Exp Brain Res (2005) 164: 194–204
DOI 10.1007/s00221-005-2242-9

RESEARCH ARTICLE

Leon Gmeindl · Andrew Rontal
Patricia A. Reuter-Lorenz

Strategic modulation of the fixation-offset effect: dissociable effects of target probability on prosaccades and antisaccades

Received: 4 August 2004 / Accepted: 13 November 2004 / Published online: 28 May 2005

Abstract In several previous experiments examining the effects of participants' expectations on oculomotor performance, the manipulation of target probability has been confounded with factors such as target occurrence and saccade frequency. We report results from three experiments that manipulated target probability in isolation from systematic variations in such bottom-up factors. We present evidence for trial-by-trial, top-down modulation of the fixation-offset effect in prosaccade latency. Furthermore, fixation-stimulus offset and target-probability manipulations had additive effects on antisaccade latency, suggesting that these factors influence separable neural processes engaged for antisaccade performance. Based on these findings, we suggest that cognitive processes utilizing target-probability information influence task processes engaged for prosaccades that differ from those engaged for antisaccades.

Keywords Brain · Control · Eye movements · Ocular fixation · Reaction time · Saccade

Saccadic eye movements are among the swiftest responses that humans can generate, in terms of both latency and duration. The superior colliculus (SC) of the midbrain has highly specialized circuitry for the rapid foveation of suddenly appearing peripheral targets (Schiller et al. 1987; Wurtz and Goldberg 1989). Stimulus-elicited saccades can be produced with diminished direct cortical input to the SC, as indicated by ablation studies in animals (e.g., Schiller et al. 1987) and by the performance of hemidecorticate humans (Reuter-Lorenz et al. 1999). In contrast, endogenously driven saccades depend on a network of eye fields in the frontal and parietal cortices (Everling et al. 1998c; Gaymard et al. 1998), and typically have long mean latencies relative to stimulus-elicited saccades.

Among the outstanding questions in eye-movement research is the extent to which top-down cognitive processes—that is, those processes that are strategic in nature and not stimulus-bound—can influence low-level oculomotor mechanisms. For example, how might one's expectations or task strategy influence the otherwise automatic workings of the eye-movement machinery? One study (Machado and Rafal 2000b) suggests a capacity for strategic modulation of the fixation-offset effect (FOE). The FOE refers to the reduction in saccade latency produced by extinguishing the fixated stimulus concurrently with the onset of the saccade target, and depends on activity within the SC. However, this and several other related studies are open to alternative interpretations because manipulations intended to influence top-down processing, such as the expectation of target presentation, covaried with bottom-up factors, such as the frequency of target presentation, that entailed systematic variations in stimulus and response processes across experimental conditions. The present research aims to manipulate and explain top-down influences on the FOE in isolation from extraneous bottom-up factors. More generally, we seek to further our understanding of the mechanisms underlying strategic control over the oculomotor system.

The effects of the presence or absence of a fixated stimulus on saccade latency have been studied extensively. When the fixated stimulus is extinguished 200–300 ms prior to the onset of a saccade target, mean latency is reduced by roughly 50 ms relative to when the fixation stimulus persists (Saslow 1967); this benefit is known as the gap effect (Reuter-Lorenz et al. 1991). Similarly, a reduction in latency, but of smaller magnitude, is observed when the fixated stimulus offsets concurrently with target onset (Klein and Kingstone 1993); this benefit is often referred to specifically as the FOE. The gap effect may be larger than the FOE because there is an inherent warning signal provided by the offset of the fixated stimulus prior to target onset

L. Gmeindl (✉) · A. Rontal · P. A. Reuter-Lorenz
Cognition & Perception, Department of Psychology,
University of Michigan, Ann Arbor, MI 48109-1109, USA
E-mail: lgmeindl@umich.edu
Tel.: +1-734-6150228
Fax: +1-734-7637480
E-mail: parl@umich.edu

(Reuter-Lorenz et al. 1995); in addition, the temporal delay following fixation-stimulus offset in the gap paradigm permits fixation-related neural activity to reach a lower level prior to target presentation.

Neurophysiological evidence suggests that the reduction in saccadic reaction time (SRT) due to fixation offset is mediated by a decrease in fixation-related neural activity that normally inhibits saccadic premotor and motor activity (Dorris and Munoz 1995). In particular, fixation neurons in the rostral SC normally inhibit the activity of more caudal buildup and burst cells that code saccade vectors. Fixation cells and vector-tuned premotor cells have also been identified in frontal cortices; antagonism within (Everling and Munoz 2000) and between (Schlag-Rey et al. 1992) these populations may also contribute to the FOE. At any rate, fixation-stimulus offset typically reduces fixation-related activity, which permits a corresponding increase in premotor activity, ultimately resulting in decreased SRT (Everling et al. 1999). Thus, the FOE is partly a stimulus-triggered phenomenon mediated by specialized circuitry within the oculomotor system.

A recent report suggesting that strategic factors can modulate the FOE is of particular interest given the documented reflexive nature of this effect. In an experiment that examined the effect of probability of target occurrence on the magnitudes of the gap effect and the FOE, Machado and Rafal (2000b) found a *decreasing* effect of fixation-stimulus offset as target probability increased. These authors suggested that when target probability is high, strategic cortical processes might tonically reduce SC fixation-cell activity, even in the presence of a fixated stimulus. This top-down process would reduce the exogenous effect of the fixation stimulus on SC activity. They proposed that the concomitant disinhibition of saccadic premotor activity would reduce SRTs and particularly so in fixation-overlap trials (i.e., when the fixation-stimulus persists following target onset), thereby resulting in a small FOE. In contrast, when target probability is low, higher levels of fixation-cell activity might be optimal, given that fixation must be maintained throughout the relatively frequent non-target trials under these conditions, thereby resulting in a larger FOE.

The Machado and Rafal (2000b) results are consistent with the view that top-down processes can influence stimulus-triggered mechanisms within the oculomotor system. However, one feature of their experimental design—that task conditions were blocked by target-probability level—permits an alternative interpretation. In the high-target-probability blocks, targets appeared in 80% of the trials, and in low-target-probability blocks, targets appeared in 20% of the trials; this means that in the former condition not only did participants expect to make saccades more frequently, but also targets occurred more frequently, and saccades were executed more frequently, than in the low-target-probability condition. The variation in frequency of target occurrence, stimulus-driven saccade execution, or both, across these trial blocks could have influenced oculomotor processes independently of any variation in the performers' expectations or strategies.

