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RESEARCH ARTICLE

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Task-switching with antisaccades versus no-go trials: a comparison of inter-trial effects

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Abstract Antisaccades involve the suppression of a pre-potent prosaccade and a vector inversion to generate the novel ocular motor response of looking away from the target. Antisaccades have also been found to prolong the latencies of saccades in upcoming trials, an effect that we attribute to a form of immediate plasticity in the ocular motor system. Our goal was to determine whether the inter-trial effects of antisaccades were similar to that of no-go trials, where subjects must suppress making a saccade when the target appears without substituting a novel ocular motor response. We tested 12 subjects with two different blocks of saccadic trials. In one, prosaccades randomly alternated with antisaccades. In the other, prosaccades alternated with no-go trials. We analyzed the error rates and latencies of prosaccades that followed antisaccades versus no-go trials, compared to repeated prosaccades, to determine if inter-trial effects were present for both types of responses that required prosaccade suppression. No-go responses increased the error rates of prosaccades in the following trial less than antisaccades did. However, no-go trials had the same effect on the latencies of upcoming prosaccades as antisaccades. The inhibitory effect that prolongs the latencies of prosaccades after antisaccades likely stems from the need to inhibit a prosaccade, a function that is also required in no-go trials. The greater impairment of prosaccade accuracy after an antisaccade may reflect either additional control mechanisms involved in vector inversion or a different form of inhibitory control that operates during antisaccades and not during no-go responses.

Keywords Antisaccade · No-go · Task-switching · Inhibition · Prosaccade

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Introduction

The usual, highly practiced saccadic response to a suddenly appearing target is to shift the fovea to the location of this new stimulus. "Prosaccades" are rapid and highly accurate. However, they are not mandatory and with instructions subjects can substitute novel saccadic responses in their place (Hallett 1978; Hallett and Adams 1980). The term "antisaccade" denotes one such novel response, in which a subject makes a saccade of similar amplitude but in the opposite direction to the target. As a novel unpracticed response, antisaccades are characterized by higher error rates and longer latencies than prosaccades (Everling and Fischer 1998).

Current concepts suggest that antisaccade generation may involve at least two processes (Munoz and Everling 2004). First, the subject must prevent the pre-potent prosaccade response from being executed, which we will refer to as "prosaccade suppression". Second, the stimulus vector must be inverted to create the volitional antisaccade. Different anatomic systems may serve these dual processes of prosaccade suppression and vector inversion, and distinguishing the different contributions of these two processes may improve our understanding of the mechanisms underlying the volitional control of eye movements.

The multiplicity of cognitive operations occurring during the antisaccade task leads to uncertainty about the origins of effects being generated during its performance. One such effect that we have been examining is "response system plasticity" (Barton et al. 2005, 2006). This stems from observations of inter-trial effects: that is, the effects of previous trials on current responses during task-switching experiments. We and others have shown that performing an antisaccade in the prior trial increases the saccadic latency in the current trial, regardless of whether the current trial is a prosaccade or an antisaccade (Cherkasova et al. 2002; Manoach et al. 2002, 2004; Fecteau et al. 2004; Barton et al. 2006). This contrasts with other models of task-switching, which generally predict that switching the response set from that of the prior trial should increase latency (Wylie and Allport 2000). The key result in our antisaccade studies is that an antisaccade preceded by an antisaccade takes longer to execute than an antisaccade preceded by a prosaccade. Thus, for latency, repeating the antisaccade task-set is disadvantageous compared to switching.

One interpretation of this finding is that antisaccades may generate a persistent inhibition of the saccadic response system, rather than of the opposing prosaccade task-set. If so, this would cause subsequent saccadic responses of either type to be delayed. Physiologic data from monkeys show that during antisaccade trials there is a generalized depression of preparatory pre-target activity in the frontal eye field (Everling and Munoz 2000) and the superior colliculus (Everling et al. 1999). As the directional characteristics of the prior trial can influence the preparatory activity in the next trial (Dorris et al. 2000), it is plausible that antisaccadic depression of pre-target activity in one trial could also persist into the next. Since depression of pre-target activity is directly related to saccadic latency (Dorris and Munoz 1998), a persistent antisaccadic depression could generate prolonged latencies in trials after antisaccades. Following Dorris et al. (2000), we suggest that this effect reflects immediate "response-system plasticity".

