Effect of Short-Term Saccadic Adaptation on Saccades Evoked by Electrical Stimulation in the Primate Superior Colliculus

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Edelman, Jay A. and Michael E. Goldberg. Effect of short-term saccadic adaptation on saccades evoked by electrical stimulation in the primate superior colliculus. J Neurophysiol 87: 1915–1923, 2002; 10.1152/jn.00805.2000. The brain maintains the accuracy of visually guided movements by using visual feedback to correct for changes in the nervous system and musculature that would otherwise result in dysmetria. In monkeys, evidence suggests that an adaptive mechanism can compensate for weakness in an extraocular muscle by changing the gain of the neural signal to the weakened muscle. The visual effects of such neuromuscular changes have been simulated using a short-term saccade adaptation paradigm, in which the target spot jumps to a new location during the initial saccade. Under these circumstances, over several hundred trials, monkeys gradually change the amplitude of their saccades so that the eye lands closer to the final location of the target spot. There is considerable evidence from lesion and single-unit recording studies that the locus of such saccade adaptation is downstream of the superior colliculus in the cerebellum. Paradoxically, previous research has indicated that saccades evoked by electrical stimulation in the superior colliculus are not modified by short-term saccade adaptation, suggesting that adaptation occurs in the oculomotor system upstream of the superior colliculus or else in a pathway that bypasses the superior colliculus. We tested whether this result was due to using suprathreshold stimulation currents. Stimulating at 44 low-threshold sites in the superior colliculi of three monkeys revealed that using low current levels evoked saccades that were modified by adaptation. Adaptation for visually guided and electrically evoked saccades had similar time courses and tended to be accomplished by a reduction in saccade velocity rather than a decrease in duration. Moreover, the more similar the velocity of electrically evoked and visually guided saccades prior to the start of saccadic adaptation the greater the effect of adaptation on electrically evoked saccades. These results suggest that the superior colliculus is indeed upstream of the locus of adaptation, corroborating previous lesion and single-cell recording studies, but that the mechanism mediating saccade adaptation is sensitive to the parameters of electrical stimulation.

INTRODUCTION

The primary purpose of saccadic eye movements is to move the eye quickly so that visual information from items of interest falls on the fovea, the most sensitive portion of the retina. Because saccades are executed too rapidly for visual feedback to ensure their accuracy, accurate movement must be maintained by an adaptive control system that uses the accuracy of recent saccades to adjust the motor program for the current saccade. Saccade dysmetria will result if changes to the properties of the system, such as those due to neuronal death and muscle damage, are not monitored and compensated for (Leigh and Zee 1991).

Previous research has demonstrated that the saccadic system can compensate for experimental lesions to the oculomotor apparatus. In monkey, Optican and Robinson (1980) showed that saccade accuracy can be restored after a horizontal rectus muscle is surgically weakened. Furthermore, they demonstrated that large aspiration lesions of the cerebellum prevented such a restoration in accuracy (Optican and Robinson 1980). These lesions were large and included both the oculomotor vermis and the deep cerebellar nuclei, areas of the cerebellum that have been shown to be involved in saccade generation (Fuchs et al. 1993; Keller 1989; Robinson et al. 1993).

Oculomotor deficits can be simulated in a standard eye-movement laboratory by shifting the location of a target during a saccade to that target (Albano and King 1989; Deubel et al. 1986; FitzGibbon et al. 1986; Fuchs et al. 1996; McLaughlin 1967; Miller et al. 1981; Straube et al. 1997). Repeated identical target shifts will cause the vector of the saccade to change gradually so as to land closer to the final target location. In monkeys, such short-term saccadic adaptation is often not completely effective; the saccade still lands some distance from the final target location even after many hundreds or thousands of trials (Straube et al. 1997). If this target shift is then removed, after repeated saccades, the changes in saccade vector will reverse and the saccades gradually return to their original size.