Indeed, in several previous studies of target-probability effects on saccade performance, the effects of strategic and bottom-up factors were confounded. For example, several studies (Basso and Wurtz 1997, 1998; Carpenter and Williams 1995; Dorris and Munoz 1998; Jüttner and Wolf 1992) have confounded the probability of a target's appearance at a particular location with the frequency of targets presented at, and saccades made to, that same location. Presumably, the targets presented at the probable location often elicited activity of neurons possessing the corresponding receptive field; neurons with the corresponding movement field likely were activated frequently as well. Consequently, stimulus-driven or response-driven neural modulation related to target-frequency and/or saccade-frequency, rather than participants' *knowledge* of target probability per se, may have produced the observed effects on SRT.

To illustrate the problem further, consider that Basso and Wurtz (1998) found reliable increases in SC buildup-neuron activity from the beginning to the end of trial blocks across which the probability of a target appearing at a given location was systematically varied. Did these changes reflect the monkeys' learning of the target probability or merely that more targets were presented at, and saccades made to, this location by the end of the trial block? Relevant to the latter possibility, single-unit recording has indicated greater pretarget activity in SC saccade-related neurons, and reduced SRT, on trials that were preceded by saccades of the same vector (Dorris et al. 2000; see also Dorris et al. 1999).

Also potentially supporting such a bottom-up explanation are results from a study conducted by Lueck et al. (1991). In this experiment, participants were required to saccade to alternating peripheral targets appearing at a frequency of either 1.15 or 0.18 Hz. While target location was equally predictable in both conditions, saccades made at the higher frequency had significantly shorter SRTs than did low-frequency saccades,[1] suggesting important factors of target and/or saccade frequency in determining SRT.

In view of the problems that complicate the interpretation of these previous studies, our goal was to design a task to assess the effects of top-down processing independently of variations in target frequency or saccade frequency. We therefore utilized a paradigm in which the probability of target appearance is manipulated on a trial-by-trial basis, such that the cumulative proportions of targets presented and saccades executed do not systematically vary as a function of target probability. An auditory cue at the beginning of each trial indicated the probability (0.8, 0.5, or 0.2) that a

[1]There appears to be no evidence for a performance tradeoff in Lueck et al. (1991), as saccade amplitude did not vary as a function of saccade frequency.

visual target would appear in the periphery. Target-probability and fixation-stimulus factors were manipulated orthogonally.

Given the possibility of strategic influence over SC activity, we predicted that FOE magnitude would decrease with increasing target probability for prosaccades (cf. Machado and Rafal 2000b). Results from two experiments indicate that the FOE can indeed be modulated by *purely* top-down influence, and suggest trial-by-trial cortical modulation of otherwise reflexive oculomotor processes underlying the FOE. Further insights into the dynamics of oculomotor control are contributed by a third experiment that examined the effects of target-probability and fixation-stimulus manipulations on the production of endogenously driven saccades, as required in the antisaccade task (Hallett 1978).

Experiment 1

Method

Participants

Nine right-handed participants (three women, six men; mean age = 22 years, SD = 3.6 years) provided informed consent prior to inclusion in this experiment, and were compensated with US $10/h for their participation. All participants reported normal hearing, no color blindness, and either normal or corrected to normal (with contact lenses) vision. The procedures in the three experiments reported here were approved by the University of Michigan Behavioral Sciences Institutional Review Board and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Apparatus

Eye-movement data were collected using infrared scleral-reflectance detectors mounted on a pair of special eyeglass frames, while the participant was seated in a dark, sound-attenuated testing booth (Model 402.A; Industrial Acoustics Company). Signal current was amplified through an Applied Science Laboratories amplifier (EYE-TRAC Model 210) and subsequently digitized with a sampling rate of 500 Hz. Stimulus light-emitting diodes (LEDs) subtending 0.5° of visual angle were driven at 1.6 lx (0.15 fc) illuminance by in-house LabVIEW 2.0 (National Instruments Corporation) computer code with a temporal resolution of 1 kHz. Two red LEDs were positioned along the horizontal axis at eye level 8.8° to the left and right of a central green LED. Auditory stimuli were presented with a small loudspeaker located directly below the central LED. (The loudspeaker was not visible in the darkness.) Each participant positioned his or her head comfortably on a chinrest, placed 60 cm from the central LED, in order to minimize movement artifacts.

Design and procedure

Subjects participated in two experimental sessions, each lasting approximately 1 h, on separate days. Each session consisted of five trial blocks, with 60 trials per block. The experimenter confirmed that each participant understood the written instructions before proceeding with testing. In the first session, participants completed one practice trial block before the test blocks were conducted.

For each trial (see Fig. 1), participants were told to look as quickly as possible at the target (illumination of a red LED) whenever it appeared, and to otherwise maintain fixation at the location of the green central LED. At the beginning of each trial, the central LED was illuminated, and a white-noise burst was presented for 200 ms, indicating that fixation had to be maintained until either a target was presented (in target trials) or the end of the trial occurred (in catch trials). Eight hundred milliseconds following the offset of the white-noise burst, one of three levels (0.8, 0.5, 0.2) of target probability [$P(T)$] was indicated validly for that trial by an auditory cue (Q_n, where n = number of tones): for $\boldsymbol{P(T \mid Q_1) = 0.2}$, one 600-ms tone was presented; for $\boldsymbol{P(T \mid Q_3) = 0.5}$, three 400-ms tones were presented with a 40-ms interstimulus interval (ISI); and for $\boldsymbol{P(T \mid Q_6) = 0.8}$, six 200-ms tones were presented with a 40-ms ISI. All tones had a frequency of 2 kHz

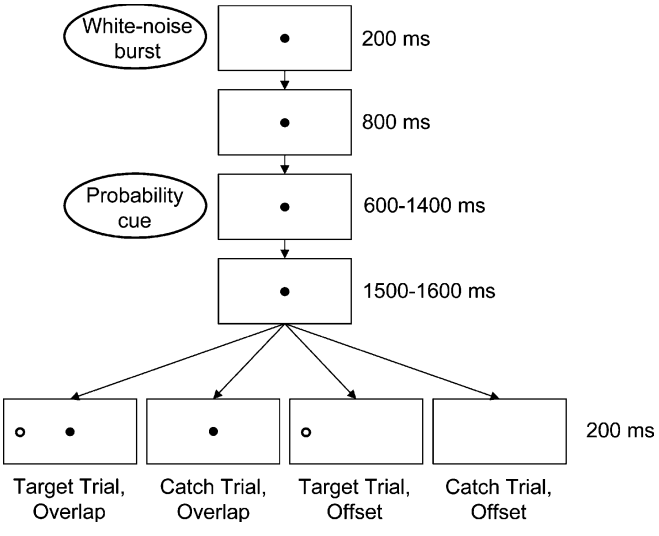

Fig. 1 Sequence of trial events. The durations of events are indicated to the *right* of the *panels*. *Large ovals* represent auditory stimuli presented centrally. *Black dots* represent the central fixation stimulus, and *black circles* represent saccade targets. The four conditions depicted in the *bottom row of panels* were interleaved within each trial block. On each target trial, target location was presented pseudorandomly 8.8° to the left or to the right of the fixation-stimulus location. The probability-cue duration depended on which cue was presented (see text for details)

and an intensity of 60 dB at 60 cm from the loudspeaker. Participants were instructed to use the target-probability information indicated by the cues to optimize their performance.[2]

An ISI varying randomly between 1,500 and 1,600 ms (in 20-ms increments) occurred between the auditory cue and the peripheral target in target trials in order to reduce predictability of target onset, and therefore to minimize potential anticipatory responses. Targets were presented for 200 ms, and target location (left or right of fixation) was randomized. Target onset (in target trials) or omission (in catch trials) was followed by a 900-ms response window and subsequent 2-s intertrial interval.