What generates this persistent antisaccade inhibition in the saccadic response system? The necessary suppression of the pre-potent prosaccade seems a likely source of inhibition, but this does not exclude the possibility that inhibition stems from an additional control process involved in creating the vector-inverted antisaccade. Linking inter-trial inhibitory effects to changes in preparatory activity in the frontal eye field does not necessarily settle this question. There is evidence that not only the lateral intraparietal area (Zhang and Barash 2000, 2004) but perhaps also the frontal eye field (Sato and Schall 2003) are involved in vector inversion. Regarding saccadic suppression, some propose that fixation neurons in the superior colliculus and frontal eye field play key roles in suppressing prosaccades, along with the participation of the dorsolateral prefrontal cortex and supplementary eye fields (Munoz and Everling 2004).

As a first step in examining the origins of persistent antisaccadic inhibition further, it would be useful to devise a paradigm that could dissociate the suppression of prosaccades from the generation of the vector-inverted antisaccade. While it is difficult to envision a trial in which the novel antisaccade response could be generated without requiring suppression of the prosaccade, it is possible to create a trial that involves only suppression of the prosaccade. That is, a subject could be required simply not to make a saccade when a stimulus appeared, sometimes termed a "no-go" trial. By contrasting the inter-trial effects of no-go trials with those of antisaccade trials, it may be possible to determine whether a general effect of prosaccade suppression may lie behind the inter-trial inhibitory effects we and others have observed.

Methods

Participants

We studied 13 healthy subjects, one of whom was excluded because of an incomplete data set. The 12 subjects in the final analysis were 8 men and 4 women, with mean age of 31 years (range 19–56). All gave informed consent according to a protocol approved by our hospital's institutional review board.

Apparatus

We recorded eye movements with a magnetic search coil technique, using 3-foot field coils (Crist Instruments, Bethesda MD, USA). A scleral coil was placed in the subject's left eye, though the subject was permitted to view the stimulus binocularly. Images generated by a Power Macintosh 9600/233 using the Vision Shell programming platform were back-projected by an Eiki LC-7000U projector onto a screen 81 cm from the subject. Participants' heads were secured in a chin-rest. Eye position was digitized at 500 samples/s and velocity was derived from eye position by a five-point central difference algorithm (Bahill and McDonald 1983). The system was calibrated for each subject by having the subject successively fixate on nine targets in a grid spanning 50°.

Eye movement protocol

Each session consisted of eight blocks, each containing 48 trials. Four of these blocks consisted of a random mixture of prosaccade and no-go trials, and four of a mixture of prosaccade and antisaccade trials. Half the subjects began with two no-go block and half began with two antisaccade blocks, and these were then alternated in blocks of two during the session.

The initial display had a dark background with a white fixation ring at center, of 0.4° diameter and luminance of 20 cd/M^2. The fixation ring was flanked by two dots of 0.2° diameter and the same luminance at 20° eccentricity right and left, which remained visible throughout the test. Each trial began when a subject's eye fell within 3° of the fixation point. After a brief period the fixation point was replaced by one of two symbols—a yellow 'O' with a surrounding ring of 0.8° diameter, or a blue 'X' spanning 0.8°. The yellow O was the cue for prosaccades, while the blue X was the cue for a response that required prosaccade suppression, either an antisaccade in the prosaccade/antisaccade blocks, or a no-go response in the prosaccade/no-go blocks. The cues lasted 200 ms and were replaced by the return of the white fixation ring at screen center for another 1,800 ms, at which point it shifted to become the target around one of the peripheral dots. The side of the target was randomly ordered. The white ring remained in the peripheral target location until either the subject's eye had fallen within 3° of the desired end position or 3 s had elapsed, then it reappeared at the central fixation point for the next trial.

Before each session all subjects did a practice session of 20 trials.

Data analysis

We identified saccades as eye movements with velocities exceeding 47°/s. The onset of a saccade was taken as a point at which the velocity of the eye first exceeded 31°/s. The first saccade after target onset was considered the saccadic response. The first saccade of each block was eliminated from analysis. We excluded trials whose saccadic responses had latencies less than 130 ms (about 1.9% of saccadic trials), as these would be anticipatory responses in advance of rather than in response to the appearance of the target (Kalesnykas and Hallett 1987). We also excluded trials with latencies greater than 800 ms (about 0.1% of saccadic trials) as being too prolonged to accurately reflect the processes we wished to isolate.