There is evidence that the cerebellum plays a role in short-term saccadic adaptation. Collicular signals can reach the cerebellum via the pons (particularly the nucleus reticularis tegmenti pontis) (Harting 1977; Huerta and Harting 1982) and possibly via cortical eye movement areas such as the frontal eye field (Sommer and Wurtz 1998), which can then relay the signals to the cerebellum through the pons. The cerebellum projects its output to the saccadic premotor burst generators in the brain stem that integrate the cerebellar modulatory and the direct signal from the superior colliculus (reviewed in Hepp et al. 1989; Keller 1989). Reversible lesions of the caudal fastigial nucleus (Robinson et al. 1993), irreversible lesions of the entire fastigial and interposed nuclei (Goldberg et al. 1993), and large permanent lesions of the oculomotor vermis in which the fastigial nucleus has been spared (Barash et al. 1999;
Takagi et al. (1998) eliminate short-term saccadic adaptation. Recent experiments in human also implicate midline cerebellar structures in saccade adaptation (Desmurget et al. 1998). Furthermore, there is evidence that the same cerebellar adaptive mechanism mediates both short-term saccade adaptation and adaptation caused by surgical weakening because these two types of adaptation progress at similar rates (Scudder et al. 1998).

The role of the superior colliculus in saccade adaptation is still unclear. It has long been known that saccades are accompanied by high-frequency discharge of neurons within a particular region of the superior colliculus starting ~25 ms prior to saccade onset, and this discharge is greatest for neurons near the center of this superior colliculus region. Conversely, for a given superior colliculus neuron, saccades to a certain region of visual space relative to present gaze, the neuron’s movement field, are accompanied by high-frequency discharge (reviewed in Sparks and Hartwich-Young 1989). Single-cell recordings provided evidence that changes in saccade vector during short-term saccadic adaptation were not accompanied by corresponding changes in the region of the colliculus active during a saccade (Frens and Van Opstal 1997). This suggests that the colliculus represents target displacement rather than actual eye displacement and thus that saccadic adaptation is mediated downstream of the superior colliculus or else in a pathway that bypasses it.

Electrical stimulation at the site of collicular presaccadic neurons evokes saccades at short latencies to a location corresponding to the center of the movement fields of these neurons (Sparks and Hartwich-Young 1989). If, as suggested by the single-cell recordings, adaptation occurs downstream of the superior colliculus, then the effects of short-term saccadic adaptation on visually guided saccades should transfer to saccades evoked by electrical stimulation. Instead, preliminary evidence from electrical stimulation studies showed the paradoxical result that saccades evoked by electrical stimulation of the superior colliculus were unaffected by short-term saccadic adaptation (FitzGibbon et al. 1985; see also Melis and van Gisbergen 1996).

The cause for this paradox between studies using single-unit recording and electrical stimulation is unclear. However, in the original FitzGibbon et al. (1985) study, only suprathreshold currents (50 μA) were used. Such high currents, while eliciting saccades with more or less normal metrics, may be activating a different ensemble of collicular activity than that active during a visually guided movement of similar vector. If the effect of adaptation on stimulated saccades depends on the ensemble of collicular activity being similar for visually guided and electrically stimulated saccades, then electrically evoked saccades may be more influenced by adaptation when they are evoked using current levels closer to the threshold for eliciting movement. In this report, we show that stimulating the colliculus at lower current intensities unMASKS a transfer of adaptation from visually guided to electrically evoked saccades.

METHODS

Animals and surgery

We electrically stimulated the intermediate layers of the superior colliculus at 52 low-threshold sites of three rhesus monkeys (Macaca mulatta). In preparation for these experiments, the monkeys were surgically implanted with a recording chamber above the dura mater at a position above the superior colliculus, a head holder that could be coupled to an animal chair to restrain the head during recordings, and scleral search coils in each eye. Eye coils were implanted using the method of Judge et al. (1980). The head holder and recording chamber were embedded in an implanted composed of dental acrylic attached to the skull by tungsten surgical-grade screws. General anesthesia was induced using ketamine (10.0 mg/kg), diazepam (1.0 mg/kg), and glycopyrrolate (0.01 mg/kg) and maintained with isoflurane. For two of the monkeys, the recording chamber was implanted several months after the head-holder device and eye coils. After surgery, animals were given the analgesic flunixin meglumine (Banamine) as needed (2.0 mg/kg). The antibiotic ampicillin (Polypelex) was administered every other day for the 2 week following surgery. Monkeys were allowed to recover 1 wk after surgery prior to their participation in these experiments. Each animal’s fluid intake, weight, and general health status were carefully monitored. All procedures were approved by the Animal Care and Use Committee of the National Eye Institute in compliance with the Public Health Service Guide for the Care and Use of Laboratory Animals.