Each level of target probability, along with its corresponding auditory cue, was presented pseudorandomly (i.e., with a constraint ensuring equal numbers of trials per level) within a trial block. Thus for any given trial, approximately one half of the preceding trials contained targets and, assuming correct responses, saccades to target locations. As a result, we were able to examine the trial-by-trial effects of knowledge of target probability on saccade performance in the absence of confounding bottom-up factors of target and response frequency.

In one half of the trials (offset), the green central LED was offset at the same time that the peripheral target was either onset (target trial; ISI = 0 ms) or omitted (catch trial). In the other half of the trials (overlap), the green LED remained illuminated for the duration of the trial, regardless of target occurrence. Fixation type (offset, overlap), target probability (0.2, 0.5, 0.8), target location (left, right), and trial type (target, catch) were all counterbalanced within each trial block.

Data analysis

Our analysis routine automatically determined saccade latency by applying a velocity criterion of 50°/s for three consecutive samples. The experimenter verified the accuracy of this routine by inspection of the digitized eye-movement waveform for each trial. Trials displaying blink artifacts or signal noise were excluded from further analysis.

Outliers from correct SRT distributions for target trials were removed according to a trimming procedure (Schumacher et al. 1999). Mean SRTs were then subjected to a repeated-measures analysis of variance (ANOVA), with fixation type (offset, overlap) and target probability (0.2, 0.5, 0.8) designated as within-subjects factors.

Counted as errors were saccades initiated before, or within 70 ms after, target onset (anticipations); omissions of saccades during target trials (misses); saccades executed in the wrong direction (direction errors); and saccades made during catch trials (false alarms). For the last two categories, saccades with latencies greater than three standard deviations above the longest correct mean RT observed in the experiment were trimmed out. Categories in which errors occurred on 1% or fewer of candidate trials were not analyzed further.

Results

Correct saccades

Latency results are plotted in Fig. 2. While mean SRTs observed here are longer than in some prosaccade studies, they are comparable to those reported in a similar study by Machado and Rafal (2000b). As predicted, the difference between overlap and offset SRTs (i.e., FOE magnitude) decreased monotonically (45.5, 26.0, and 21.8 ms, respectively), as target probability increased from 0.2 to 0.5 to 0.8; the corresponding fixation type × target probability interaction was reliable, $F_{(2,16)} = 3.15$, $p = 0.035$ (one-tailed). Pairwise contrasts (Bonferroni-corrected $\alpha = 0.017$) revealed a reliably smaller FOE magnitude for $P(T \mid Q_6) = 0.8$ compared with $P(T \mid Q_1) = 0.2$, $t(8) = 2.65$, $p = 0.015$ (one-tailed); FOE magnitude did not differ reliably between $P(T \mid Q_6) = 0.8$ and $P(T \mid Q_3) = 0.5$, $t(8) = 0.43$, $p = 0.34$ (one-tailed), or between $P(T \mid Q_3) = 0.5$ and $P(T \mid Q_1) = 0.2$, $t(8) = 1.68$, $p = 0.07$ (one-tailed). The fixation type × target probability interaction was driven by a greater reduction in overlap SRT (46.1 ms) than in offset SRT (22.3 ms) as target probability increased from 0.2 to 0.8.

Additionally, there were main effects of fixation type, with offset SRTs reliably shorter than overlap SRTs (252.0 vs 283.1 ms, respectively), $F_{(1,8)} = 25.23$, $p = 0.001$,

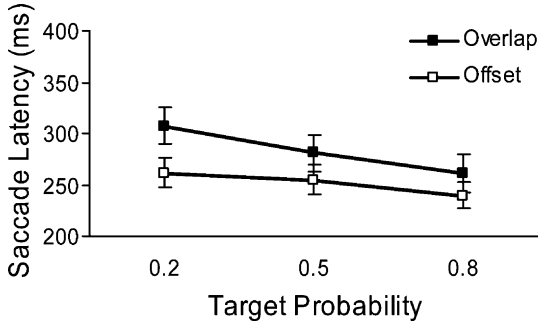

Fig. 2 Experiment 1, mean SRT (±SE) as a function of target probability and fixation type

[2]To confirm that these auditory cues were easily distinguishable, and therefore could be relied upon to convey target-probability information, a control experiment utilizing identical stimulus presentation parameters as in experiment 1 was conducted. There, six participants were required to report vocally "one," "three," or "six" immediately after the presentation of Q_1, Q_3, or Q_6, respectively, at the beginning of each of 60 trials. These participants were required to saccade to targets when presented, and to otherwise maintain fixation, just as were the participants in experiment 1, although they were not informed of the tone-to-probability mapping. For these control participants, no vocal-response errors were made, indicating that the auditory cues were highly distinguishable.

and of target probability, with SRT decreasing as target probability increased from 0.2 to 0.5 to 0.8 (284.6 vs 267.6 vs 250.4 ms, respectively), $F_{(2,8)} = 25.93$, $p < 0.001$.

Errors

In general, few errors were made. Anticipations, direction errors, and misses occurred on 1% or fewer of candidate trials. However, more false alarms occurred on offset trials than on overlap trials, χ^2 (1, $N = 244$) = 126.95, $p < 0.001$, and this held for each of the target-probability levels (all p values < 0.001).[3] This result is consistent with increased movement-cell activity triggered by removal of the fixation stimulus.

Discussion

In experiment 1, FOE magnitude was modulated by target probability, despite the absence of any systematic variation in the cumulative proportion of targets and saccades across different levels of target probability. This suggests that the FOE can be modulated by purely top-down processing. Furthermore, comparison of mean latencies (see Fig. 2) indicates a greater reduction in SRT for overlap trials than for offset trials as target probability increased. This interaction was unlikely to be due to a floor effect at high target probability, as the shortest observed mean SRTs (i.e., at $P(T \mid Q_6) = 0.8$) were longer than those found in studies of express saccades (Kalesnykas and Hallett 1987; see also Reuter-Lorenz et al. 1991). Instead, this interaction is consistent with the proposal that strategic processes can modulate SC fixation-cell activity, even in the presence of a fixated stimulus (Machado and Rafal 2000b).