Each trial was classified by its conditions: block type (go/no-go vs. prosaccade/antisaccade), saccade type (prosaccade vs. "suppressive" response, which in the go/no-go blocks were the no-go responses and in the prosaccade/antisaccade blocks were the antisaccade responses), and prior-trial type (prosaccade vs. "suppressive" response). The analysis was limited to trials that had been preceded by correct responses. While this eliminates a number of trials, the remaining data are more likely to reflect the true influences of prior responses.

For accuracy we analyzed mean accuracy rates for each subject. For prosaccades and antisaccades, accuracy was judged simply by whether the saccade was in the correct direction; for no-go trials, a correct response was no saccade. We performed two ANOVA analyses, one on prosaccadic responses, which are most relevant to the question posed, and one on inhibitory responses (antisaccades or no-go trials). Both analyses had two main factors of block type and prior-trial type, with subjects as a random effect. We focused on specific a priori linear contrasts to compare prosaccades preceded by prosaccades with prosaccades preceded by responses requiring prosaccade suppression (either antisaccade or no-go response).

For latency, the analysis was further restricted to trials that had correct responses. We analyzed prosaccade trials only, since there are no latencies for correct no-go responses by definition. The analysis focused on our specific hypotheses. First, we anticipated reproducing our prior finding that prosaccades preceded by antisaccades would have longer latencies than prosaccades preceded by prosaccades. If so, would we then also find that prosaccades would have longer latencies if they were preceded by a no-go response? If there was one, would this be equivalent to the effect generated by a preceding antisaccade trial? We used ANOVA to examine the prosaccade data with the two main factors of block type and prior-trial type, with subjects as a random effect. We focused on specific a priori linear contrasts to compare trials with prior prosaccades and trials with prior suppressive responses.

Results

For accuracy (Fig. 1), ANOVA of prosaccadic trials showed a significant effect of prior-trial type ($F_{(1,11)} = 11.5$, $P < 0.0018$), with switched trials 4.5% less accurate that repeated trials. There was a trend to a significant effect of block type ($F_{(1,11)} = 3.98$, $P = 0.054$) with prosaccades from antisaccade blocks 2.7% less accurate that prosaccades from go/no-go blocks. Similarly there was a trend to an interaction between prior-trial type and block type ($F_{(1,11)} = 3.26$, $P = 0.079$). While repeated prosaccades had similar accuracy rates in both the go/no-go and antisaccade blocks, switched prosaccades were less accurate in the antisaccade blocks than in the go/no-go blocks ($t = 2.69$, $P < 0.012$).

The ANOVA of the accuracy of inhibitory trials (i.e., no-go and antisaccade trials) also showed a significant effect of prior-trial type ($F_{(1,11)} = 14.4$, $P < 0.0006$) with switched trials 7% less accurate than repeated trials. However, there was also a significant effect of block type ($F_{(1,11)} = 14.7$, $P < 0.0005$), with antisaccades 8% less accurate than no-go trials. There was no significant interaction, as both antisaccades and no-go trials showed a similar effect of switching on their error rates.

For latency (Fig. 2), ANOVA showed a significant effect of prior-trial type ($F_{(1,11)} = 11.57$, $P < 0.0007$), with switched responses 13 ms faster than repeated ones. However, there was no significant effect of block type, or significant interaction between block type and prior trial type. Our planned linear contrasts showed that switched trials differed significantly from repeated trials in both

go/no-go blocks ($t = 2.54$, $P < 0.012$) and antisaccade blocks ($t = 2.27$, $P < 0.024$), and that switched trials and repeated trials gave nearly identical mean latencies in go/no-go and antisaccade blocks.

Discussion

Our findings show that, while a no-go response impairs the accuracy of a following prosaccade less than an antisaccade, its influence on the latency of that following prosaccade is virtually identical to that of a preceding antisaccade.

There are no neurophysiologic experiments that provide direct contrasts between antisaccades and no-go trials. Antisaccades are associated with a directionally non-specific depression of preparatory pre-target neuronal activity in the frontal eye field and superior colliculus (Everling et al. 1999; Everling and Munoz 2000). This moves neural activity further away from the threshold to trigger a saccade. Failure to achieve sufficient pre-target inhibition leads to increased error rates (Dorris and Munoz 1998; Everling et al. 1998). Successful pre-target inhibition allows time for vector inversion to proceed and generate sufficient neural activity to eventually trigger an antisaccade, but at a cost of some increase in latency.