Physiological methods

GENERAL PROCEDURES. Monkeys were housed unrestrained either singly or in pairs in between recording sessions. During recording sessions, the monkey sat comfortably with head restrained in a primate chair. The monkeys’ heads were restrained by attaching a metal post to the implanted head holder and using a metal sleeve to couple the post with another post attached to the chair. Neural activity was monitored and saccades electrically evoked using monopolar tungsten microelectrodes (Frederick Haer, Bowdoin ME) manipulated by an electric microdrive system. Electrodes had an impedance of 500 KΩ to 1 MΩ measured at 1 kHz. Electrodes were positioned within the recording chamber by being placed in a 23-gauge stainless steel guide tube and inserted into a hole of a plastic grid fastened inside the cylinder (Crist et al. 1988). A second guide tube inserted into the saline-filled chamber and resting above the dura served as the ground electrode.

ELECTRICAL STIMULATION. Constant-current electrical stimulation was applied using a two-channel stimulator connected to a pair of stimulus isolation units (Grass S88). Stimulation pulses were applied biphasically, positive first. Each positive and negative pulse was 0.25 ms in duration, and the negative pulse started immediately after the positive pulse ended. The pulse pairs were applied at 500 Hz. Electrical current varied from twice stimulus threshold to 50 μA but was kept constant during a session. Stimulation trains lasted for 50–120 ms, set to be long enough to ensure that evoked saccades would not be prematurely truncated by the cessation of stimulation. Current levels were monitored by measuring the voltage across a 1 kΩ resistor placed in series with the current flowing through the electrode. To select stimulation sites in the motor (intermediate and deep) layers of the superior colliculus, we advanced an electrode slowly into the superior colliculus while monitoring multiunit activity in a visually guided delayed-saccade task (Edelman and Goldberg 2001; Fischer and Boch 1981). The electrode tip was passed through the superficial layers to a depth 500 μm beyond the location at which we first observed perisaccadic discharge until we observed saccade-related discharge that dwarfed the temporally separate visual response. Stimulation threshold was defined as the current that elicited saccades on >50% of stimulation trains with amplitudes >50% of the saccades evoked by suprathreshold currents.

Experimental control and data acquisition

Experiments were controlled and data were collected using the REX (Real Time Experimental) control language (Hays et al. 1982) running on a Hewlett-Packard HP Vectra 486/337 computer
under the QNX operating system. Eye position was sampled and stored at 1000 Hz.

**Stimulus presentation**

Visual stimuli were generated by back projecting red-light-emitting diodes (LEDs) or red laser pointers (Edmond Scientific) onto a tangent screen located 57 cm away from the monkey (Crist and Robinson 1989). The positions of the projected light spots were controlled using two pairs of servo-controlled mirror galvanometers (General Scanning). The galvanometers could move a spot 20° in 8 ms. The intensity of the LEDs or laser spots was 1.0–1.3 cd/m². Experiments were run in complete darkness.

**Trial types**

Experiments were run after a suitable electrical stimulation site was found in the superior colliculus. Throughout the experiment four trial types were used. These were as follows.

**SINGLE JUMP.** In these trials, the target was presented to elicit saccades with a vector approximately that of the saccades evoked by electrical stimulation. Trials began with the appearance of a fixation point at the center of the screen. The monkey was required to fixate in a 2 × 2° “window” surrounding this point within 500 ms after its appearance. Three hundred to 550 ms after the eye entered this window the fixation point disappeared and a target appeared at the same location as the end point of the electrically stimulated saccades (Fig. 1A). The monkey was required to make a saccade to the target within 400 ms of its appearance. The saccade had to land within a window surrounding the target; the size of this window varied from 2 × 2 to 8 × 8°, depending on the radial eccentricity of the target. After fixating this target for 300 ms the monkey received a water reward.