To rule out alternative explanations based on the contribution of stimulus-driven factors for the reduction in FOE magnitude, we considered the hypothesis that the auditory cues signaling target probability presented at the beginning of each trial could have produced greater or lesser physiological arousal, or other unintended alerting effects, that may have influenced saccade latency. For example, the cue indicating $P(T \mid Q_6) = 0.8$, given its longer duration and the tones' multiple sudden onsets, may have been more alerting than the single tone for $P(T \mid Q_1) = 0.2$. This possibility seemed unlikely to account for the results, however, since at least 1,500 ms preceded target onset (see Nickerson 1967). Nevertheless, we conducted a second experiment in which the tone-to-probability mapping was reversed. Here, we omitted the 0.5-probability condition, as experiment 1 indicated that a comparison of the 0.8-probability and 0.2-probability conditions was sufficient to reveal differences in FOE magnitude as a function of target probability. This change also reduced the discriminative processing required of participants to utilize the information conveyed by the auditory cues, and increased the power of the most sensitive probability manipulation.

[3] Because small numbers of false alarms (e.g., five) were observed for at least one condition of interest in each of the three experiments reported here, despite collapsing across subjects, we do not present statistical analyses of false alarm latency.

Experiment 2

Method

The materials and methods in experiment 2 were identical to those in experiment 1, except for the following modifications: (1) the $\boldsymbol{P(T \mid Q_3) = 0.5}$ condition was omitted, and (2) the tone-to-probability mapping was reversed, so that $\boldsymbol{P(T \mid Q_6) = 0.2}$, and $\boldsymbol{P(T \mid Q_1) = 0.8}$.

Participants

Five right-handed participants (two women, three men; mean age = 20 years, SD = 0.4 years) who did not participate in experiment 1 provided informed consent to participate in this experiment, and were compensated with US $10/h. All participants reported normal hearing, no color blindness, and either normal or corrected to normal (with contact lenses) vision.

Results

Correct saccades

Latency results are plotted in Fig. 3. The FOE magnitude decreased from 81 to 28 ms as target probability increased from 0.2 to 0.8; the corresponding fixation type × target probability interaction was reliable, $F_{(1,4)} = 8.27$, $p = 0.023$ (one-tailed). Also replicating the pattern of results from experiment 1 was a greater reduction in overlap SRT (76 ms) than in offset SRT (23 ms) as target probability increased from 0.2 to 0.8.

Additionally, there were reliable main effects of fixation type, with offset SRTs reliably shorter than overlap SRTs (261 vs 315 ms, respectively), $F_{(1,4)} = 14.54$, $p = 0.02$, and of target probability, with SRT decreasing as target probability increased from 0.2 to 0.8 (313 vs 263 ms, respectively), $F_{(1,4)} = 33.61$, $p < 0.01$.

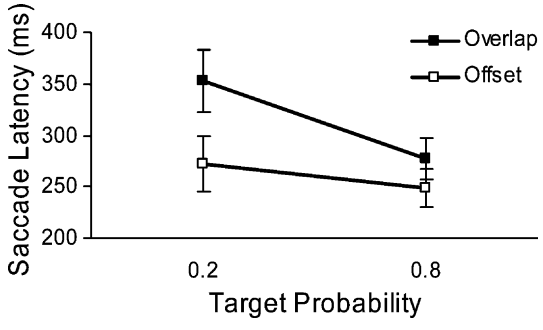

Fig. 3 Experiment 2, mean SRT (±SE) as a function of target probability and fixation type

Errors

Anticipations and direction errors occurred on 1% or fewer of candidate trials. As observed in experiment 1, more false alarms occurred on offset trials than on overlap trials, χ^2 (1, $N = 165$) = 107.21, $p < 0.001$, and this difference was reliable for each of the target-probability levels (both p values < 0.001). As stated above, this result is consistent with increased movement-cell activity triggered by removal of the fixation stimulus. In addition, after normalizing for the proportions of target trials presented in each target-probability condition, over three times as many misses occurred for $P(T \mid Q_6) = 0.2$ than for $P(T \mid Q_1) = 0.8$, χ^2 (1, $N = 55$, normalized) = 15.97, $p < 0.001$. This result is consistent with decreased stimulus-detection and/or movement-related preparation in the low-target-probability condition. No other reliable effects were observed.

Discussion

The results from experiment 2 replicate the reduction in FOE magnitude with increasing target probability observed in experiment 1, despite the reversal of the tone-to-probability mapping. This finding rules out alternative explanations of FOE modulation based on differential alerting effects of the auditory cues. Importantly, these data provide further confirmatory evidence for purely top-down modulation of the FOE. Moreover, the greater reduction in overlap SRT than in offset SRT as target probability increased again suggests a modulation of fixation-related neural activity despite the persistence of a fixated stimulus.

An important question that bears on the theoretical significance of our findings for distinguishing between alternative models of oculomotor control concerns whether the dependence of the FOE magnitude on target probability is restricted to prosaccades alone, or applies also to saccades requiring more extensive voluntary control, such as those made in the antisaccade task—a task in which the performer must execute a saccade to the location opposite that of a suddenly appearing peripheral target (Hallett 1978).

To perform the antisaccade task, participants must inhibit reflexive saccades toward suddenly appearing peripheral targets. How might this be accomplished? Neuropsychological and neurophysiological research provides evidence for a critical role of cortical structures in inhibiting reflexive saccades. For example, some studies (e.g., Guitton et al. 1985; Pierrot-Deseilligny et al. 1991) have shown that frontal cortical damage can lead to a deficit in inhibiting stimulus-directed saccades. Microstimulation of frontal areas, in contrast, can arrest prosaccades (Burman and Bruce 1997; Schlag-Rey et al. 1992). In addition, several cortical regions of the frontal and parietal lobes project either directly or via subcortical pathways to the SC, providing both inhibitory and excitatory modulation of SC activity (Segraves and Goldberg 1987; Selemon and Goldman-Rakic 1988; Sommer and Wurtz 2000; Sparks and Hartwich-Young 1989). Furthermore, hemidecorticate patients produce frequent contralesional prosaccade errors in antisaccade tasks (Reuter-Lorenz et al. 1999), indicating a lateralized cortical inhibition of oculomotor mechanisms.

