Functional Specialization within Macaque Dorsolateral Prefrontal Cortex for the Maintenance of Task Rules and Cognitive Control

Sabeeha Hussein1,2, Kevin Johnston1,2, Brandon Belbeck1,2, Stephen G. Lomber1,2,3, and Stefan Everling1,2,3

Abstract
■ The abilities of switching between and maintaining task rules are fundamental aspects of goal-oriented behavior. The PFC is thought to implement the cognitive processes underlying such rule-based behavior, but the specific contributions of the several cytoarchitecturally distinct subfields of PFC remain poorly understood. Here, we used bilateral cryogenic deactivation to investigate the relative contributions of two regions of the dorsolateral PFC (dlPFC) — the inferior dlPFC (idlPFC) area, consisting of the cortex lining the caudal principal sulcus, and the dorsally adjacent superior dlPFC (sdlPFC) — to different aspects of rule-based behavior. Macaque monkeys performed two variants of a task that required them to alternate unpredictably between eye movements toward (prosaccade) or away from (antisaccade) a visual stimulus. In one version of the task, the current rule was overtly cued. In the second, the task rule was uncued, and successful performance required the animals to detect rule changes on the basis of reward outcome and subsequently maintain the current task rule within working memory. Deactivation of the idlPFC impaired the monkeys’ ability to perform pro- and antisaccades in the uncued task only. In contrast, deactivation of the sdlPFC had no effect on performance in either task. Combined deactivation of idlPFC and sdlPFC impaired performance on antisaccade, but not prosaccade, trials in both task variants. These results suggest that the idlPFC is required for mnemonic processes involved in maintenance of task rules, whereas both idlPFC and sdlPFC together are necessary for the deployment of the cognitive control required to perform antisaccades. Together, these data support the concept of a functional specialization of subregions within the dlPFC for rule-guided behavior.

INTRODUCTION
Goal-oriented behavior requires the ability to apply rules that specify the most appropriate response to a stimulus within a given context. Rules may be externally cued with fixed, relatively simple stimulus–response mappings, such as go when a traffic light is green and stop when it is red. In other instances, the appropriate rule is not directly specified by environmental stimuli, but must be selected, maintained, or switched on the basis of behavioral outcomes. Such uncued rule-related processes are commonly assessed using the WCST (Milner, 1963), which requires subjects to acquire a task rule by trial and error and either maintain or switch rules depending on “stay” or “switch” feedback.

Single neuron recordings in the macaque monkey have found neural correlates of both cued and uncued rule representations in PFC (Tsujimoto, Genovesio, & Wise, 2012; Johnston, Levin, Koval, & Everling, 2007; Johnston & Everling, 2006b; Everling & Desouza, 2005; Genovesio, Brasted, Mitz, & Wise, 2005; Wallis & Miller, 2003; Wallis, Anderson, & Miller, 2001; Asaad, Rainer, & Miller, 2000; White & Wise, 1999). In general, these studies suggest little differentiation of such representations across the several subregions comprising this area in primates. In contrast, lesion studies of macaque PFC have provided compelling evidence for regional specialization of cued and uncued rule representations. Ventral prefrontal and orbitofrontal areas are critical for the application of cued rules (Bussey, Wise, & Murray, 2001; Murray, Bussey, & Wise, 2000; Passingham, Toni, & Rushworth, 2000), whereas dorsolateral PFC (dlPFC) lesions either do not or only mildly impair this ability (Gaffan & Harrison, 1989; Petrides, 1982). Recently, Buckley and colleagues trained monkeys on a simplified analog of the WCST that required switching between shape and color matching rules during selection of visual stimuli and investigated the effects of lesions of several prefrontal subregions on task performance (Buckley et al., 2009). Lesions of inferior dlPFC (idlPFC) in the area of the principal sulcus were found to selectively increase error rates after imposed delay periods between trials. Accordingly, the authors proposed that this area is functionally specialized for the selection and active maintenance of uncued rules in working memory. Lesions of cortex dorsal to the principal sulcus, which they labeled
superior dlPFC (sdlPFC), had no effects. Such regional specialization of function is consonant with the well-established anatomical segregation of PFC in primates, based on cytoarchitecture and connectivity (Petrides & Pandya, 1999; Preuss & Goldman-Rakic, 1991; Barbas & Pandya, 1989).

An important aspect of rule-based behavior not captured by the WCST is the relative automaticity of certain stimulus–response pairings that is characteristic of more naturalistic situations. Some rules may be overlearned and more automatic, whereas others require more control. Both Stroop (Stroop, 1935) and stimulus–response compatibility tasks (Hommel & Prinz, 1997) require subjects to override automatic processes in favor of controlled responses. In these tasks, incongruent stimulus–response processes are characterized by increases in RT and performance decrements relative to congruent processes. Functional imaging studies in humans have shown that the dlPFC is activated during delay periods in the Stroop task when subjects have to prepare to name the print color of a color word (Donohue, Wendelken, & Bunge, 2008; MacDonald, Cohen, Stenger, & Carter, 2000) and in the antisaccade task (Munoz & Everling, 2004) when they prepare to look away from a subsequently presented visual stimulus (Brown, Vilis, & Everling, 2007; Desouza, Menon, & Everling, 2003). On the basis of these findings, it has been proposed that the ventrolateral PFC is involved in rule maintenance for stimulus–response associations, whereas the dlPFC is engaged in rule maintenance when subjects must maintain the goal of overriding a strong response tendency (Bunge, 2004).

