ERP indices of persisting and current inhibitory control: A study of saccadic task switching

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ABSTRACT

Previous studies have found that inhibition of a biologically dominant prepotent response tendency is required during the execution of a less familiar, non-prepotent response. However, the lasting impact of this inhibition and the cognitive mechanisms to flexibly switch between prepotent and non-prepotent responses are poorly understood. We examined the neurophysiological (ERP) correlates of switching between prosaccade and antisaccade responses in 22 healthy volunteers. The behavioural data showed significant switch costs in terms of response latency for the prosaccade task only. These costs occurred exclusively in trials when preparation for the switch was limited to 300 ms, suggesting that inhibition of the prepotent prosaccade task either passively dissipated or was actively overcome during the longer 1000 ms preparation interval. In the neurophysiological data, a late frontal negativity (LFN) was visible during preparation for a switch to the prosaccade task that was absent when switching to the antisaccade task, which may reflect the overcoming of persisting inhibition. During task implementation both saccade types were associated with a late parietal positivity (LPP) for switch relative to repetition trials, possibly indicating attentional reorienting to the switched-to task, and visible only with short preparation intervals. When the prosaccade and antisaccade task were contrasted directly during task implementation, the antisaccade task exhibited increased stimulus-locked N2 and decreased P3 amplitudes indicative of active inhibition. The present findings indicate that neurophysiological markers of persisting and current inhibition can be revealed using a prosaccade/antisaccade-switching task.

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Introduction

The ability to control one's actions in accordance with internal goals is pivotal for human behaviour. However, how flexibly we can react to our environment depends on how familiar or biologically hard-wired any alternative, competing response is. The presence of competing responses requires that the cognitive control mechanisms allow both non-prepotent responses to be executed and prepotent responses to be re-enabled when necessary. This study examines the electrophysiological (ERP) indices of these mechanisms.

An extreme example of a hard-wired, prepotent response is a saccade. Saccades are ballistic eye movements, which are executed about 150,000 times a day (Schiller, 1998). In the laboratory, the tendency to execute an eye movement towards an object which abruptly appears (the prosaccade) is much stronger than the tendency to make an eye movement away from the object (the antisaccade; Hallett and Adams, 1980). It has been suggested that when an antisaccade is executed the prosaccade response is suppressed (for review see Munoz and Everling, 2004). Suppression of the prosaccade response on an antisaccade trial, however, may have a persisting negative effect on subsequent response latency (Fecteau and Munoz, 2003; Manoach et al., 2007).

A number of behavioural studies of non-saccadic tasks have examined the importance of task strength (i.e. task prepotency) on task switching performance. They have mainly demonstrated larger switch costs (increased reaction time or errors when the task switches relative to when it is repeated) for the stronger, prepotent task (Allport et al., 1994; MacLeod, 1991; Meuter and Allport, 1999). Arguably, during the execution of a weaker task, the stronger task has to be inhibited. This inhibition is thought to persist such that switching back to the stronger task requires the sustaining inhibition to be overcome, bringing a cost to the speed and/or accuracy of performance (e.g. Allport et al., 1994). A similar pattern of switch costs is observed for saccadic tasks when only a short period (200 ms) is available to prepare for a switch of task. Antisaccades, like the weaker task in the non-saccadic switching studies, show smaller latency switch costs relative to the cost associated with the switching to prosaccades (Barton et al., 2006). However, with longer preparation intervals a switch benefit for the antisaccade task has been observed (antisaccade switch latencies faster and errors lower than antisaccade repeat latencies and errors...
An fMRI study of saccadic switching has highlighted a distinction between persisting and current inhibition (Manoach et al., 2007). During preparation for an antisaccade repeat trial, reduced BOLD activity in the frontal eye fields (FEF), supplementary eye fields (SEF) and parietal eye fields (PEF) was observed (relative to the antisaccade switch trial). In contrast, during preparation for a switch prosaccade trial (relative to repeat prosaccade), reduced activity was found only in SEF. These differences were interpreted in terms of maintaining suppression of the prosaccade response during preparation to repeat the antisaccade task, and dissipating suppression during preparation to switch to the prosaccade task. When prosaccades and antisaccades were compared directly, activity for antisaccades was increased in the FEF, possibly reflecting the current firing of afferent inhibitory neurones. Other studies have highlighted the crucial role of the SEF in the control of eye movements during such response conflict (Husain et al., 2003; Parton et al., 2007).