**DOUBLE-JUMP TRIALS.** These trials were like the single-jump trials except that when an on-line saccade detector detected the start of the saccade (saccade speed >50°/s), the target LED was turned off. After this saccade was complete (25 ms after saccade speed dropped <50°/s), the target reappeared at a new location with the same direction as the initial target but with an eccentricity 50% of that of the initial target (Fig. 1B). To help ensure that saccades of only one vector were adapted, the initial target location was adjusted from trial-to-trial to take into account the small eye position variations in the monkey’s initial fixation. The target would only appear at the final location if the initial saccade landed in a wedge-shaped window surrounding the initial and final target locations. This window had an angular extent of 20° and extended in eccentricity from 2° less than that of the final target position to 2° more than that of the initial target position. Within 400 ms after the end of the first saccade the monkey’s eye position had to be located in a square window surrounding the final location; the size of this window varied from 3 × 3 to 5 × 5°, depending on the radial eccentricity of the target. The monkey could get into this final window by virtue of a second saccade if the first saccade did not land in this window. Eye position had to remain in this window for 400 ms before receiving a water reward.

**STIMULATION TRIALS.** These proceeded like the single- and double-jump trials up until the disappearance of the fixation point (Fig. 1C). One hundred fifty to 300 ms later a train of high-frequency stimulation was applied, using the parameters described above. 100 ms after the end of stimulation the monkey received a reward regardless of the effect of stimulation.

**PERPENDICULAR TRIALS.** These trials were identical to the single-jump trials except that the targets were presented so as to elicit a saccade with a direction approximately perpendicular to the direction of the electrically evoked saccades (Fig. 1D). We found that augmenting the experiment by increasing the variety of trial types enhanced the monkeys’ motivation. These trials were not analyzed.

If, in any of the trial types described, the monkey violated any of the corresponding temporal or spatial restrictions, the fixation or target LEDs were turned off and the monkey received no reward. An additional 800 ms period of darkness followed unsuccessful trials.

**Block types**

Experiments consisted of two or three blocks run in the order that they are described in the following text. Each block consisted of one or more of the trial types listed in the preceding text. To increase the uncertainty of trial type presentation and to help assess the relative time courses of the effects of adaptation on visually guided and electrically stimulated saccades, trial types for all blocks were run intermixed.

**PREADAPTATION BLOCK.** After the selection of a superior colliculus site for stimulation, 200–500 trials were run, ~55% of which were single-jump trials, ~10% of which were stimulation trials, and ~35% were perpendicular trials. If necessary, we adjusted the target position of the single-jump trials during this block so that the visually guided saccades matched the vector of the electrically stimulated saccades as closely as possible. After adjustment was complete we ran ≥30 single-jump trials before completing the preadaptation block.

**ADAPTATION BLOCK.** Seven hundred to 1,500 trials were run, ~55% of which were double-jump trials, ~10% of which were stimulation trials, and ~35% were perpendicular trials.

**POSTADAPTATION BLOCK.** If a monkey was still eager to work at the end of the adaptation block, we performed a block of trials with proportions of trials identical to the preadaptation block; ≤1,000 trials were run, depending on the monkey’s motivation. During all blocks, trial types were presented pseudo-randomly in accordance with the percentages described in the preceding text.

**Data analysis**

For each site, we determined a measure of the magnitude of adaptation for visually guided (single jump and double jump) and
For visually guided saccades the gain change is defined as

$$100\times (VG_{PRE} - VG_{ADP}) / (1\text{st target jump})$$

where $VG_{PRE}$ is mean saccade amplitude of the last 30 correct single-jump trials in the preadaptation block and $VG_{ADP}$ is mean saccade amplitude of the initial saccade in the last 100 correct adaptation trials in the adaptation block. First target jump refers to the difference between the fixation point and the initial target position in the single- and double-jump trials.

For electrically evoked saccades

$$100\times (ES_{PRE} - ES_{ADP}) / (1\text{st target jump})$$

where $ES_{PRE}$ was the average amplitude of all stimulation trials in the preadaptation block and $ES_{ADP}$ was the average amplitude of the stimulation trials whose trial numbers were within the range spanned by the last 100 double-jump trials in the adaptation block.

