remapping that extended well beyond the adapted horizontal meridian (recall that adaptation fields extend some distance from the adapted saccade). To evaluate the maximum possible contribution of visual remapping, we tested the amplitudes of single saccades made directly to the final target location after the second target step in the double-step paradigm. The amount of adaptation transfer to the horizontal component of these oblique saccades was ∼44%. Thus, some of the adaptation transfer seen in the double-step experiments could be due to the adaptation field, and therefore might be sensory. However, since the amount of transfer to the horizontal component of the oblique saccade was only ∼50% of the amount of transfer during the double-step paradigm, a substantial part of the adaptation is motor.

Similar double-step experiments with humans also yielded evidence that adaptation is a motor phenomenon, although the data are confounded by the possibility that the subjects could predict the location of the adapted stimulus (the target appeared in the same spatial location on every trial; Frens and van Opstal, 1994). Predictability of the target location could introduce a strategic component to the adaptation process. However, these authors further supported their conclusion by adapting targeting saccades and observing partial adaptation transfer to saccades elicited by auditory stimuli. Although these latter data are limited, statistics are not provided, and the decrease in amplitude of the auditory saccades is modest, these results also support the notion that amplitude adaptation is largely a motor event rather than a visual event.

Another approach has been to assume that any adaptation that produces a general reorganization of the representation of the visual world will affect all visuomotor behavior. Consequently, a variety of studies have asked whether saccadic adaptation transfers to other visually guided movements, such as head movements and finger pointing (McLaughlin et al., 1968; Bekkering et al., 1995; de Graaf et al., 1995; Kröller et al., 1996, 1999; Phillips et al., 1997). In humans, adaptation of targeting saccades did not transfer to head movements in the dark, which were guided on a trial-by-trial basis by verbal commands dictating when to start and stop moving the head. Nor did adaptation transfer to head movements to flashed visual targets, when the subjects were instructed to point their heads at the location of the flash (Kröller et al., 1996). In contrast, amplitude reduction of targeting saccades in the monkey does transfer (by 81%) to head-free gaze shifts and vice versa (75% transfer; Phillips et al., 1997).

The difference in the results of these two studies may be methodological since the types of head movements generated were quite different. In the human study, subjects slowly guided their heads towards the target under instruction or tried to point their heads at a flashed target. Such movements are slow enough to be guided by proprioceptive feedback from the neck, which may reduce or eliminate the effect of the adaptation. Also, an awareness of the head movements, as presumably occurs during the human study, may allow the subjects to cancel any adaptive changes. In contrast, during the monkey experiments, the head movements were components of a more natural horizontal gaze shift.

Studies of the transfer of saccadic adaptation to finger-pointing movements also yield conflicting results. McLaughlin et al. (1968) found that finger pointing to a target in an otherwise dark room was unaffected by a reduction in saccadic amplitude. In contrast, de Graaf et al. (1995) found that subjects with heads either fixed or free pointed short of a target when targeting saccades were reduced in size. In their most recent paper, however, they reported a transfer of <15%, which they concluded is "seemingly too small to have a clear functional meaning for gaze and hand coordination" (Kröller et al., 1999, p. 359).

An experiment described previously (see Section 4.5) also bears on the issue of whether adaptation is motor or sensory. In that experiment, subjects mislocated a test target relative to the saccade target in the same direction as the adapted saccade, leading the authors to suggest that the perception was influenced by information about the intended saccade (to the original target) rather than the actual adapted saccade

(Bahcall and Kowler, 1999). They concluded that because the perception was not affected by the adaptation, adaptation must have occurred after an efferent copy of the desired saccade, a premotor command, was sent to the perceptual system. However, the same findings would have resulted if adaptation had been completely sensory, in which case the eye movement command and the perception would remain in register and mislocations of the target would follow the direction of adaptation, as observed.

In a direct test of visual remapping, Moidell and Bedell (1988) asked subjects to judge the distance of a target from a central fixation point before and after adaptation of saccadic amplitude. A very modest but significant mislocation of the target in the direction of the adaptation did occur. Therefore, because no eye movements were made during this test paradigm, the authors suggested that amplitude adaptation could be due, in part, to a perceptual remapping of the visual world.

After considering the evidence from all the above experiments, we think that, at least for monkey, only a part of the adaptation process can be accounted for by a remapping of the neuronal representation of the visual field, and that most of the adaptation occurs where the signals in the saccadic pathway are in motor coordinates.

### 5.2. Behavioral experiments addressing the site of adaptation

#### 5.2.1. Adaptation transfer experiments in humans

As described previously (Section 3), we suggest that saccades of different cognitive complexities, as reflected in part by their latencies, might be subserved by different pathways within the saccadic system. Therefore, it is possible that the adaptive mechanism is acting at different loci for different types of saccade. If this is true, adaptation at a locus that affects one type of saccade may not transfer, or transfer only partially, to another type of saccade. Alternatively, adaptation may occur only after all the saccadic pathways converge, in which case adaptation of every type of saccade will transfer completely to every other. We now examine experiments that consider these possibilities.