In conjunction with reflexive-saccade inhibition, the spatial components (i.e., amplitude and direction) of the correct antisaccade must be computed. Again, several cortical regions (parietal cortex: Everling et al. 1998c; Matthews et al. 2002; supplementary eye fields: Schlag-Rey et al. 1997; frontal eye fields: Schlag-Rey et al. 1992) are likely to play important roles in the endogenous determination of antisaccade vectors.

How might the cortical processes responsible for endogenously directed saccades influence the reflexive processes underlying the FOE? Several previous studies (e.g., Abrams et al. 1998; Craig et al. 1999; Reuter-Lorenz et al. 1991, 1995) have found unreliable, or relatively small, effects of fixation-stimulus offset in antisaccade tasks. This is consistent with the possibility that the output of collicular motor processes, or the collicular processes themselves, may be suppressed by the cortex and/or other structures (e.g., substantia nigra pars reticulata: Basso and Wurtz 2002; Hikosaka and Wurtz 1983; omnipause neurons in the pons: Everling et al. 1998b; Moschovakis and Highstein 1994) while the antisaccade vector is computed and subsequently driven by the cortex (Everling and Munoz 2000; Schlag-Rey et al. 1992, 1997). Extended voluntary maintenance of SC fixation-cell activity following target onset could provide a mechanism for the inhibition of reflexive saccades during the (relatively slow) cortical computation of the antisaccade vector (Forbes and Klein 1996; Machado and Rafal 2000a). However, Everling et al. (1999) have shown that SC fixation-cell activity drops during the temporal gap following fixation-stimulus offset for both prosaccades and antisaccades in the gap paradigm. In addition, single-unit recordings have demonstrated activity corresponding to correct antisaccade vectors in SC buildup and burst cells (Everling et al. 1998a, 1999), indicating that SC motor-related processes are not quiescent for antisaccades, although they are less active than for prosaccades. These results suggest that the SC may play a functional role in the preparation and execution of antisaccades.

But if this is the case, then why is FOE magnitude typically smaller for antisaccades than for prosaccades? Some researchers (e.g., Trappenberg et al. 2001) have claimed that because it takes longer to initiate an antisaccade than a prosaccade, the effect of fixation-stimulus offset on neural activity occurs too early in the course of a trial to produce large effects on the processes responsible for executing antisaccades. Recent behavioral evidence (Machado and Rafal 2000a) suggests, however, that fixation-stimulus offset has different effects on the processes or neural structures engaged for voluntary saccades from those responsible for reflexive saccades; as a result, the FOEs observed in different studies may

reflect the workings of different saccade mechanisms, depending on the task demands and on the strategies employed.

This evidence, along with task analysis, suggests that information about the probability of target presentation might have different effects on FOE magnitude for antisaccades than for prosaccades: if high-target-probability cues in the prosaccade task are used to reduce fixation-related neural activity (e.g., in the SC), as is consistent with experiments 1 and 2, whereas this information is used in the antisaccade task to modulate activity in brain structures (e.g., in cortex) distinct from those reflexively driven by the presence of a fixation stimulus, one might predict that target probability and fixation type factors would have additive effects on antisaccade SRT (for additive-factors logic, see Sternberg 1969). Indeed, we arrived at this prediction based on the performer's need in the antisaccade task always to inhibit reflexive saccades in target trials and to maintain fixation in catch trials.[4] Accordingly, a high rate of fixation-cell firing may be maintained prior to target onset, regardless of target probability, thereby producing an invariant FOE magnitude. In experiment 3, we combined the target-probability and fixation-stimulus manipulations used in experiment 2 with an antisaccade task to test this hypothesis.

Experiment 3

Method

The materials and method in experiment 3 were identical to those in experiment 2, except that participants were required to saccade to the location opposite that in which the target appeared. Additionally, 40 rather than 60 trials were presented in each of the trial blocks; however, a third session was added to the design in order to equate the statistical power across experiments 2 and 3 for observing any variation in FOE magnitude as a function of target probability within subjects.

Participants

Ten right-handed participants (six women, four men; mean age = 20 years, SD = 0.9 years) who did not participate in the previous experiments provided informed consent and were compensated with US $10/h. All participants reported normal hearing, no color blindness, and either normal or corrected to normal (with contact lenses) vision.

[4]Everling et al. (1999) found greater SC fixation-cell activity prior to fixation-stimulus offset for antisaccades than for prosaccades, indicating a higher level of saccade inhibition in the former task.

Results

Correct saccades

Latency results are plotted in Fig. 4. As predicted, there was no reliable difference in FOE magnitude as a function of target probability, $F_{(1,9)} = 0.05$, $p = 0.41$ (one-tailed), indicating additivity of target probability and fixation type factors. There was, however, a reliable main effect of target probability, with SRT decreasing as target probability increased from 0.2 to 0.8 (365 vs 324 ms, respectively), $F_{(1,9)} = 21.57$, $p = 0.001$. As discussed below, the shortest mean SRT (310 ms at $P(T \mid Q_1) = 0.8$ with fixation offset) was reliably longer for antisaccades than the corresponding mean SRT in experiment 1 (239 ms), $t(17) = 2.91$, $p = 0.01$; this difference was marginally reliable for the corresponding mean SRT in experiment 2 (249 ms), $t(13) = 1.98$, $p = 0.07$. There was also a reliable main effect of fixation type in the present experiment, with mean offset SRT reliably shorter than mean overlap SRT (331 vs 359 ms, respectively), $F_{(1,9)} = 8.98$, $p = 0.02$. Also discussed below, this FOE (28 ms) is statistically no greater in magnitude than the smallest FOE observed for prosaccades in both experiment 1 (22 ms), $t(17) = 0.47$, $p = 0.64$, and experiment 2 (28 ms), $t(13) = 0.03$, $p = 0.98$.

Errors

Anticipations and misses occurred in 1% or fewer of candidate trials. As observed in experiments 1 and 2, more false alarms occurred on offset trials than on overlap trials, χ^2 (1, $N = 394$) = 250.24, $p < 0.001$, and this difference was reliable for each of the target-probability levels (both p values < 0.001). After normalizing for the proportions of catch trials presented in each target-probability condition, there were also more false alarms for $P(T \mid Q_6) = 0.2$ than for $P(T \mid Q_1) = 0.8$, χ^2 (1, $N = 290$, normalized) = 6.08, $p = 0.01$. The greatest proportion of false alarms occurred for offset trials with $P(T \mid Q_6) = 0.2$. The mean SRT (467 ms) of these most frequent errors is substantially longer than even the longest mean correct antisaccade SRT (379 ms) observed in experiment 3.