At this time it is unclear whether the no-go response is associated with similar pre-target inhibition in the same neural structures and to the same degree as antisaccades. Similar no-go paradigms to ours have been used to demonstrate that visual responses in the frontal eye field are not dependent on saccadic programming (Thompson et al. 1997), and there is one abstract reporting that no-go trials do not affect preparatory activity in the superior colliculus (Sommer et al. 1997). Otherwise, though, specific contrasts between no-go trials and antisaccades have not yet been done.

How can we explain the puzzling combination of a similar effect on prosaccade latency but a reduced effect on accuracy from no-go responses compared to antisaccades? One possibility may lie in the contrast between the two components necessary for antisaccade production, namely suppression of the reflexive prosaccade and vector inversion to generate the novel antisaccade. Given that both no-go responses and antisaccades entail a suppression of prosaccades, it may be that this function is responsible for the increased latencies following antisaccades that we previously reported. On the other hand, generating a vector-inverted response may introduce a degree of instability into the saccadic system that interferes with prosaccadic commands, so that more prosaccade errors occur after an antisaccade than after a no-go response, which does not involve any vector-inverting processes.

However, another possibility may lie in the nature of the inhibition involved in no-go and antisaccade responses. While it is true that both responses require suppression of the prosaccade, it may not be that such suppression is quantitatively or qualitatively equivalent in no-go and antisaccade trials. Indeed, this is suggested by the fact that significantly more errors were made during antisaccade trials than during no-go trials.

Can a quantitative difference in inhibition explain our findings? Suppression of prosaccades might be more powerful and more complete during no-go trials than antisaccade trials. Since there is no requirement that any saccade be generated in a no-go trial (unlike the case

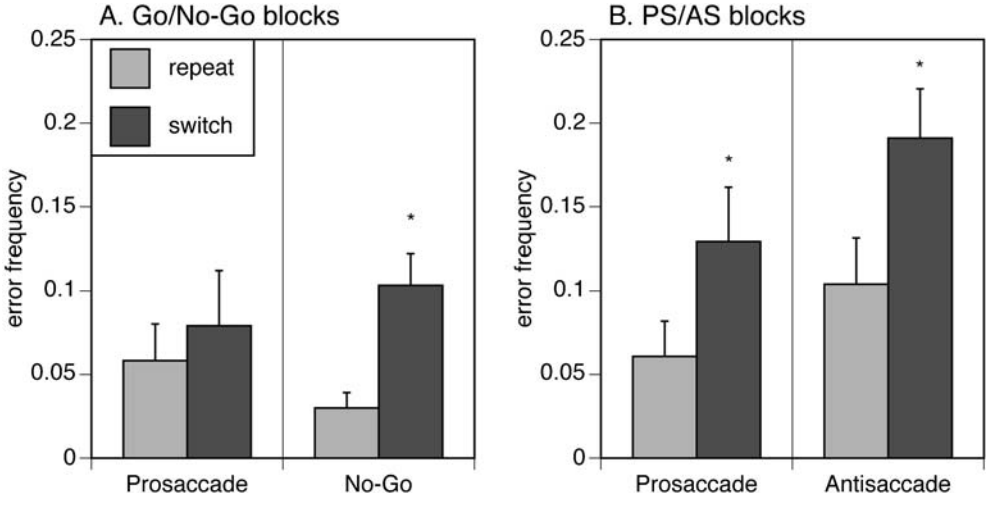

Fig. 1 Accuracy data. Mean and one standard error are shown for error frequency. **a** Go/no-go blocks. Prosaccade (go) errors are shown on *left*, no-go errors on the *right*. *Light bars* indicate data for repeated trials and *dark bars* the data for switched trials. **b** Prosaccade/antisaccade blocks. Prosaccade errors are shown on *left*, antisaccade errors on the *right*. Note, first, the lower error rate of no-go trials compared to antisaccade trials, and second, the increased error rate of prosaccades after an antisaccade trial but not after a no-go trial. *Asterisks* indicate antisaccade results that differed significantly from prosaccades