We will present these transfer experiments by considering that saccades belong to one of two categories: (1) *reactive*, i.e., targeting and express, and (2) *higher-order*, i.e., delayed, memory-guided and scanning (Pierrot-Deseilligny et al., 1991; Deubel, 1995b). This dichotomy is based primarily on the latency of the saccade and its perceived degree of difficulty (see Section 2). Although future experiments may eventually prove that this dichotomy is too naïve, we think it provides a useful structure to allow us to understand the complicated results of the published transfer experiments. We will first discuss data that deal with amplitude adaptation transfer within each category and then highlight data that address amplitude adaptation transfer between categories.

*5.2.1.1. Transfer within a category.* Adaptation transfer between targeting and express, i.e., *reactive*, saccades is quite robust (Frens and van Opstal, 1994; Deubel, 1999; Hopp and Fuchs, 2002). In most cases, the amount of transfer between these two types of saccade was essentially 100% (Hopp and Fuchs, 2002), whether the transfer was from targeting to express or vice versa. Table 1 presents a summary of the amount of adaptation transfer produced by amplitude reductions of the various types of saccade in different studies.

The amount of adaptation transfer between various *higher-order* saccades is more variable and can depend on which saccade was adapted and which was tested. Deubel (1995b, 1999) reported that adaptation of scanning saccades transferred robustly to both delayed and memory-guided saccades (average transfer was 76 and 90%, respectively), but when memory-guided saccades were adapted, scanning saccades showed no significant adaptation.[2]

The amount of adaptation transfer from memory-guided to delayed saccades varies from one laboratory to another. Deubel (1995b, 1999) found that reducing the amplitude of memory-guided saccades did not cause significant reductions in the amplitudes of delayed saccades. On the other hand, Fujita et al. (2002) showed a significant, but only small, amplitude reduction in delayed saccades after adaptation of memory-guided saccades (average transfer 17%); therefore, transfer was only partial. In the reverse direction, reductions in the amplitudes of delayed saccades produced significant decreases in the amplitudes of memory-guided saccades; in four of six experiments the average transfer (32%) was partial (Fujita et al., 2002).

*5.2.1.2. Transfer across categories.* The amount of adaptation transfer between reactive and higher-order saccades also varies between laboratories. After adaptation of targeting saccades, Deubel (1995b, 1999) found no significant adaptation of memory-guided saccades. In contrast, Fujita et al. (2002) found that adaptation of saccades to flashed targets (saccades that presumably are similar to targeting saccades) produced significant changes in the amplitude of memory-guided saccades in the majority of either amplitude-increasing (2/2) or -decreasing (8/10) experiments. The average amount of adaptation transfer (∼50%) again was partial.

In the reverse direction, Deubel's (1995b, 1999) reductions in the amplitude of memory-guided saccades did not produce a significant amount of adaptation in targeting saccades. In contrast, when Fujita et al. (2002) reduced the amplitude of memory-guided saccades, they found significant adaptation of saccades to flashed targets in half of the experiments; however, transfer was only partial (31% on average). After memory-guided saccades were adapted to have *increased* amplitudes, only one of their four experiments in

[2] 'Significant adaptation' means there was a significant reduction in the amplitude of saccades.

Table 1
Adaptation transfer between different types of saccades in humans

| Tested Saccade Type \ Adapted Saccade Type | Targeting | Express | Scanning | Delayed | Memory-guided |
|---|---|---|---|---|---|
| **Targeting** | | 87% / 100%* | 37% / 31%** | 25% | NS / 31% |
| **Express** | 86% / 100%* | | ND | ND | ND |
| **Scanning** | NS | ND | | ND | NS |
| **Delayed** | NS / 26% | ND | 76% | | NS / 17% |
| **Memory-guided** | NS / 50% | ND | 90% | 32% | |

Thick solid lines separate reactive from higher-order saccades. Data presented above the slash in each box are from Deubel (1995, 1999). Data below the slash are from either Fujita et al. (2002), (∗) Hopp and Fuchs (2002), or (∗∗) Erkelens and Hulleman (1993). ND: no data available; NS: no significant reduction in the amplitude of the tested saccade type.

two subjects showed significant changes in the amplitudes of saccades to flashed targets.

The transfer of adaptation of targeting saccades to delayed saccades also varies between laboratories. When targeting saccades were decreased in amplitude, Deubel (1995b, 1999) found no significant adaptation of delayed saccades. Conversely, Fujita et al. (2002) found significant decreases in the amplitude of delayed saccades in four of six experiments; the average transfer in these experiments was partial (∼26%). When delayed saccades were adapted, half of the experiments showed only a partial transfer (average 25%) to saccades elicited by flashed targets (Fujita et al., 2002).

Finally, adaptation of scanning saccades transfers poorly to targeting saccades. Reduction of the amplitude of scanning saccades made between two constantly illuminated targets, both of which were shifted during the saccade, caused a small (average 5%), but usually significant, reduction in the amplitude of targeting saccades (average transfer ∼31%; Erkelens and Hulleman, 1993). A similar scanning-saccade adaptation paradigm with six targets also caused a small but significant reduction in the amplitudes of targeting saccades (average 7%) with an average transfer of 37% (Deubel, 1995b, 1999). In the reverse direction, no significant reduction in amplitude occurred in scanning saccades after adaptation of targeting saccades (Deubel, 1995b, 1999). Because the amount of transfer between scanning and targeting saccades was modest at best, both laboratories concluded that scanning and targeting saccades could be adapted independently.