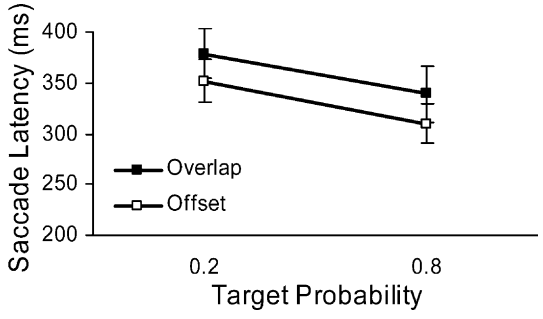

Fig. 4 Experiment 3, mean SRT (±SE) as a function of target probability and fixation type

More direction errors occurred on offset trials than on overlap trials, χ^2 (1, $N = 77$) = 3.75, $p = 0.05$ (Table 1). However, whereas this difference held for $P(T \mid Q_6) = 0.2$, χ^2 (1, $N = 18$) = 5.56, $p = 0.02$, it was not reliable for $P(T \mid Q_1) = 0.8$. After normalizing for the proportions of target trials presented in each target-probability condition, the corresponding interaction was marginally reliable, χ^2 (1, $N = 65.5$, normalized) = 3.55, $p = 0.06$. The greatest proportion of direction errors occurred for offset trials with $P(T \mid Q_6) = 0.2$. Consistent with a stimulus-driven basis for these prosaccade errors, in contrast to the long mean latency of false alarms observed for offset trials (see above), the mean direction error SRT was 249 ms, which is comparable to the shortest mean latencies observed for correct prosaccades in experiments 1 and 2 (239 and 249 ms, respectively). This mean latency was also shorter than all mean correct antisaccade latencies. There were no reliable differences in direction error SRT among the different conditions. No other reliable effects were observed in experiment 3.

Discussion

The results of experiment 3 indicate that for antisaccades, while a reliable FOE was observed, and while increasing the target probability reduced saccade latency, the magnitude of FOE did not vary as a function of target probability, consistent with our prediction. This additivity implies that our fixation type and target probability manipulations affected separable task processes engaged in antisaccade performance (Sternberg 1969). For example, target-probability information may be used to modulate SC fixation-cell activity for prosaccades; however, this mechanism would likely not be optimal for antisaccade tasks, where regardless of target probability, one must always either inhibit reflexive saccades (on target trials) or maintain fixation (on catch trials). Accordingly, a high level of fixation-related activity may be invoked by cortical control processes prior to fixation-stimulus offset for all probability levels, resulting in an invariant FOE magnitude.

We propose that high target probability may prompt one to specify cortically one or more of the antisaccade vector components (amplitude, direction) in advance of target appearance, resulting in reduced SRT. Relevant to this possibility is evidence that amplitude and direction can be prepared independently in advance of target presentation, while spatial components also can be specified independently of saccade timing (Abrams and Jonides 1988; Findlay 1981; Findlay and Walker 1999). In contrast, the interaction observed for prosaccade latency in experiments 1 and 2 suggests that fixation-type and target-probability manipulations affected at least one task process in common (Sternberg 1969). For example, fixation-stimulus offset and high target probability both may lead to reduced fixation-related activity in the same neural structure(s), thereby disinhibiting stimulus-directed saccades.

Also noteworthy in the results of experiment 3 is that while the shortest mean antisaccade SRT was longer than the corresponding mean SRT for prosaccades, the FOE magnitude was, however, no greater than the smallest FOEs observed in experiments 1 and 2. If the reduction in FOE with increasing target probability observed in the previous experiments were due simply to a floor effect (i.e., at $P(T \mid Q_n) = 0.8$ with fixation offset), then FOE magnitude should be larger when observed mean SRTs are longer than in the previous experiments. In contrast, the current finding that FOE magnitude did not increase with longer mean SRT provides additional support for the hypothesis that the target probability × fixation type interactions observed in experiments 1 and 2 were unlikely due to floor effects with high target probability (Reuter-Lorenz et al. 1991).

The target probability × fixation type interaction observed for the frequency of direction errors in experiment 3 suggests that errors (prosaccades) are most likely to occur when the fixated stimulus disappears and when participants are not expecting a target. Under these conditions, it is likely that participants were not fully prepared to inhibit stimulus-elicited prosaccades. In contrast, one might consider the alternative explanation that these data reflect not the degree of prosaccade inhibition per se, but rather the results of parallel computation of exogenously elicited prosaccades and endogenously computed antisaccades. Specifically, it may be the case that when an experimental manipulation, such as low target probability and/or fixation overlap, increases the duration of antisaccade computation, the probability of prosaccade execution is increased, thereby increasing the frequency of direction errors. However, this hypothesis predicts increased error rate with increasing mean antisaccade SRT, and counter to this prediction there was a small negative correlation ($\rho = -0.27$) between frequency of direction errors and antisaccade SRT. Nevertheless, the marginal significance of the observed interaction and the paucity of direction errors observed in this experiment warrant cautious interpretation.

The greatest proportion of false alarms occurred for offset trials with low target probability. It is possible that, rather than this reflecting a failure to maintain voluntary fixation, participants simply assumed that the trial had ended, and therefore disengaged fixation following fixation-stimulus offset. However, the greater

Table 1 Frequencies and reaction times of direction errors in experiment 3. Reaction times are presented in milliseconds. *M* mean, *SD* standard deviation

Fixation type	Target probability								
	0.2			0.8			Mean		
	Error	M	SD	Error	M	SD	Error	M	SD
Overlap	1.3%	288	106	2.2%	245	108	1.8%	266	107
Offset	4.7%	279	80	2.8%	237	91	3.7%	258	86
Mean	3.0%	284	93	2.5%	241	100	2.7%	262	96

incidence of false alarms for offset trials with low than with high target probability suggests that participants may have been more prone to noise-driven saccades in the former condition. Accordingly, the hypothesis that participants are most likely to insufficiently suppress saccade-related activity when target probability is low, and when the fixated stimulus is removed, is consistent with the false alarm data, and perhaps with the direction error data as well.

General discussion

By manipulating the probability of target appearance on a trial-by-trial basis, we found that people can modulate the magnitude of the prosaccade FOE through purely top-down influences. Specifically, in experiments 1 and 2, FOE magnitude decreased as target-probability increased. Because our paradigm permitted us to examine top-down influences in isolation from systematic variations in bottom-up factors confounded in previous studies, this finding indicates clearly that humans can endogenously alter otherwise-reflexive neural activity within oculomotor mechanisms underlying the FOE. Indeed, this conclusion is consistent with evidence from several saccade studies (Basso and Wurtz 1998; Dorris and Munoz 1998; Everling et al. 1998a, 1998c, 1999; Everling and Munoz 2000; Schlag-Rey et al. 1997) that investigated changes in brain activity as a function of either target probability or task type (e.g., prosaccade and antisaccade).