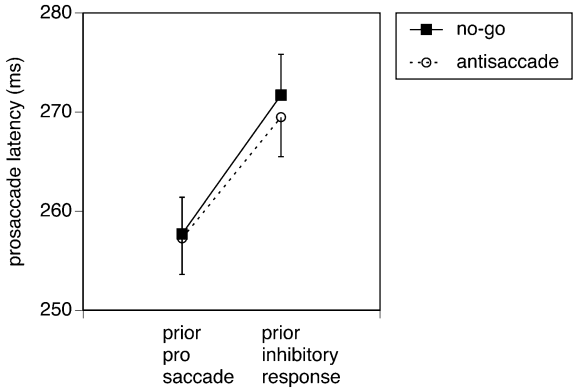

Fig. 2 Latency data for prosaccades. Means and one standard error are shown. On the *left* are the data for prosaccades preceded by prosaccades (i.e., repeated prosaccades), on the *right* are data for prosaccades preceded by a suppressive response (i.e., prosaccades switched from either a prior antisaccade or prior no-go response). The results from go/no-go blocks and prosaccade/antisaccade blocks are virtually identical

with antisaccade trials), it may be permissible for the system to suppress saccadic activity completely. This might be reflected in greater depression of pre-target activity during the next trial in structures like the frontal eye field and superior colliculus. This difference in pre-target activity would predict that, compared to preceding antisaccades, preceding no-go trials should cause future prosaccades to have (a) smaller error rates, which we did find, and (b) longer latencies, which we did not find. Therefore, our results do not seem compatible with this explanation.

What about a qualitative difference? It is possible that different inhibitory processes are required for no-go responses than for antisaccades. To prevent a prosaccade and yet allow the alternative antisaccade is probably a more complex cognitive task than the generalized suppression of all saccades during a no-go trial. Thus, the more precise cognitive control required by an antisaccade may be more difficult to achieve, and thus would be associated with higher error rates during antisaccades than no-go trials, as we found.

This distinction between the type of suppression involved with antisaccades and in no-go ocular responses has parallels in the literature on manual responses. De Jong and colleagues have proposed the existence of multiple inhibitory mechanisms, including a "selective, central and a global peripheral inhibition mechanism", based on behavioral and ERP studies (De Jong et al. 1990, 1995). They suggested that the selective central mechanism is involved in "stop-change" trials, when one response must be halted while another substituted for it (as with the antisaccade task). The global peripheral inhibition mechanism, which may be the inhibition of the transmission of motor commands from central to peripheral structures, is involved in "stop-all" trials, when one must simply prevent any response (as with the no-go task). Their measures showed that lateralized readiness potentials over motor cortex were still present when the peripheral mechanism was operating during stop-all trials, whereas these potentials were attenuated during stop-change trials. If an analogy holds for ocular motor responses, then antisaccades should be associated with stronger inhibition in central motor structures like the frontal eye field, whereas no-go responses may use a fast peripheral mechanism that operates downstream of these central structures. To explain our results, one could speculate that either central or peripheral inhibition may prolong the latency of upcoming responses, but the generation of specific commands to create an accurate response is affected primarily by the inhibition of central structures like the frontal eye field.

Our study differs significantly in methodology from a few prior studies of countermanding in manual task switching (Schuch and Koch 2003; Kleinsorge and Gajewski 2004). In those studies subjects had two tasks of equivalent difficulty that were repeated or switched back and forth. On a certain percentage of trials a stop signal was presented at the same time as the stimulus, shortly after the cue indicating the response required. The object was to see whether preparation or response selection processes were responsible for switch costs. The comparisons were between no-go trials that cancelled the same task-set as the current trial, and no-go trials that cancelled the opposite task-set. The results showed that the type of task-set cancelled had no effect on the next trial's latency.

This contrasts with our study, which compared the inter-trial effects of prosaccade suppression versus antisaccade generation. To this end, we used the no-go task as one of the two tasks to be switched, rather than as a stop signal to cancel one of two tasks being switched. Although there are no studies similar to our design, a secondary finding in one of those two prior reports was that latencies after no-go trials were elevated compared to latencies after go trials (Schuch and Koch 2003), similar to our data. The authors speculated that this might indicate priming of go and no-go decisions by the prior trial type.

Our results show that the priming of prosaccadic latency is similar for both no-go and antisaccade responses, but the effects on prosaccadic accuracy are more deleterious for prior antisaccades than prior no-go responses. This suggests that, despite the close relation between speed and accuracy in the trade-offs correlated with pre-target preparatory activity in structures like the superior colliculus and frontal eye field, there may be distinctly different effects on these two parameters from the different cognitive processes involved in antisaccade and no-go generation. Whether these are due to differences between prosaccade inhibition and vector inversion, or between central and peripheral inhibitory mechanisms, remains to be determined.