*5.2.1.3. The existence of partial transfer.* In many human experiments, transfer appears to be partial (Table 1), but is partial transfer a methodological artifact or is it real? The partial transfer reported in some studies can be attributed to averaging over many experiments with different amounts of transfer (often ranging from 0 to 100%). However, in other studies, including unpublished data from our own lab, transfers of less than 100% do occur for specific experiments on individual subjects. Such true partial transfers are most likely to occur when the most difficult types of saccade are considered. Memory-guided saccades, for example, not only are inherently more variable but also are more difficult to adapt. For example, in our own unpublished experiments in which we employ identical 33% adaptation steps, the amount of adaptation ranges from 0 to 30% for memory-guided saccades, versus 9–18% for targeting saccades. The large variability of individual memory-guided saccades coupled with highly variable amounts of adaptation makes it difficult to establish a statistical difference between the adapted and tested saccades. Despite these caveats, we believe that partial transfer between certain types of human saccades does exist.

If partial transfer does exist, it implies that adaptation occurs at multiple sites in the saccadic system (Deubel, 1995b, 1999). Multiple sites of adaptation could also account for cases in which adaptation of one type of saccade transferred to another but the transfer was not as pronounced when the adapted and tested saccades were reversed. For example, if memory-guided saccades were adapted at a higher cortical area, there might not be adaptation of lower-order saccades, such as targeting saccades that are not routed through the same neuronal regions. However, if targeting saccades were adapted at a location that was part of the pathway for memory-guided saccades, there could be partial adaptation transfer from targeting saccades to memory-guided saccades. In this scenario, complete transfer would not be

expected because the generation of memory-guided saccades has an additional contribution from higher cortical areas, loci that would be unaffected by the adaptation of targeting saccades.

Because the existence of partial transfer imposes a major constraint on models of saccadic adaptation, future experiments must be designed to reveal under which conditions and to what degree adaptation transfer is partial. In particular, we need to determine the amount of transfer between saccades that clearly involve the cortex (e.g., memory-guided) and those that do not (e.g., express). In such experiments, combining data across all subjects, directions, and amplitudes for a specific experiment (e.g., memory-guided adaptation transfer to targeting saccades) should be avoided.

#### 5.2.2. Adaptation transfer experiments in monkeys

Transfer between various types of saccade in monkeys is quite different from that in humans. In our laboratory, transfer of targeting-saccade adaptation to all other types of saccade was very strong. It was essentially complete to delayed saccades (average transfer across experiments was ∼96%), express saccades (96%) and memory-guided saccades (88%; Fuchs et al., 1996). Transfer to scanning saccades, while less complete, was still substantial (average ∼69%); humans, on the other hand, exhibited no transfer at all in exactly the same conditions (Fuchs et al., 1996). Finally, we observed substantial transfer (average ∼75%) from targeting saccades to the saccades required to catch up to a smoothly moving target. It is important to realize, however, that these averages may be biased towards higher values because transfer was considered to be 100% whenever the amount of adaptation of the test saccades was not significantly different from that of the targeting saccades.

In contrast to the robust transfer described above, adaptation of targeting saccades did not transfer to the fast phases of either vestibular or optokinetic nystagmus, patterns of eye movements consisting of slow movements in one direction interrupted by rapid saccade-like movements in the other (Fuchs et al., 1996). Perhaps this is not very surprising because fast phases need only re-center the eye approximately; they do not need to be accurate or of a particular size, and they are not elicited by a specific visual target in space.

Because adaptation in monkeys is probably a motor event (Wallman and Fuchs, 1998), the monkey transfer experiments suggest that the locus of adaptation is at a site, such as the SC, common to the generation of all types of saccade. On the other hand, the locus of adaptation does not seem to reside in pathways associated with the fast phases of nystagmus.

#### 5.2.3. Adaptation occurs where saccades are still represented as vectors

At more central locations in the saccadic circuitry, neuronal discharge reflects the vector properties of the saccade. For example, neurons in the SC fire best for saccades of a specific amplitude and direction. Thus, the signals from these neurons are in vector coordinates (Sparks et al., 1976). At more peripheral locations, neurons in the pontine (BBG) and mesencephalic reticular formations discharge best for either horizontal or nearly vertical saccades, respectively or the horizontal and vertical components of oblique saccades. Therefore, at this level of the saccadic circuitry, the neural representation of the saccade has been broken down into its horizontal and vertical coordinates. Insight into the site of saccadic adaptation could be gained if we knew whether adaptation occurred when the saccade was represented as a vector or as vector components.