Finally, we define the effect of adapting the visually guided saccades on electrically evoked saccades as percentage of adaptation transfer, the change in electrically evoked saccade amplitude divided by the change in visually guided saccade amplitude.

Adaptation transfer = $100\times (ES_{PRE} - ES_{ADP}) / (VG_{PRE} - VG_{ADP})$

For the purposes of measuring these values, we eliminated trials for which amplitude was $>3$ SD different from the mean for the particular data subset. This step resulted in the elimination of $\sim 2\%$ of the trials.

Data analysis was performed using MATLAB and custom-written software running on a Pentium PC-compatible computer running Windows NT 4.0.

**RESULTS**

**Effect of short-term saccadic adaptation on saccades evoked by electrical stimulation in the motor layers of the superior colliculus**

We studied the effects of saccadic adaptation on the eye movements evoked by electrical simulation at 52 low-threshold sites (6–10 $\mu$A) in the motor layers of the superior colliculi of three monkeys. Data from five sites at which the saccade amplitude of electrically evoked saccades decreased significantly either as soon as the experiment began or else at a point not corresponding to the start of the adaptation block were not analyzed. Furthermore, during three sessions, the monkeys’ visually guided saccades failed to adapt significantly ($t$-test comparing saccade amplitude before and after adaptation—see METHODS). We analyzed data from the 44 remaining sites. Adaptation of visually guided saccades varied considerably from monkey to monkey and session to session; saccade amplitude typically reached an asymptote after several hundred trials.

**Dependence of adaptation transfer of electrically evoked saccades on stimulus current**

Short-term saccade adaptation affected electrically evoked saccades at most sites at which current was low (Fig. 2A). For sessions in which we observed such adaptation transfer (and in which we ran postadaptation trials), we noted that the saccade amplitude of electrically evoked saccades increased during the postadaptation block. Adaptation transfer was more likely to be minimal, or even negative (so that the amplitude of electrically evoked saccades increased during saccade adaptation), at high-current sites (Fig. 2B).

The relationship between adaptation transfer and stimulation current is shown for all 44 sites in Fig. 3 (see also Table 1). Note that for low currents, adaptation transfer approached, but rarely exceeded, a value of 100%. At high currents, there was considerable variability in the adaptation transfer. Across the 44 sites, adaptation transfer was inversely dependent on current (Pearson product-moment correlation coefficient, $r = -0.51, P < 0.001$).
is observed for the site portrayed in Fig. 2

trically evoked saccades, the time courses of electrically evoked saccades is also responsible for the change in amplitude of electrically evoked saccades. The mechanism modifying both visually guided and electrically evoked saccades due to short-term saccadic adaptation using first-order declining exponentials for the 11/44 sites at which adaptation transfer was >50% (curve fits of adaptation of electrically evoked saccades at sites with less adaptation transfer tended to have low goodness of fit). The mean rate constant for visually guided saccades, 121 trials, and that for electrically evoked saccades, 117 trials, were approximately equal (P = 0.79, by paired t-test). Furthermore, the rate constants for the visually guided and electrically stimulated saccades were correlated with each other across the 11 sites (R = 0.86, P < 0.01, Pearson product-moment correlation, Fig. 4). Finally, direct comparisons of the rate constants for each of the 11 sites revealed not a single statistically significant difference (at \( \alpha = 0.05 \)). These results are consistent with the existence of a single mechanism modifying both visually guided and electrically evoked saccades.

Does short-term saccade adaptation affect the saccade velocity and duration of the two types of saccades similarly?