The target probability × fixation type interaction we found and replicated for prosaccade latency was driven by a greater reduction in overlap SRT than in offset SRT as target probability increased, suggesting that fixation-related neural activity can be modulated endogenously even in the presence of a fixated stimulus (cf. Machado and Rafal 2000b). Accordingly, when one is informed that a prosaccade target is likely to appear, cortical preparatory mechanisms might inhibit SC fixation cells, thereby disinhibiting SC movement cells and ultimately reducing saccade latency. A direct result of this preparatory modulation is that a diminished effect on SRT (i.e., a smaller FOE) is incurred by removal of the fixated stimulus, the presence of which normally evokes substantial activity in these cells.

We found in experiment 3, in contrast, that target-probability and fixation-type manipulations had additive effects on *anti*saccade SRT: fixation-stimulus offset and high target probability each reduced mean SRT, but the magnitude of the FOE did not vary with the probability of target presentation. This additivity suggests that these factors had their effects on separable processes (Sternberg 1969) engaged during antisaccade performance. Moreover, the results of the three experiments *together* imply that cognitive processes utilizing target-probability information exert control over different task processes engaged for prosaccades from those engaged for antisaccades.

A parsimonious explanation of this additivity is that elevated levels of fixation-related neural activity prior to the completion of saccade programming are likely optimal for all target-probability levels in the antisaccade task, given its requirement to always inhibit reflexive saccades (in target trials) and noise-driven saccades (in catch trials). Instead of modifying fixation-related activity, target-probability information may be used in the antisaccade task to specify components of the antisaccade vector prior to target onset, in the service of movement preparation. As a result, these two component processes (i.e., prosaccade inhibition and antisaccade-vector preparation) may be performed in independent, parallel stages. In experiment 3, because target eccentricity was constant (8.8°), whereas target location (left or right of fixation stimulus) was randomized, participants may have prepared the amplitude component of the antisaccade vector when target probability was high. For prosaccades, in contrast, a representation of the correct saccade vector is provided by the target stimulus itself (i.e., exogenously), eliminating the need for cortical vector specification. Moreover, the hypothesized modulation of SC fixation-cell activity as a function of target probability in the prosaccade task involves the same neural machinery that is reflexively driven by the presence of the fixation stimulus, thus providing a structural locus for the interaction of factors observed in experiments 1 and 2.

Convergent evidence strongly suggests a critical role of frontal cortical regions for the use of abstract information in determining task strategy and employing executive control (Alivisatos and Milner 1989; Miller 1999; Milner 1963; Wallis et al. 2001). We accordingly hypothesize that a subset (e.g., dorsolateral prefrontal cortex) of these brain regions modulates activity in cortical (e.g., frontal and parietal eye fields) and subcortical (e.g., SC) oculomotor-specific neural populations given the goals of the performer, task demands, and the availability of task-relevant information (e.g., target probability) useful in optimizing performance (cf. Henik et al. 1994; Machado and Rafal 2004a, 2004b; Ro et al. 1997).

Acknowledgements Funding for this research was provided to Leon Gmeindl by fellowships from the National Science Foundation and the Horace H. Rackham School of Graduate Studies, University of Michigan, and to Patricia A. Reuter-Lorenz by the University of Michigan Office of the Vice President for Research and by NIH AG18286. The authors wish to thank David E. Meyer, John Jonides, Rachael Seidler, members of the University of Michigan Cognitive and Affective Neuropsychology Laboratory, two anonymous reviewers, and Robin Walker for comments on previous versions of this paper, and Matt Jones for playing devil's advocate.

References

Abrams RA, Jonides J (1988) Programming saccadic eye movements. J Exp Psychol Hum Percept Perform 14(3):428–443

Abrams RA, Oonk HM, Pratt J (1998) Fixation point offsets facilitate endogenous saccades. Percept Psychophys 60(2):201–208