Three studies have yielded evidence that adaptation acts on the saccadic signal while it is still encoded as a vector. Deubel (1987) adapted oblique saccades made along an axis ∼20° clockwise of vertical and tested whether the adaptation transferred to oblique saccades made along an axis ∼20° counterclockwise of vertical. In his illustration of a single experiment in only one human, adaptation of the clockwise saccade indeed seemed to transfer to the counterclockwise saccade. Such transfer could not be explained by adaptation of the rightward horizontal component because adaptation of rightward horizontal saccades does not transfer to leftward horizontal saccades. Therefore, adaptation of only the entire clockwise saccadic *vector* would produce adaptation of saccades made to the counterclockwise target. Unfortunately, it was not clear whether there were significant changes in the individual horizontal and vertical components. Deubel (1987) suggests that a similar result is obtained in the monkey.

Wallman and Fuchs (1998) provide indirect evidence that adaptation occurs as a vector. Following adaptation of saccades to 10° horizontal target steps, there was only a ∼44% transfer to the horizontal component of oblique saccades elicited by oblique target steps with a 10° horizontal component. If adaptation had occurred on the horizontal and vertical components separately, an adaptation transfer of 100% to the horizontal component of the oblique saccade would have occurred.

Finally, as stated previously (Section 5.1), Phillips et al. (1997) reported that amplitude reductions of head-unrestrained gaze shifts in monkeys caused changes in both the eye and head components of the gaze shift. The most parsimonious explanation of these data is that adaptation occurs before the gaze command is separated into eye and head components and thus when gaze is still encoded as a vector.

Taken together, these studies suggest that adaptation of saccadic amplitude occurs at or upstream of the SC or at collicular descending pathways where the saccade is still encoded as a vector.

### 5.3. Neurophysiological investigations of the adaptation locus

The neuronal site of adaptation also has been investigated in a variety of neurophysiological preparations. The roles of

various saccadic structures, principally the SC and the oculomotor cerebellum, have been examined in recording, stimulation, and lesion studies on monkeys. Human patients with naturally occurring lesions of saccadic structures, as well as normal human subjects undergoing fMRI during adaptation, also have been studied.

#### *5.3.1. Studies on monkeys: involvement of the superior colliculus*

As a major descending source of saccade signals, the SC was an obvious structure to examine for involvement in saccadic adaptation. The SC projects either directly or through one or two interneurons to the burst generator, and many neurons in the SC discharge a burst of spikes with saccades (Sparks et al., 1976 and many others). As discussed earlier, saccade-related SC neurons have movement fields in that they discharge their highest-frequency bursts for saccades of an optimal vector and lower-frequency bursts for saccades that are larger or smaller or in a different direction than the optimal vector (Sparks et al., 1976).

Adaptation of saccadic amplitude apparently does not alter the behavior of burst neurons in the SC. Once Frens and van Opstal (1997) had determined a neuron's movement field, they reduced the amplitude of saccades of the optimal vector. For the two SC neurons that they illustrated in detail, the bursts for optimal vector saccades before adaptation were qualitatively similar to the bursts made for reduced-amplitude (sub-optimal vector) saccades made after the adaptation. Because similar bursts occurred for different-sized saccades to the same target step, the authors concluded that SC activity remained true to the desired, not actual, saccade size. Fitzgibbon et al. (1986) reported similar anecdotal data.

Frens and van Opstal (1997) quantified the effect of adaptation on the firing rate of a SC neuron by comparing, for each saccade during adaptation, the burst rate expected if the discharge were related either to desired eye displacement (i.e., the size of the target step) or to actual eye displacement. The residuals of these comparisons revealed significant correlations of burst rate with desired eye displacement and not with actual eye displacement, but in only ∼37% of their SC neurons. No cell showed the opposite correlation, i.e., a significant correlation of burst rate with actual eye displacement and not with desired eye displacement. Most (∼63%) cells, however, did not show significant correlations of burst rate with *either* desired or actual eye displacement. Nevertheless, the authors concluded that activity in the SC better reflects the desired eye displacement than the actual eye displacement and suggested that adaptation occurs at a site downstream of the SC.

To eliminate the possibility that the input signal to the SC had itself already undergone adaptation, in which case adaptation would have occurred upstream of the SC, Melis and van Gisbergen (1996) attempted to adapt saccades produced by direct stimulation of the SC. If, after a saccade was elicited in the dark by electrical stimulation, a target spot was made to appear either farther than or short of the saccade's expected landing point, saccadic amplitudes gradually increased or decreased, respectively. The course of these adaptations was slow and gradual, as in behavioral adaptation paradigms. Adaptation of these electrically evoked saccades suggests that adaptation occurs at or downstream of the SC. Furthermore, it supports the notion that adaptation is motor, not visual, because electrically evoked saccades are generated without a visual stimulus, so they could not be the result of a remapping of the visual world.

Adaptation of electrically evoked saccades transfers significantly, albeit incompletely, to targeting saccades. It is possible that targeting saccades, elicited by a visual stimulus, can utilize a non-collicular pathway, e.g., a direct projection from the FEF to the brainstem burst generator. In this scenario, partial transfer of adaptation might be explained if adaptation of electrically evoked saccades affects only saccadic pathways through the SC while pathways utilizing other structures remain unchanged. If a targeting saccade is generated using a signal from the SC *and* another structure(s), its amplitude will be only partially adapted because only the SC contribution has been adapted. This suggestion of distributed adaptation sites in the monkey is consistent with the possibility suggested earlier (Section 5.2.1) that adaptation occurs at multiple sites in the human saccadic system.