It is still controversial whether changes in visually guided saccade amplitude resulting from short-term saccadic adaptation are due to changes in saccade velocity, saccade duration, or both (Abrams et al. 1992; Straube and Deubel 1995; Straube et al. 1997). Whatever the nature of the mechanism underlying visually guided saccade adaptation in our experiments, the hypothesis that the adaptive mechanism modifies visually guided and electrically evoked saccades similarly predicts that the relative changes in velocity and duration during and after adaptation should be similar for visually guided and electrically evoked saccades. We therefore measured visually guided and electrically evoked saccade peak velocity and duration before and after adaptation and computed their differences for the 11 low-threshold sites in the intermediate layers of the superior colliculus at which adaptation transfer was >50%. For both visually guided and electrically evoked saccades, we generally found that decreases in saccade amplitude were accompanied by decreases in saccade velocity. Indeed, considering the two types of saccades together, there was a consistent relationship between the reduction in saccade amplitude and velocity (Fig. 5A). In contrast, adaptation had little or no effect overall on the durations of electrically evoked or visually guided saccades (Fig. 5B). These results suggest that the amplitudes of both visually guided and electrically evoked saccades decrease due to reductions in saccade velocity rather than by shortened saccade durations. Like the findings from the analysis of time courses of adaptation described in the preceding text, they suggest that the mechanism entrained by the adaptation procedure processes collicular signals resulting from electrical stimulation as if they were saccades elicited by visual stimuli.

Dependence of adaptation transfer on differences in peak velocity prior to adaptation

What is still a mystery after these analyses is why there is so much variability in adaptation transfer when the current was high (50 \( \mu \)A). We noticed that at some sites the velocities of electrically evoked saccades prior to the onset of adaptation were much higher than those of visually guided saccades prior to adaptation. At other sites the velocities were much more similar. We speculated that if electrically and visually guided saccades had similar vectors and similar velocities then they might arise from similar ensembles of activity in the superior colliculus, regardless of the stimulation current used. If so, then in these experiments transfer of adaptation may be higher the more similar the velocities of visually guided and electrically evoked saccades prior to adaptation. We tested this idea by determining whether the amount of adaptation transfer for the 50 \( \mu \)A sites depended inversely on the difference between the peak velocities of the two classes of saccades (as measured prior to the onset of adaptation). An inverse-dependence of adaptation transfer on the difference in peak velocity was found for the 50 \( \mu \)A sites. For the 23 sites in the intermediate layers at which the stimulation current was 50 \( \mu \)A, adaptation transfer and the difference in peak velocity were significantly negatively correlated (\( r = -0.47, P = 0.02 \), Fig. 6).

Do stimulation latency or other factors influence the level of adaptation transfer?

Stimulation latency (the time between the onset of electrical stimulation and the onset of the saccade) of electrically evoked saccades may also influence the amount of adaptation transfer from visually guided to electrically evoked saccades. Low-frequency activity in the motor layers of the superior colliculus precedes the high-frequency perisaccadic burst (Glimcher and Sparks 1992; Munoz and Wurtz 1995). If the cerebellum is responsible for saccade adaptation, adaptation might require cerebellar circuitry to be entrained or otherwise activated by this low-level saccade-related activity. If so, then the lack of...
low-frequency activity sent from the colliculus to the cerebellum prior to electrically evoked saccades might result in lowered adaptation transfer. However, electrical stimulation could have a greater chance of engaging adaptive circuitry in the cerebellum if it endures longer prior to the actual onset of the saccade. This would predict that greater stimulation latency should result in a higher adaptation transfer. To test this, we assessed the relationship between adaptation transfer and stimulation latency. Because stimulation latency might also depend on current level, we confined our analysis to the 23 sites at which we used a current of 50 μA. Surprisingly, we found a modest negative correlation between stimulation latency and adaptation transfer for the 23 50-μA sites (r = -0.44, P = 0.03), with a 5.9% decrease in the value of adaptation transfer for every extra millisecond of latency.

Other factors could also influence the amount of adaptation transfer of electrically evoked saccades. Because large-amplitude gaze shifts are more likely to have a head movement component suppressed when the head is fixed, it is conceivable that the adaptation of small- and large-amplitude saccades are mediated by different mechanisms. If so, adaptation transfer may depend on the amplitude of the adapted saccade. However, across the 44 sites, this dependence was not found (r = -0.11, P > 0.48).