Similarly, electrophysiological recordings in the monkey have documented reduced FEF activity during preparation for antisaccades, (Everling and Munoz, 2000). Event-related potentials in humans (ERP) have characterised the sensorimotor transformation associated with shifting from a prosaccade to an antisaccade, and the inhibitory processes involved with the shift from a prosaccade to a NoGo response (Matthews et al., 2002), but not the switch to a prosaccade. A large number of recent studies have examined the ERP effects of switching between cognitive tasks during both task preparation and implementation stages, usually with manual responses and tasks which are symmetric, rather than asymmetric, in terms of overall difficulty (Mueller et al., 2007; Rushworth et al., 2002; Swainson et al., 2003). Enhanced late frontal negativities (LFN) have been reported during the later stages of task preparation that are modulated by whether tasks were changed or repeated. They are seen to vary depending on the response demands of the preceding trial as well as the extent to which responses are shared between tasks and may reflect processes associated with encountering inhibition of the switched-to task-set (Astle et al., 2006). ERP components associated with active inhibitory processes during the implementation phase are thought to be reflected in the N2/P3 complex (Jackson et al., 1999) possibly mirroring activations in prefrontal cortex and motor areas during go and no-go (i.e., inhibited) trials (Liddle et al., 2001). Finally, a switch-related enhanced late parietal positivity (affecting the later part of the P3 component, LPP) has been widely reported during both the preparation and implementation phases. The LPP component, however, is unlikely to reflect inhibition and instead may index attentional shifting (Astle et al., 2008b; Nicholson et al., 2003).

We sought to characterise the temporal dynamics of the control mechanisms involved in switching between asymmetric tasks using dense-sensor ERPs and a mixed pro-/antisaccade task. Based on prior findings, we expected carry-over effects of the previous antisaccade to be visible in a sustained LFN specifically for switching to prosaccades but not antisaccades during saccade preparation (Astle et al., 2006, 2008a). We predicted that current inhibitory processes required for the implementation of antisaccades would be apparent in an increased N2 but decreased P3 components (relative to prosaccade) as previously seen for no-go responses (Jackson et al., 1999; Thorpe et al., 1996). It was also anticipated that a change in task would generate a late parietal positivity (LPP) that would be more increased for switch relative to repetition trials during either preparation or implementation and affecting both types of saccade (Rushworth et al., 2002; Swainson et al., 2003).

Materials and methods

Twenty-two neurologically healthy participants (9 males, mean age 22±2.6 years) with normal or corrected-to-normal vision participated in the study. All participants were right-handed (Edinburgh Handedness Inventory, Oldfield, 1971) and received £10. Ethical guidelines of the University of Nottingham were followed and participants provided written consent. One participant had to be excluded from analysis due to excessive artefacts in the EEG.

Stimuli were projected onto a white wall in a dimly lit room 1.7 m away from the subject. A coloured cue (red or green) consisting of a fixation cross (2.4°) was presented in the centre of the screen on a black background. The cue was presented for one of two cue-to-target intervals (CTIs, 300 ms or 1000 ms), randomised from trial to trial: while the long CTI would allow us to observe ERP effects of preparation prior to target onset, the short CTI would encourage speedy preparation on all trials and allow us to examine the extent to which subjects prepared for a change in task (shown by the reduction in switch cost from short to long CTI). The white target box (1.85°) then appeared on either the left or the right hand side of the fixation cross (15°) and was displayed for 700 ms. Participants were instructed to make an eye movement towards the target box when the fixation cross (cue) was green (prosaccade trial) and an eye movement away from the target box equidistant into the opposite direction when the fixation cross was red (antisaccade trial). They were instructed to hold their fixation there until the target box disappeared and then return to the central fixation cross. The interval between the disappearance of a target stimulus and the appearance of the next cue was jittered between 2000 and 2400 ms in 100 ms increments in order to avoid anticipation of cue onset. To achieve equal trial durations across trial types, on trials with a 300 ms CTI an additional 700 ms passed before presentation of the next cue.