The complementary experiment of evaluating saccades evoked by electrical stimulation of the SC after adaptation of targeting saccades has produced inconclusive results. Early studies, which used currents of 50 μA (up to five times threshold), indicated that adaptation does not transfer from targeting saccades to those evoked by electrical stimulation (Fitzgibbon et al., 1986; Melis and van Gisbergen, 1996). These results suggest that saccadic amplitude adaptation occurs upstream of the SC, in marked contrast to the conclusion suggested by single-unit recording studies. Because it is likely that such large currents activated extensive patches of the SC, potentially masking the effects of the adaptation, Edelman and Goldberg (2002) used currents smaller than those used by their colleagues (Fitzgibbon et al., 1986). At 7 of 10 sites where currents of two times threshold for eliciting saccades on 50% of trials (<20 μA) were used, adaptation of targeting saccades caused >50% transfer of adaptation to electrically evoked saccades. In contrast, Melis and van Gisbergen (1996) found no adaptation transfer at two sites where stimulation was two times the threshold for eliciting saccades on 70% of trials. At sites where stimulation currents were much more than two times threshold (30–50 μA), adaptation transfer ranged from substantial (>50%), to none, to transfer in the wrong direction (Edelman and Goldberg, 2002). These results are perplexing because the amount of transfer, even for low currents, ranged from ∼22–100%, and even at high currents (>30 μA), there was substantial transfer at some sites. Also, under apparently similar experimental conditions, the study by Melis and van Gisbergen (1996) showed no transfer of adaptation whereas the study

by Edelman and Goldberg (2002) showed as much as 100% transfer. To resolve this discrepancy, it would be informative to vary stimulation strengths at a single site and determine the relation between stimulation strength and the amount of adaptation transfer.

It is difficult to draw a firm conclusion from the limited and conflicting evidence about the locus of adaptation relative to the SC. The two electrical stimulation studies have produced completely opposite results with respect to the transfer of adaptation from targeting to electrically evoked saccades (Melis and van Gisbergen, 1996; Edelman and Goldberg, 2002). Of course, there always is the question of whether electrical stimulation engages the natural saccade-generating mechanism. The unit-recording data (Frens and van Opstal, 1994) are problematic for a number of reasons. First, the authors' conclusions are convincing for only a third of their neurons. Second, even for these neurons, there were often very few adaptation trials so it is possible that the adaptation was not very robust; a robust behavioral adaptation is a desirable prerequisite to demonstrate a convincing effect on unit activity. Third, the analysis of the residuals is an uncommon technique that is not clearly presented; furthermore, the results derived from the analysis vary greatly between neurons.

The finding that a neuron's firing rate is the same before and after adaptation does not necessarily mean that the unit activity encodes desired eye displacement. An alternative explanation is that the movement field shifts toward a smaller preferred amplitude during the adaptation. In this scenario, adaptation would occur at the SC or at a site that contributes an input to the SC to regulate its topographic organization. To test whether the entire movement field shifts during adaptation, one could cause saccades in the same direction but with greater amplitude than the optimal vector of a neuron to undergo amplitude reduction. If the entire movement field indeed shifted during adaptation, the weak response for saccades with amplitudes much less than the optimal amplitude of the neuron should be enhanced. It also is possible that adaptation simply changes the shape of the movement field. Although a change in the shape might be difficult to detect, its occurrence would be consistent with a site of adaptation at the SC. Indeed, all the other data we have described for the monkey would be compatible with this suggestion.

*5.3.2. Studies on monkeys: involvement of the cerebellum*

The cerebellum has been implicated as a likely player in saccadic adaptation for several reasons. First, it is involved in other forms of motor learning in the vestibuloocular reflex, the blink reflex (Raymond et al., 1996), and the somatosensory system (Martin et al., 1996). Second, human patients with cerebellar lesions exhibit saccadic dysmetria, which often does not resolve substantially with time (Zee et al., 1976; Straube et al., 1995; Waespe and Müller-Meisser, 1996), suggesting that the establishment and maintenance of normal, accurate saccades requires a functioning cerebellum. Third, neurons in the midline cerebellum, including the CFN and overlying oculomotor vermis (OMV), lobules VI and VII, discharge saccade-related bursts whose timing variations could be used to adjust saccadic duration and hence amplitude (Fuchs et al., 1993; Ohtsuka and Noda, 1992). Indeed, consistent with this suggestion, specific lesions of the CFN (Villis and Hore, 1981; Robinson et al., 1993, 2002; Iwamoto and Yoshida, 2002) and OMV (Ritchie, 1976; Barash et al., 1999) in the monkey produce very dysmetric saccades, indicating that without the oculomotor cerebellum, the brainstem burst generator alone is incapable of producing accurate saccades. Fourth, the CFN projects directly to brainstem burst neurons involved in saccade generation (Scudder and McGee, 2000; Noda et al., 1990); therefore, changes in CFN activity can have a rapid influence on saccadic accuracy.