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References

Bahill T, McDonald J (1983) Frequency limitations and optimal step size for the two-point central difference derivative algorithm with applications to human eye movement data. IEEE Trans Biomed Eng 30:191–194

Barton J, Cherkasova M, Lindgren K, Goff D, Manoach D (2005) What is perseverated in schizophrenia? Evidence of abnormal response plasticity in the saccadic system. J Abnormal Psychol 114:75–84

Barton J, Greenzang C, Hefter R, Edelman J, Manoach D (2006) Switching, plasticity, and prediction in a saccadic task-switch paradigm. Exp Brain Res 168:76–87

Cherkasova M, Manoach D, Intriligator J, Barton J (2002) Antisaccades and task-shifting: interactions in controlled processing. Exp Brain Res 144:528–537

De Jong R, Coles M, Logan G, Gratton G (1990) In search of the point of no return: the control of response processes. J Exp Psychol Hum Percept Perform 16:164–182

De Jong R, Coles M, Logan G (1995) Strategies and mechanisms in nonselective and selective inhibitory motor control. J Exp Psychol Hum Percept Perform 21:498–511

Dorris M, Munoz D (1998) Saccadic probability influences motor preparation signals and time to saccadic inhibition. J Neurosci 18:7015–7026

Dorris M, Paré M, Munoz D (2000) Immediate neural plasticity shapes motor performance. J Neurosci 20:RC52

Everling S, Fischer B (1998) The antisaccade: a review of basic research and clinical studies. Neuropsychologia 36:885–899

Everling S, Munoz DP (2000) Neuronal correlates for preparatory set associated with pro-saccades and anti-saccades in the primate frontal eye field. J Neuriosci 20:387–400

Everling S, Dorris MC, Munoz DP (1998) Reflex suppression in the anti-saccade is dependent on prestimulus neural processes. J Neurophysiol 80:1584–1589

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 19:2740–2754

Fecteau J, Au C, Armstrong I, Munoz D (2004) Sensory biases produce alternation advantage found in sequential saccadic eye movement tasks. Exp Brain Res 159:84–91

Hallett P (1978) Primary and secondary saccades to goals defined by instructions. Vis Res 18:1279–1296

Hallett P, Adams B (1980) The predictability of saccadic latency in a novel voluntary oculomotor task. Vis Res 20:329–339

Kalesnykas R, Hallett P (1987) The differentiation of visually guided and anticipatory saccades in gap and overlap paradigms. Exp Brain Res 68:115–121

Kleinsorge T, Gajewski P (2004) Preparation for a forthcoming task is sufficient to produce subsequent shift costs. Psychonom Bull Rev 11:302–306

Manoach D, Lindgren K, Barton J (2004) Deficient saccadic inhibition in Asperger's disorder and the social-emotional processing disorder. J Neurol Neurosurg Psychiatry 75:1719–1726

Manoach DS, Lindgren KA, Cherkasova MV, Goff DC, Halpern EF, Intriligator J, Barton JJS (2002) Schizophrenic subjects show deficient inhibition but intact task-switching on saccadic tasks. Biol Psychiatry 51:816–825

Munoz D, Everling S (2004) Look away: the anti-saccade task and the voluntary control of eye movement. Nat Rev Neurosci 5:218–228

Sato T, Schall J (2003) Effects of stimulus-response compatibility on neural selection in frontal eye field. Neuron 38:637–648

Schuch S, Koch I (2003) The role of response selection for inhibition of task sets in task shifting. J Exp Psychol Hum Percept Perform 29:92–105

Sommer M, Paré M, Wurtz R (1997) Instructional dependence of preparatory discharges of superior colliculus neurons. Soc Neurosci Abstr 23:333–335

Thompson K, Bichot N, Schall J (1997) Dissociation of visual discrimination from saccade programming in macaque frontal eye field. J Neurophysiol 77:1046–1050

Wylie G, Allport A (2000) Task switching and the measurement of "switch costs". Psychol Res 63:212–233

Zhang M, Barash S (2000) Neuronal switching of sensorimotor transformations for antisaccades. Nature 408:971–975

Zhang M, Barash S (2004) Persistent LIP activity in memory antisaccades: working memory for a sensorimotor transformation. J Neurophysiol 91:1424–1441