Alivisatos B, Milner B (1989) Effects of frontal or temporal lobectomy on the use of advance information in a choice reaction time task. Neuropsychologia 27(4):495–503
Basso MA, Wurtz RH (1997) Modulation of neuronal activity by target uncertainty. Nature 389:66–69
Basso MA, Wurtz RH (1998) Modulation of neuronal activity in superior colliculus by changes in target probability. J Neurosci 18(18):7519–7534
Basso MA, Wurtz RH (2002) Neuronal activity in substantia nigra pars reticulata during target selection. J Neurosci 22(5):1883–1894
Burman DD, Bruce CJ (1997) Suppression of task-related saccades by electrical stimulation in the primate's frontal eye field. J Neurophysiol 77(5):2252–2267
Carpenter RHS, Williams MLL (1995) Neural computation of log likelihood in control of saccadic eye movements. Nature 377(6544):59–62
Craig GL, Stelmach LB, Tam WJ (1999) Control of reflexive and voluntary saccades in the gap effect. Percept Psychophys 61(5):935–942
Dorris MC, Munoz DP (1995) A neural correlate for the gap effect on saccadic reaction times in monkey. J Neurophysiol 73(6):2558–2562
Dorris MC, Munoz DP (1998) Saccadic probability influences motor preparation signals and time to saccadic initiation. J Neurosci 18(17):7015–7026
Dorris MC, Taylor TL, Klein RM, Munoz DP (1999) Influence of previous visual stimulus or saccade on saccadic reaction times in monkey. J Neurophysiol 81(5):2429–2436
Dorris MC, Paré M, Munoz DP (2000) Immediate neural plasticity shapes motor performance. J Neurosci 20(1):RC52 (51–55)
Everling S, Munoz DP (2000) Neuronal correlates for preparatory set associated with pro-saccades and anti-saccades in the primate frontal eye field. J Neurosci 20(1):387–400
Everling S, Dorris MC, Munoz DP (1998a) Reflex suppression in the anti-saccade task is dependent on prestimulus neural processes. J Neurophysiol 80(3):1584–1589
Everling S, Paré M, Dorris MC, Munoz DP (1998b) Comparison of the discharge characteristics of brain stem omnipause neurons and superior colliculus fixation neurons in monkey: implications for control of fixation and saccade behavior. J Neurophysiol 79(2):511–528
Everling S, Spantekow A, Krappmann P, Flohr H (1998c) Event-related potentials associated with correct and incorrect responses in a cued antisaccade task. Exp Brain Res 118(1):27–34
Everling S, Dorris MC, Klein RM, Munoz DP (1999) Role of primate superior colliculus in preparation and execution of anti-saccades and pro-saccades. J Neurosci 19(7):2740–2754
Findlay JM (1981) Spatial and temporal factors in the predictive generation of saccadic eye movements. Vis Res 21(3):347–354
Findlay JM, Walker R (1999) A model of saccade generation based on parallel processing and competitive inhibition. Behav Brain Sci 22(4):661–721
Forbes K, Klein RM (1996) The magnitude of the fixation offset effect with endogenously and exogenously controlled saccades. J Cogn Neurosci 8(4):344–352
Gaymard B, Ploner CJ, Rivaud S, Vermersch AI, Pierrot-Deseilligny C (1998) Cortical control of saccades. Exp Brain Res 123(1–2):159–163
Guitton D, Buchtel HA, Douglas RM (1985) Frontal-lobe lesions in man cause difficulties in suppressing reflexive glances and in generating goal-directed saccades. Exp Brain Res 58(3):455–472
Hallett PE (1978) Primary and secondary saccades to goals defined by instructions. Vis Res 18(10):1279–1296
Henik A, Rafal R, Rhodes D (1994) Endogenously generated and visually guided saccades after lesions of the human frontal eye fields. J Cogn Neurosci 6(4):400–411
Hikosaka O, Wurtz RH (1983) Visual and oculomotor functions of monkey substantia nigra pars reticulata, IV: relation of substantia nigra to superior colliculus. J Neurophysiol 49(5):1285–1301
Jüttner M, Wolf W (1992) Occurrence of human express saccades depends on stimulus uncertainty and stimulus sequence. Exp Brain Res 89(3):678–681
Kalesnykas RP, Hallett PE (1987) The differentiation of visually guided and anticipatory saccades in gap and overlap paradigms. Exp Brain Res 68(1):115–121
Klein R, Kingstone A (1993) Why do visual offsets reduce saccadic latencies? Behav Brain Sci 16(3):583–584
Lueck CJ, Crawford TJ, Hansen HC, Kennard C (1991) Increase in saccadic peak velocity with increased frequency of saccades in man. Vis Res 31(7–8):1439–1443
Machado L, Rafal RD (2000a) Control of eye movement reflexes. Exp Brain Res 135(1):73–80
Machado L, Rafal RD (2000b) Strategic control over saccadic eye movements: studies of the fixation offset effect. Percept Psychophys 62(6):1236–1242
Machado L, Rafal RD (2004a) Control of fixation and saccades during an anti-saccade task: an investigation in humans with chronic lesions of oculomotor cortex. Exp Brain Res 156(1):55–63
Machado L, Rafal RD (2004b) Control of fixation and saccades in humans with chronic lesions of oculomotor cortex. Neuropsychology 18(1):115–123
Matthews A, Flohr H, Everling S (2002) Cortical activation associated with midtrial change of instruction in a saccade task. Exp Brain Res 143(4):488–498
Miller EK (1999) Prefrontal cortex and the neural basis of executive functions. In: Humphreys GW, Duncan J, Treisman A (eds) Attention, space, and action: studies in cognitive neuroscience. Oxford University Press, New York, pp 250–272
Milner B (1963) Effects of different brain lesions on card sorting. Arch Neurol 9:100–110
Moschovakis AK, Highstein SM (1994) The anatomy and physiology of primate neurons that control rapid eye-movements. Annu Rev Neurosci 17:465–488
Nickerson RS (1967) Expectancy, waiting time and the psychological refractory period. Acta Psychol 27:23–34
Pierrot-Deseilligny C, Rivaud S, Gaymard B, Agid Y (1991) Cortical control of reflexive visually-guided saccades. Brain 114:1473–1485
Reuter-Lorenz PA, Hughes HC, Fendrich R (1991) The reduction of saccadic latency by prior offset of the fixation point: an analysis of the gap effect. Percept Psychophys 49(2):167–175
Reuter-Lorenz PA, Oonk HM, Barnes LL, Hughes HC (1995) Effects of warning signals and fixation point offsets on the latencies of pro- versus antisaccades: implications for an interpretation of the gap effect. Exp Brain Res 103(2):287–293
Reuter-Lorenz PA, Herter T, Ptito M, Ptito A, Guitton D (1999) The effect of hemispherectomy on pro- and anti-saccades to auditory targets in the gap paradigm. Paper presented at the annual meeting of the Society for Neuroscience, Miami, FL
Ro T, Henik A, Machado L, Rafal RD (1997) Transcranial magnetic stimulation of the prefrontal cortex delays contralateral endogenous saccades. J Cogn Neurosci 9(4):433–440
Saslow MG (1967) Effects of components of displacement-step stimuli upon latency for saccadic eye movement. J Opt Soc Am 57(8):1024–1029
Schiller PH, Sandell JH, Maunsell JH (1987) The effect of frontal eye field and superior colliculus lesions on saccadic latencies in the rhesus monkey. J Neurophysiol 57(4):1033–1049
Schlag-Rey M, Schlag J, Dassonville P (1992) How the frontal eye field can impose a saccade goal on superior colliculus neurons. J Neurophysiol 67(4):1003–1005
Schlag-Rey M, Amador N, Sanchez H, Schlag J (1997) Antisaccade performance predicted by neuronal activity in the supplementary eye field. Nature 390(6658):398–401
Schumacher EH, Lauber EJ, Glass JM, Zurbriggen EL, Gmeindl L, Kieras DE, Meyer DE (1999) Concurrent response-selection processes in dual-task performance: evidence for adaptive executive control of task scheduling. J Exp Psychol Hum Percept Perform 25(3):791–814

Segraves MA, Goldberg ME (1987) Functional properties of corticotectal neurons in the monkey's frontal eye field. J Neurophysiol 58(6):1387–1419

Selemon L, Goldman-Rakic P (1988) Common cortical and subcortical targets of the dorsolateral prefrontal and posterior parietal cortices in the rhesus monkey: evidence for a distributed neural network subserving spatially guided behavior. J Neurosci 8(11):4049–4068

Sommer MA, Wurtz RH (2000) Composition and topographic organization of signals sent from the frontal eye field to the superior colliculus. J Neurophysiol 83(4):1979–2001

Sparks DL, Hartwich-Young R (1989) The deep layers of the superior colliculus. In: Wurtz RH, Goldberg ME (eds) The neurobiology of saccadic eye movements: reviews of oculomotor research, vol 3. Elsevier, Amsterdam, pp 213–256

Sternberg S (1969) The discovery of processing stages: extensions of Donders' method. Acta Psychol 30:276–315

Trappenberg TP, Dorris MC, Munoz DP, Klein RM (2001) A model of saccade initiation based on the competitive integration of exogenous and endogenous signals in the superior colliculus. J Cogn Neurosci Spec Issue 13(2):256–271

Wallis JD, Anderson KC, Miller EK (2001) Single neurons in prefrontal cortex encode abstract rules. Nature 411(6840):953–956

Wurtz RH, Goldberg ME (eds) (1989) The neurobiology of saccadic eye movements. Elsevier, New York