The cerebellum is required not only for the short-term control of saccadic accuracy but for saccadic adaptation as well. When oculomotor muscles (OCM) were surgically weakened, the hypometric horizontal saccades in the impaired viewing eye increase in amplitude over several days (Optican and Robinson, 1980; Snow et al., 1985). When the now hypermetric good eye became the viewing eye, saccadic amplitude decreased. After total ablation of the cerebellum, saccades of the viewing good eye became hypermetric with amplitudes that were two to three times normal. The hypermetria, which varied in magnitude with saccadic direction, amplitude and starting positions, was not corrected over time (2 months for one animal and 4 months for another). When the patch was switched to cover the normal eye, the amplitudes of saccades in the weakened viewing eye also showed no compensation (Optican and Robinson, 1980).

Similar results were found in animals with partial ablation of the cerebellum involving just the OMV and the fastigial nuclei (Optican and Robinson, 1980). The hypermetria, resulting from the ablation, was not corrected after either eye was patched.

Smaller lesions confined specifically to the fastigial and interpositus nuclei also impair a monkey's ability to adapt saccades (Goldberg et al., 1993; Robinson et al., 2002). After reversible inactivation of one CFN, saccades ipsiversive to (i.e., toward) the side of the injection became hypermetric while contraversive (away from the side of the injection) saccades became hypometric (Robinson et al., 2002). These animals were unable to adjust their saccades to simple target steps to compensate for the dysmetria after up to ~1000 trials in each direction. Recall that normal animals can reduce artificial dysmetrias substantially within 1000 trials (Fig. 3). Bilateral injections produced hypermetric saccades in both directions, and this dysmetria persisted after >1500 trials in each direction. Even when such monkeys experienced adaptation steps, they showed no evidence of any change in saccadic amplitude (Goldberg et al., 1993).

Robinson et al. (2002) further examined whether adaptation had indeed occurred during the tracking of simple target steps but could not be expressed through the inactivated cerebellum. They placed animals, whose CFNs had been inactivated bilaterally, in the dark so that the inactivation, and

thus the hypermetria, wore off in the absence of any visual feedback of the saccadic dysmetria. Afterwards, target steps that had elicited normetric saccades before inactivation now elicited hypometric ones, although it is not clear if the amplitude reduction was significant. This experiment suggests that the cerebellum delivers to the brain-stem burst generator adapted saccadic command signals that have been generated at some site upstream of the CFN, possibly in the OMV.

The effect of a compromised OMV on the ability to adapt saccades also has been studied, with inconsistent results. In one study, aspiration of the OMV produced disparate findings, which included no deficit in adaptation in one monkey, an initial deficit that resolved within 3 months in another monkey, and a complete deficit in a third (Takagi et al., 1998). In a second study, saccades tested 2 weeks after aspiration of the OMV were hypometric and had more variable amplitudes than normal (Barash et al., 1999). After 2 months or more, the average amplitude of saccades had returned to normal, but the variability remained. In addition, in the late post-lesion period, the animals were unable to adapt the amplitude of their saccades when exposed to adaptation steps. Furthermore, the amplitude of saccades to target steps of a fixed size and direction decreased over many identical trials, suggesting an inability to compensate for fatigue. In response to similar repeated target steps, no decrease in saccadic amplitude was observed in a monkey with an intact cerebellum. Taken together, data from this latter study suggest that lesions of the OMV spare a long-term mechanism for amplitude adaptation but eliminate short-term adaptive capabilities. Furthermore, short-term adaptation seems to be associated with the regulation of saccadic variability and compensation for the effects of fatigue. Finally, short-term adaptation depends on an intact OMV.

All monkey studies involving inactivation of the cerebellum by either reversible injections or lesions, produce grossly dysmetric saccades with overshoots or undershoots of >50% of the target steps. Perhaps such dysmetrias drive the adaptive mechanism out of its normal operating range, thereby eliminating its ability to function properly. Indeed, adaptation steps greater than ~50% of the target amplitude produce little adaptation (see previous discussion, Section 4.2.3, Robinson et al., 2003).

Because changes in saccadic amplitude can be produced within 1000 adaptation trials in the monkey and the activity of single units in the cerebellum often can be recorded for that long, it has been possible to examine changes in the discharge patterns of burst neurons in the CFN during adaptation. As ipsiversive horizontal saccades of 10° underwent behavioral amplitude reduction, Inaba et al. (2003) found a concomitant increase in the average discharge rate of the initial part of the burst in the six units studied. Also, the time of peak burst firing appeared to occur earlier for some units (two/three shown), although any timing differences in the associated burst would be difficult to ascertain because the adapted smaller saccade was barely shorter in duration. However, after the amplitude of larger (often ~30°) ipsiversive saccades was reduced by as much as 30% in animals with weakened eye muscles, Scudder and colleagues (Scudder, 2002; Scudder and McGee, 2003) showed that the burst began earlier than that of preadapted saccades in a majority of their 10 neurons. The earlier burst would be appropriate to help terminate the shorter-duration, adapted saccade. After contraversive saccades underwent either increases or decreases in amplitude, there were robust increases and decreases, respectively, in the number of spikes and the peak frequency of the burst. Because of the direct projections from the CFN to the brainstem burst generator (Scudder and McGee, 2000; Noda et al., 1990), it is reasonable to suggest that the changes in CFN activity with adaptation could be responsible for the changes that occur in saccade size.