Finally, we tested whether the monkey could be using different mechanisms to alleviate the dysmetria imposed by the
adaptation task on different days. If this was the case, then adaptation transfer could depend on characteristics of the visually guided saccade adaptation, such as the change in saccade amplitude due to adaptation and rate of decrease of saccade amplitude during adaptation. Across the 44 sites, we did not find statistically significant dependencies of adaptation transfer on the amount of adaptation of visually guided saccades ($r = 0.02, P > 0.5$) nor on the rate constants of visually guided adaptation as calculated in the preceding text ($r = -0.08, P > 0.5$).

**DISCUSSION**

**Modification of saccades evoked by electrical stimulation in the SC by short-term saccadic adaptation**

This study has demonstrated that saccades evoked by electrical stimulation of the superior colliculus can be affected by short-term saccadic adaptation of visually guided saccades. We found that adaptation transfer was larger for currents near the threshold for electrically evoking saccades than for higher currents. In addition, we obtained evidence that visually guided and electrically evoked saccades are modified by similar mechanisms: rates of adaptation were similar for visually guided and electrically evoked saccades, and both types of saccades decreased in amplitude due to decreases in peak velocity rather than to decreases in saccade duration. These results now bring electrical stimulation studies into agreement with single-neuron studies in the superior colliculus (Frens and Van Opstal 1997) and lesion studies in the cerebellum (Barash et al. 1999; Goldberg et al. 1993; Robinson et al. 1993; Takagi et al. 1998), which suggest that the mechanism responsible for mediating short-term saccadic adaptation is located downstream of the superior colliculus.

**Relation to models of saccade adaptation**

Melis and Van Gisbergen (1996) demonstrated that saccades evoked by electrical stimulation could also be modified by an analogue of the short-term saccade adaptation procedure described here. They modified the amplitude of electrically stimulated saccades by adjusting the amplitude of the electric current, and observed a decrease in saccadic peak velocity.

**FIG. 4.** Comparison of rate constants of adaptation of electrically evoked saccades to those of visually guided saccades for the 11 sites at which adaptation transfer was >50% (see text for details).

**FIG. 5.** A: plots of relationship between the adaptation-induced reductions in peak velocity and saccade amplitude for visually guided and electrically stimulated saccades from data for the 11 sites at which adaptation transfer was >50%. For each type of saccade, 1 mark represents data for a single site. B: relationship between reduction in saccade duration and saccade amplitude. Same conventions as in A.

**FIG. 6.** Relation between adaptation transfer of electrically evoked saccades and difference in peak velocity of visually guided and electrically evoked saccades prior to onset of adaptation (during preadaptation block) for 23 sites at which stimulation current was 50 μA. Peak velocity difference is the absolute value of the difference in peak velocities between the stimulation trials and the single-jump trials divided by the peak velocities of the single-jump trials, expressed as percent. ○, data for a single site. See text for details.
evoked saccades by presenting a visual target immediately after the end of an electrically stimulated saccade at a location consistently different from that of the saccade end point. They also showed that adaptation of electrically stimulated saccades partially transferred to visually guided saccades. These authors used these findings to extend a model of saccade adaptation by Dean (1995). In this model (Melis and Van Gisbergen 1996), the frontal eye fields and superior colliculus provide crude and independent saccade displacement signals to the brain stem saccade burst generator and to a cerebellar adaptive mechanism. They reasoned that adaptation transfer is always partial because visually guided saccades utilize both the frontal eye field and superior colliculus pathways, whereas saccades evoked by electrical stimulation in the superior colliculus do not involve the frontal eye field pathway. Similar reasoning would argue that the adaptation of visually guided saccades should also result in some transfer to electrically stimulated saccades, and the authors pointed out that the findings showing no such adaptation transfer (FitzGibbon et al. 1985) (which they replicated but only at 2 sites) therefore did not fit the model.

In the sense that we show that electrically stimulated saccades can be affected by short-term saccade adaptation, contradicting the results of FitzGibbon et al. (1985), and that this adaptation transfer is very rarely as large as the adaptation for visually guided saccades, our data support the Melis and Van Gisbergen (1996) model. However, our data suggest that adaptation transfer depends on the level of activity in the superior colliculus and not simply whether or not the colliculus and frontal eye field are both activated.

How finicky is the mechanism mediating saccade adaptation?