The experiment consisted of two parts. A single task and a mixed task block were recorded, the order of which was counterbalanced. However, only the data from the mixed blocks will be presented here given that the primary focus of this study lay on trial transitions. The mixed block consisted of 180 experimental trials with prosaccades and antisaccades being randomised from trial to trial. Because the saccade type (prosaccade or antisaccade) was selected at random on each trial, mixed blocks included equal numbers of ‘switch’ (where the current saccade type differs from that on the previous trial) and ‘repetition’ trials (where the previous saccade type is repeated on the current trial). Consequently, switch versus repetition trials comprise the ‘transition’ factor. The block was repeated twice to give participants the opportunity to have a break in between.

Procedure

Analysis

Behavioural data

For analysis of the behavioural data (response latency and error percentage), a 2×2×2 repeated-measures ANOVA was conducted with the factors of transition (switch vs. repetition), CTI (300 vs. 1000) and saccade task (prosaccade vs. antisaccade). Planned comparisons were made to correspond to the ERP analyses and therefore examined the effects of transition within each saccade type and CTI, as well as the effects of saccade type at each CTI (collapsed across saccade type). For each subject, the first four trials were considered practice and removed from analysis.

ERP data

The horizontal electrodes that are usually used for monitoring eye movements of the EEG (HEOG, EGI sensors 125 and 128) were used to retrieve the latency and accuracy data, and saccades were scored manually offline using Matlab (Mathworks, Natick, MA). In order to increase the signal-to-noise ratio of the EEG data for the scoring of the behavioural data only, a Chebychev 2 filter was applied in addition to a standard noise filter for EEG data. The filter was arrived
at experimentally and was found to lead to the least distortion in signal (Mueller, 2006).

ERP recording

Dense-sensor ERPs were recorded with a 128-channel geodesic sensor net (Electrical Geodesics Inc., Oregon). Impedances were kept below 50 kΩ. Where this was not possible channels were excluded before analysis. EEG was recorded and digitized at 125 Hz with a high-pass filter of 0.01 Hz. Data was pre-processed with a low-pass filter at 45 Hz. In order to reduce the number of trials containing movement artefacts, which were excluded during pre-processing, participants were asked to relax, and to minimize body and head movements. Continuous EEG data was segmented into cue-locked (were asked to prepare for the upcoming change of task, because switch costs were present at the short CTI but eliminated at the long CTI. Response

ERP analysis

To analyse statistical significance of the ERP effects, a measure of consecutive significance was used (Rugg et al., 1993; Swainson et al., 2003). Two types of comparison were of interest: the effect of transition (switch versus repetition) within each saccade type, and the effect of saccade type (prosaccades versus antisaccades) collapsed across transition. In each case, we carried out separate analyses for each CTI and for cue-locked and target-locked epochs. In the case of the target-locked saccade type contrast, data were collapsed across short and long CTI trials, as no a priori hypotheses with regards to CTI existed. Pairwise comparisons between the experimental conditions of interest were run with t-tests at each time point. An effect was considered significant if it was present for at least 40 consecutive ms or more, and if it was present over at least two neighbouring electrodes. Only significant effects are reported here. In the short cue-locked epoch, transition effects were only analysed for significance until 80 ms post-target (Matthews et al., 2002), i.e., from 0 to 380 ms post-cue. In the long cue-locked epoch, transition effects were considered until target onset (1000 ms post-cue). However, for better visualization the first 500 ms after cue onset are displayed in the short CTI and until 1200 ms in the long CTI, i.e., in each case including a 200 ms post-target period at the end of the epochs. To facilitate comparison with other studies, standard ten-twenty equivalents of the dense-sensor net are given (Luu and Ferree, 2005). Trials with errors were not analysed separately due to lack of statistical power.