Finally, stretching the extraocular muscles produces evoked potentials in the feline oculomotor vermis (Fuchs and Kornhuber, 1969; Baker et al., 1972). However, it is unlikely that such proprioceptive afferents to the cerebellum participate directly in saccadic adaptation because monkeys can still adapt after deafferentation (Lewis et al., 2001).

#### 5.3.3. Studies on humans: involvement of the cerebellum

The importance of the cerebellum for normal saccadic adaptation also has been demonstrated in humans. Like monkeys, human patients with cerebellar lesions have saccadic dysmetria that does not resolve over time, suggesting that the cerebellum has a role in maintaining saccadic accuracy (Zee et al., 1976; Straube et al., 1995; Waespe and Müller-Meisser, 1996). Unfortunately, there is no way to control for the extent of lesions in human patients. Nevertheless, most patients with a variety of cerebellar problems, including cerebellar degeneration, congenital malformations, and cerebellar infarcts could adapt their saccades when exposed to an adaptation paradigm but always by a lesser amount than could the average normal control subject (Straube et al., 2001). Patients with cerebellar cortical atrophy, on the other hand, were completely unable to undergo behavioral amplitude reduction (Waespe and Baumgartner, 1992). A patient with a superior cerebellar artery infarct involving folia VI and VII had normetric ispsiversive saccades, which she could adapt about half as well as normal subjects, and hypometric contraversive saccades, which she was unable to adapt at all (Waespe and Müller-Meisser, 1996). Finally, differential PET scans of normal subjects showed greater increases in metabolic changes in the medioposterior cerebellar cortex when the subjects experienced only backward adaptation steps than when they experienced intermixed forward and backward adaptation steps (Desmurget et al., 1998, 2000). No significant metabolic changes occurred in the SC, FEF, cerebellar nuclei, or parietal eye fields during adaptation.

Damaging the inputs to the oculomotor cerebellum also impairs the adaptation of saccadic amplitude. Patients with Wallenberg's syndrome, a lateral medullary lesion believed to interrupt olivo-cerebellar connections, show enduring

saccadic dysmetria (Waespe and Baumgartner, 1992; Waespe, 1995). The enduring dysmetria suggests that this interrupted input is important for the long-term maintenance of saccadic accuracy. The nature of the saccadic dysmetria seems to affect a patient's ability to adapt. Patients who primarily undershot the target (although overshoots also were observed) with both ipsiversive and contraversive saccades showed a reduced ability to adapt ipsiversive saccades and normal adaptive abilities for contraversive saccades. Patients who routinely overshot the target on ipsiversive saccades and undershot the target on contraversive saccades also showed a decreased ability to adapt ipsiversive saccades, but no adaptation was seen for the hypometric contraversive saccades.

*5.3.3.1. Insights from cerebellar models of saccadic plasticity.* Several of the neurophysiological studies described above implicate the cerebellum as the site of saccadic plasticity (Zee et al., 1976; Optican and Robinson, 1980; Waespe and Baumgartner, 1992; Straube et al., 1995; Waespe and Müller-Meisser, 1996; Desmurget et al., 1998, 2000; Takagi et al., 1998; Barash et al., 1999; Scudder et al., 2002; Scudder and McGee, 2003; Inaba et al., 2003). Two studies have examined the plausibility of this notion by incorporating the cerebellum into models for saccade generation (Dean et al., 1994; Schweighofer et al., 1996a,b). Both used episodic signals, provided by climbing fiber inputs to Purkinje cells from the inferior olive to enhance or depress sensory inputs that arrive via mossy fiber afferents. In both models, the "teacher" that enhances the efficacy of the mossy fiber to Purkinje cell synapse is a motor error signal associated with the corrective saccade that occurs after a saccadic dysmetria. In one model, the motor error signal originates in the SC (Dean et al., 1994), whereas in the other it originates in muscle stretch afferents (Schweighofer et al., 1996a). The changes in the responsiveness of Purkinje cells occasioned by saccadic motor learning alter some aspects of CFN discharge, such as burst rate (Schweighofer et al., 1996b), which then either alters the gain of the feedback loop (Dean et al., 1994) or alters the signal of putative premotor burst neurons that reside outside the feedback loop (see Schweighofer et al., 1996a for details).

Both models can simulate some aspects of saccadic adaptation. For example, one model replicates the course of behavioral adaptation in the monkey (Schweighofer et al., 1996b) and the other simulates both the oculomotor learning after muscle weakening in the monkey and the course of behavioral amplitude reduction in humans (Dean et al., 1994). Moreover, one model predicts that robust adaptation is possible even with a crude error signal that indicates only the sign of the error (Dean et al., 1994). Both also are able to produce saccades that have learned to compensate for the non-linearities associated with different orbital starting positions.