Congruent with evidence presented here and in the experiments of Melis and Van Gisbergen (1996) and Frens and Van Opstal (1997) that saccade adaptation takes place downstream of the superior colliculus, there is strong evidence that saccadic adaptation is mediated by cerebellar structures adjusting their processing to minimize saccade dysmetria (Barash et al. 1999; Desmurget et al. 1998; Goldberg et al. 1993; Robinson et al. 1993; Takagi et al. 1998). This cerebellar mechanism may be too complicated to be modeled as a mere gain, especially because adapting saccades of one vector have an effect only on saccades of similar vectors (Albano 1996; Frens and Van Opstal 1994). In general, this mechanism must handle dysmetrias that may result from complex constellations of changes in relative strengths of eye muscles and saccade-related neural activity. It is thus possible that the saccadic adaptive mechanism is quite sensitive to the properties of the inputs.

If the adaptive mechanism has such sensitivity, it may influence saccade vector only if it receives a pattern of inputs similar to that which it was trained by short-term saccade adaptation to recognize. If so, the amount of adaptation transfer of saccades evoked from the superior colliculus would be greater with increasing similarity between the pattern of activity resulting from superior colliculus stimulation to that present during a visually guided saccade.

Our use of low-intensity current may provide such a replica of the activity present during a visually guided saccade. Evidence suggests that increasing the current of electrical stimulation progressively recruits neurons further and further from the stimulation site (McIlwain 1982; Tehovnik 1996). This implies that using suprathreshold currents activates a population of neurons that is much larger than that observed for visually guided saccades. Although we did find occasional sites where adaptation transfer was high even with suprathreshold currents, prior to adaptation the saccades evoked at such sites tended to have velocities similar to visually guided saccades of the same vector. This similarity in velocity suggests that the ensembles of neurons active for visually guided and electrically evoked saccades were similar, even for high currents.

How well can electrical stimulation substitute for naturally occurring neural signals?

Electrical stimulation of neural tissue has long been a favored tool for studying neural mechanisms in the intact brain (Tehovnik 1996). Eye-movement studies involving stimulation of the monkey superior colliculus have confirmed and extended findings gained from extracellular single-unit recording, namely that the superior colliculus can be represented as a motor map coding for saccade vector (Robinson 1972; Stryker and Schiller 1975) and that the level of superior colliculus activity influences saccade velocity (Stanford et al. 1996; Van Opstal et al. 1990).

However, other results from electrical stimulation experiments in the primate superior colliculus are in conflict to some degree with single-unit studies addressing the same questions. Besides prior experiments exploring mechanisms of saccade adaptation, it has been shown that saccade vectors evoked by electrical stimulation are much more dependent on orbital position than is neural activity (Azuma et al. 1996; Segraves and Goldberg 1992). A similar discrepancy holds for experiments exploring superior colliculus involvement in saccades generated in quick succession: stimulation studies have shown that the relationship between stimulation site and evoked saccade changes radically in the immediate wake of a previous saccade (Kustov and Robinson 1995; Nichols and Sparks 1995), whereas neurons in the superior colliculus appear to encode each saccade of a rapid double saccade sequence veridically (Goossens and Van Opstal 1997). Interestingly, in all of these studies, with the exception of that of Kustov and Robinson (1995), suprathreshold currents of \( \geq 40 \mu \text{A} \) were used.

The cerebellum may be involved in both compensating for the initial orbital position of the eye (Optican and Robinson 1980; Takagi et al. 1998), and in the brain stem saccadic feedback loop (Barash et al. 1999; Goldberg et al. 1993; Robinson et al. 1993; Takagi et al. 1998) (see also Quaia et al. 1999). Therefore it is possible that these prior collicular stimulation studies used currents that evoked cerebellar activity different from those for naturally occurring saccades. Use of currents closer to threshold in such experiments may yield results more congruent with single-unit studies. Our results provide a clear cautionary note that electrical stimulation cannot exactly mimic the ensemble of neuronal activity that occurs in association with a given behavior in real life. To avoid making erroneous conclusions about neural function based on the results of electrical stimulation, it may prove useful to probe such mechanisms using currents close to threshold and determine the sensitivity of results of electrical stimulation experiments to stimulation parameters.

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