Results

Behavioural

Latency

As expected, saccade-transitions (switch versus repetition of saccade task) affected performance. Moreover, the direction of change (from a prosaccade to an antisaccade or vice versa) and the amount of time for preparation were also important as reflected in a significant three-way interaction (F(1,20)=5.56, p<.05) (see Fig. 1). A significant cost of switching was evident only for prosaccades at the short CTI (t(20)=4.0, p<.001). In comparison, there was no significant effect of transition for antisaccades at the short CTI (t(20)=−.29, ns) or for either saccade task at the long CTI (prosaccades: t(20)=.75, ns; antisaccades: t(20)=.90, ns). When the data were collapsed across transition, prosaccades were, as expected, faster than antisaccades at both CTIs (300 ms: F(1,20)=4.86, p<.05; 1000 ms: F(1,20)=6.68, p<.05).

Errors

There was not a significant 3-way interaction in the error data but two 2-way interactions were significant: CTI and switch (F(1,20)=13.1, p<.01) and CTI by task (F(1,20)=4.6, p<.05). Switch costs were significant for both saccade types at the short CTI (prosaccades: t(20)=2.9, p<.01; antisaccades: t(20)=3.8, p<.001) but for neither at the long CTI (prosaccades: t(20)=.92, ns; antisaccades: t(20)=1.5, ns). At both CTIs, antisaccades produced more errors than prosaccades (300 ms: t(20)=−3.6, p<.01; 1000 ms: t(20)=−2.3, p<.05).

In summary there was evidence that subjects were using the cue to prepare for the upcoming change of task, because switch costs were present at the short CTI but eliminated at the long CTI. Response

Fig. 1. Reaction times (upper panel) and error rates (lower panel) for the saccadic switching task. Error bars denote 95% confidence intervals (Loftus and Masson, 1994).
latency was affected by switching task only for prosaccades and only at the short preparation interval. Both tasks showed a significant reduction in accuracy for switch versus repetition trials but again only with the short preparation interval.

**ERP effects**

**Cue-locked ERP effects**

The transition comparison for each saccade type in the electro-physiological data during the preparation phase (cue-locked epochs) revealed a late frontal negativity (LFN) for switch relative to repetition trials over frontal scalp (AFz, EGI sensor 16) which was confined to prosaccades (Fig. 2). This extended from 812 ms to target-onset at 1000 ms (and therefore was only present in trials with a long CTI). No significant switch-related effects were observed in the cue-locked epoch for the antisaccade task.

When saccade types were compared directly (collapsed over transition), prosaccades were associated a larger positive modulation over frontal scalp (Fz, EGI sensor 11) than antisaccades in an interval ranging from 260–380 ms (Fig. 3).

**Stimulus-locked ERP**

During the task implementation phase (stimulus-locked epochs), significant effects of transition were only observed with the 300 ms CTI. A sustained late parietal positivity was seen over central scalp (CPz; EGI sensor 55) over the interval 432–724 ms for prosaccades (Fig. 4A upper half) and 532–588 ms for antisaccades (Fig. 4B upper half). No significant effects of switching were found for either type of saccade for stimulus-locked epochs that were preceded by the long preparation interval (Figs. 4A and B lower halves for prosaccades and antisaccades, respectively).

The direct comparison between saccade types indicated an increased N2 negativity (180–244 ms) and subsequent reduced P3 positivity (292–492 ms) for antisaccades over parietal scalp (Pz; EGI sensor 62; Fig. 5).

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**Fig. 2.** Cue-locked waveforms and scalp maps at the long (1000 ms) CTI, showing the anterior frontal negativity (LFN) for prosaccade switch versus repetition trials which is absent for antisaccades. The black bar underneath the waveform indicates the period of consecutive significance. Scalp maps show voltage differences (switch–repetition) across the scalp (colour indicates magnitude) and sensors with a significant switch versus repetition difference (circles for switch positivity and squares for switch negativity, relative to repetition); star indicates site of plotted waveforms.