However, recent observations pose problems for both models. As we discussed above, adaptation can be made to occur without the presence of a corrective saccade (Wallman and Fuchs, 1998; Bahcall and Kowler, 2000; Noto and Robinson, 2001) and also without feedback from extraocular muscle afferents (Lewis et al., 2001). Also, neither of the models predicts the changes in timing of CFN discharges that accompany the saccadic amplitude changes in behavioral adaptation. (Admittedly, the model of Dean et al. (1994) does not attempt to simulate discharge patterns.) Also, many of the assumptions about the physiology are somewhat speculative. Nevertheless, these models serve to demonstrate that the cerebellum at least *could* implement amplitude adaptation.

*5.3.4. Studies on humans: involvement of non-cerebellar sites*

The capability of undergoing saccadic amplitude adaptation also has been examined in humans with lesions of saccadic sites other than the cerebellum. Patients with Parkinson's disease adapt targeting saccades as well as do age-matched controls (MacAskill et al., 2002). Memory-guided saccades, however, adapt more than demanded when patients are subjected to an amplitude-decreasing paradigm. Furthermore, even an amplitude-increasing paradigm induced a modest amplitude reduction in these patients. These data suggest that there are separate pathways for the adaptation of memory-guided and targeting saccades: the former utilizes the basal ganglia whereas the latter does not.

Patients with lesions in the cerebellar-recipient part of the thalamus, which receives the largest projection from the CFN (F.R. Robinson, personal communication), are able to adapt targeting saccades, but the amount of adaptation is less than normal for ipsiversive saccades and greater than normal for contraversive saccades (Gaymard et al., 2001). Patients with lesions to the part of the thalamus not associated with the cerebellum showed normal adaptation. These data suggest that a cerebello-thalamo-cortical loop plays a role in saccadic adaptation and are consistent with the notion that sites of adaptation are distributed throughout the saccadic system.

## 6. Conclusion

Most of our understanding about the neuronal mechanisms underlying motor learning is the result of experiments on motor reflexes such as the blink reflex and the vestibulo-ocular reflex. This review demonstrates that the saccadic system provides a unique opportunity to study motor learning of a voluntary, precise movement. Saccadic adaptation, at least the rapid component, occurs over a short period of time so that single units may be recorded while the adaptation actually is occurring. Because arguably more is known about the neuronal substrate of saccades than about any other voluntary motor response, many of the possible neural structures where adaptation might be implemented

already are well known. Furthermore, the roles of these structures in the generation of the wide variety of types of saccade have been documented.

Equipped with this basic knowledge, the oculomotor community has begun to make progress in understanding the characteristics and neuronal substrate of saccadic adaptation. Not surprisingly, this review has shown that there is some disagreement about the sites and mechanisms of saccadic adaptation. Nevertheless, we feel that the experiments to date have identified several issues that need to be resolved.

First, it is not obvious why the rates of rapid saccadic adaptation differ in monkeys and humans. This issue might be resolved by further experiments on the multiple adaptation processes with different rates (at least rapid and slow) that have been demonstrated in both species. Furthermore, the different adaptation processes may serve different aspects of saccadic adaptation, e.g., the rapid process primarily might control saccadic accuracy and the slow process might regulate saccadic variability (Barash et al., 1999). Finally, we must determine which neuronal structures serve the various adaptation processes in both species.

Second, transfer experiments in humans indicate that transfer within the reactive and higher-order category generally is stronger than that across categories. In contrast, monkeys show a robust transfer between adapted targeting saccades and all other types of saccade. The data on humans suggest that adaptation may be distributed to different sites within the saccadic system according to the type of saccade, whereas data in monkeys suggest a common site of adaptation at a location where descending commands for all types of saccade have converged. Specific experiments are needed to resolve these apparent differences. For example, in monkeys, it is necessary to perform transfer experiments in which higher-order, and not just targeting, saccades have been adapted. Such experiments may reveal selective or partial transfer between certain types of saccades. Furthermore, in humans, the possible existence of partial transfer between certain types of saccade must be substantiated because the existence of partial transfer would form the foundation for models of saccadic adaptation.

Third, to date only the neuronal correlates of the adaptation of reactive targeting saccades have been examined. The behavioral experiments on humans suggest that there are distributed adaptation sites for different types of saccade. Therefore, it will be important to reexamine sites such as the SC and CFN to determine whether those structures might participate in the adaptation of reactive saccades but not higher-order saccades or vice versa.

Fourth, the location of the site of adaptation in primates even for simple targeting saccades is unclear. In either species, we believe it has not been demonstrated adequately that adaptation occurs outside the SC for at least three reasons. First, in monkeys, there is robust transfer of adaptation from targeting saccades to a variety of other types of saccade whose generation involves the SC. Second, adaptation seems to occur when saccades are still in vector coordinates. Third, the results of the various neurophysiological studies that attempt to localize the site of adaptation relative to the SC in monkeys have produced conflicting or unconvincing results.

Finally, although several lines of evidence converge on the oculomotor vermis as the site of adaptation of targeting saccades, future experimenters should monitor the activity of Purkinje cells as adaptation occurs. In those experiments, the probability of occurrence of climbing fiber spikes should be altered as adaptation proceeds if they do indeed provide the error signal that drives this kind of motor learning.

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