**Fig. 3.** Waveform and scalp map for the significant cue-locked anterior positivity for prosaccades relative to antisaccades. Scalp map shows voltage differences between saccade types (prosaccade–antisaccade) and sensors with a significant prosaccade versus antisaccade difference (circles prosaccades more positive than antisaccades and squares antisaccades more negative than prosaccades).
Fig. 4. A. Target-locked voltage difference scalp map and waveform showing the late parietal positivity (LPP) in the prosaccade task when preceded by a short (300 ms CTI) preparation interval, which is absent for the long (1000 ms) interval. B. Same, but showing the smaller LPP for the antisaccade task.

Fig. 5. Waveforms and difference scalp maps for the target-locked prosaccade versus antisaccade comparison (data collapsed across CTI), showing the increased target-locked N2 and reduced P3 components for antisaccades relative to prosaccades over parietal scalp.
Discussion

It was hypothesised that distinct neurophysiological markers related to inhibition would be apparent in a saccadic switching task with asymmetrically strong responses. As predicted, during the preparation phase for a shift to the prosaccade task, a switch-specific late frontal negativity (LFN) was visible that was not present for the switch to the antisaccade task. This component may index the encountering or overcoming of persisting suppression of prosaccades applied during the performance of an antisaccade to prevent the incidental triggering of a prosaccade. Current suppression of the prosaccade response during an antisaccade trial may be indexed by the increased N2 and decreased P3 (target locked N2/P3 complex) for the antisaccade task relative to prosaccade task. A delayed late parietal positivity (LPP) was found during task implementation following the short preparation interval (switch versus repeat within each task). This waveform was more sustained for the prosaccade than the antisaccade task and importantly occurred after mean response onset. Each of these effects is discussed in turn after the summary of the behavioural results.

As expected, the behavioural data showed that the effect of trial history on performance depended on both the prepotency of the task and the time available for preparatory activity. When the preparation time was limited, the latency of responses with a switch to prosaccades but not to antisaccades was slowed (relative to repetition of the same saccade type). At the short preparation interval, prosaccade switch trials were as slow as antisaccade switch trials. However, there was a significant reduction in response latency for prosaccades with repetition which can either be seen as a repetition benefit or a switch cost. Such a reduction in latency was not present for antisaccades. With regards to overall accuracy, switching between tasks was associated with a significant decline in error rates for both saccade types when preparation time was limited. By comparison, when an extended period was available for advance preparation, neither task showed a decline in latency or accuracy on switch trials. These findings are in line with previous studies that have shown that switch costs are typically larger for prosaccade than antisaccade and may be reversed (switch benefit) or absent when preparation time is increased (Barton et al., 2006; Hodgson et al., 2004).

Matthews et al. (2002) previously reported a cue-locked increased negativity (306–380 ms) over central and fronto-central sensors, following a change of cue that indicated a switch to an antisaccade task, relative to a cue change during a block of prosaccade trials that did not require a change of task. He suggested this difference was a marker of suppression of the prepotent prosaccade. In the current study we also found that the antisaccade task was more negative than the prosaccade task over a comparable period (260–380 ms) and sensors, which is shown in the topographic plot of Fig. 3 as a relative positivity for prosaccades. Given that this effect was not modulated by switching tasks supports the notion that this waveform reflects the suppression of the prosaccade response, which would be required on any antisaccade trial.

As expected, we observed a progressive LFN for switch trials relative to repetition trials from 812 ms to target onset, which was only present in the prosaccade task. We have previously observed the switch-related LFN in circumstances where competition between tasks to control motor output is increased. For example, it has been observed during preparation to switch tasks following a go response but not a no-go response (Astle et al., 2006) or when an overt but not a covert shift of task is planned (Astle et al., 2008a). When each task is associated with a unique set of responses, a switch related LFN is either missing (Mueller et al., 2007) or else is less sustained (Astle et al., 2008a). We suggest that in the current study the LFN observed for the shift to the prosaccade task reflects the presence of persisting prosaccade task suppression that was applied during the preceding antisaccade trial.

This suppression may be necessary to prevent the accidental triggering of a prosaccade during execution of the antisaccade task, and because it persists, it affects the shift back to the prosaccade task (e.g. Allport et al., 1994). Of note, the LFN is unlikely to reflect the execution of an inhibitory process itself, because that would have occurred on the preceding trial. Instead, it may reflect activity related to encountering or overcoming persisting suppression. By comparison, during the shift to the antisaccade task, no prior suppression from the prosaccade task may need to be resolved as it was never present. As a consequence, the same switch-modulated effect is not seen for antisaccades.

Given the difference of techniques we cannot say whether the ERP effects observed in the current study reflect the same functions or brain sources observed in saccadic functional imaging studies. Manoach and colleagues have reported a reduction of activity in the FEF on antisaccade trials following an antisaccade response (antisaccade repeat trial), which they attributed to sustained suppression of prosaccade responses (Manoach et al., 2007). Other evidence from functional imaging and neuropsychology suggest that the SEF, a part of the medial frontal cortex, is critically involved in resolving conflict when faced with a discrepancy in oculomotor action plans, although the timing of this activity is unclear (Nachev et al., 2005; Parton et al., 2007). The SEF may be part of a wider medial frontal cortex system for error monitoring and conflict resolution (Ridderinkhof et al., 2004). Manoach and colleagues reported that activity in SEF was decreased on trials following an antisaccade. This evidence is consistent with a decrease in error monitoring and motor conflict following an antisaccade response.

During task implementation (i.e., in the stimulus-locked waveforms) we found a switch-related positivity for both types of saccade for the short preparation interval, resembling the late parietal positivity seen in previous studies (LPP; e.g. Swainson et al., 2006). Previous task switching studies have reported this effect with a wide range of tasks (Nicholson et al., 2005; Rushworth et al., 2002, 2005; Swainson et al., 2006). Some authors have attributed this component to anticipatory task-set reconfguration since its timing is related to when participants know what task to perform (Nicholson et al., 2005). In the current study the LPP for switch trials occurred too late to be a marker of advance task set reconfguration. The mean RT for prosaccades was 432 ms, and for antisaccades 451 ms while the LPP became significant from 430 ms onwards for prosaccades and from 532 ms onwards for antisaccades. The onset of this component was similarly later than the mean response time in a previous study where participants switched between two manual tasks that differed in terms of prepotency (Swainson et al., 2006). In the current study, the LPP was absent from both the target- and cue-locked data when preceded by long preparation intervals. These findings are inconsistent with the view that this component is a marker of advance reconfguration, since its occurrence is clearly not necessary for a shift of task to occur. Instead, we suggest that the LPP reflects the biasing of attention to the now relevant task set, a process that can occur after response execution, and which will then benefit subsequent task-repetitions (Astle et al., 2008b).

During the implementation phase, markers of current inhibition that suggest a requirement for additional control for antisaccadic trials were evident in the N2/P3 complex. Studies have documented these neurophysiological markers of response inhibition using the Go–Nogo task (Eimer, 1993; Jackson et al., 1999; Thorpe et al., 1996). Both an increased negativity during the N2 waveform (Thorpe et al., 1996) and a decreased positivity during the P3 waveform (Jackson et al., 1999) have been reported for Nogo-relative to Go trials. Previous behavioural studies have noted the similarity between Nogo responses and antisaccades (Barton et al., 2005). As such, an increased N2 with a decreased P3 for antisaccades relative to prosaccades is consistent with findings from the Go–Nogo literature. Some investigators have argued that the N2 reflects a response to conflict information while
the reduced P3 reflects control of this conflict when conflict levels are high (Chen et al., 2008).

In summary, we found two neurophysiological markers of persisting (LFN) and current (N2/P3) inhibition when switching between two strongly asymmetric tasks. The former may reflect the active overcoming of suppression applied during the antisaccade trial, and the later the active inhibition of the prosaccade during the antisaccade trial. The results demonstrate the utility of saccadic tasks for examining the temporal brain dynamics of behavioural control in the presence of hard-wired biological response tendencies.

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References