Taken together, evidence from lesion studies in monkeys and fMRI investigations in human participants suggests a parcellation of rule-related processes in PFC. The relative contribution of dlPFC subregions to rule-based behavior under conditions requiring maintenance and switching of automatic and controlled processes, however, remains poorly understood. To address this, we reversibly and separably deactivated parts of the idlPFC and sdlPFC while monkeys performed tasks requiring the implementation of cued or uncued rules. We used bilaterally implanted cryoloops (Lomber, Payne, & Horel, 1999) to independently deactivate the idlPFC (cortex in the caudal principal sulcus) or the dlPFC (cortex dorsal to the principal sulcus; Figure 1A). The area of cortex deactivated by these loops was consistent with, but of lesser area, than the idlPFC and sdlPFC lesions in the study of Buckley et al. (2009). Animals performed a task that required them to switch between blocks of prosaccades (requiring a saccade toward a flashed peripheral stimulus) and antisaccades, which required the suppression of a saccade toward the stimulus in favor of one toward the opposite direction (Everling & Desouza, 2005; Figure 1B). In a cued condition, the color of the fixation point instructed the monkeys which task to perform on each trial. In an uncued condition, the animals had to acquire the current rule based on reward feedback delivered following each trial. After 15–25 correct trials, the rule was changed without warning and the animals had to switch to the other rule. This task thus required the animals to switch between and maintain within working memory task rules specifying relatively automatic and more controlled responses under externally cued and uncued conditions.

**METHODS**

**Surgeries**

Data were collected from two male rhesus monkeys (Macaca mulatta) weighing 10 and 12 kg. In a third rhesus monkey, one of the idlPFC loops became plugged immediately after the cooling loop surgery, and no data could be obtained from this animal for this study. All procedures were carried out in accordance with the guidelines of the Canadian Council of Animal Care Policy on the Use of Laboratory Animals and a protocol approved by the Animal Use Subcommittee of the University of Western Ontario Council on Animal Care. In the first aseptic surgery, a plastic head restraint was implanted (for details, see Johnston & Everling, 2006a). Animals received analgesics and antibiotics postoperatively and were closely monitored by a university veterinarian. Following recovery, monkeys were trained to perform the cued pro/antisaccade and uncued pro/antisaccade tasks. After the animals reached a criterion of ∼75% correct performance in the uncued task, they underwent a second surgery in which stainless steel cryoloops (6 mm × 3 mm) were implanted bilaterally into the posterior portion of the principal sulcus (idlPFC loop, covering parts of area 46 and 9/46 and anterior parts of area 8A) and bilaterally on the cortex that lies immediately dorsal to the principal sulcus (dlPFC loop, covering parts of area 9/46d and area 9; Figure 1A). On the basis of a spread of devascularization of 2 mm around the loops (Lomber et al., 1999), we estimated that the idlPFC loop deactivated portions of areas 46, 9/46d and v, and 8, whereas the sdlPFC loop deactivated portions of areas 46, 9, 9/46d, and 8 (Figure 1B). Cryoloops were constructed from 23-gauge hypodermic stainless steel tubing. The procedures for the manufacturing, surgery, and use of cryoloops have been described in detail (Lomber et al., 1999).

**Task**

Figure 1C illustrates the pro/antisaccade switch task. Each trial began with the presentation of a fixation spot at the center of a CRT monitor screen. The animals were required to fixate it within a 0.5° × 0.5° window for a random period of 1100–1400 msec. A visual stimulus (0.2") was then presented pseudorandomly with equal probability 8° to the left or right of the fixation spot. To obtain a liquid reward, monkeys were required to generate a saccade within 500 msec, either to the stimulus

*Hussein et al.* 1919
location on prosaccade trials or away from the stimulus to
its mirror location on antisaccade trials (within a 5° × 5°
window). On successful trials, a liquid reward was given
200 msec after saccade end. Task switches occurred
on a random trial once animals had performed between
15 and 25 correct responses. In the cued task, a green
fixation spot instructed prosaccades and a red fixa-
tion spot was the instruction to perform antisaccades
for Monkey G. These instructions were reversed for
Monkey B. In the uncued task, the fixation spot was
always white, and the monkeys had to acquire the task
rule based on reward delivery ("stay") or omission
("switch"). Horizontal and vertical eye positions were
recorded at 500 Hz using an Eyelink II system (SR
Research, Kanata, Canada).

Prefrontal Deactivations

We collected data from a total of 103 sessions in which
either (1) no area was deactivated, (2) the idlPFC was
bilaterally deactivated, (3) the sdlPFC was bilaterally de-
activated, or (4) both areas were bilaterally deactivated.
Cued and uncued versions of the switch task were run
on separate days. During cooling sessions, methanol at
room temperature was pumped through teflon tubing
passing through a methanol ice bath, which was re-
duced to subzero temperatures by the addition of dry
ice. Chilled methanol was then pumped through a cryo-
loop and returned to the same reservoir from which
it came. Cryoloop temperature was monitored by an
attached microthermocouple. At the beginning of each
cooling session, either two or four pumps (one for each
cyroloop) were turned on. It took on average of 85 sec
to lower the temperature of the loops to 3°C. After 3–
5 min, the experimental task began. We maintained cryo-
loop temperature in the range of 1–5°C by adjusting
the flow rate of the pump. This range was chosen to inactivate
as large an area of cortical tissue as possible (the extent
of inactivated tissue is limited to a range of ∼2 mm when
cryoloop temperature is reduced to 1–3°C; Lomber et al.,
1999) while avoiding potentially harmful subzero tem-
peratures at the cortical surface. This ensured that the
cortical tissue adjacent to the cryoloop reached tempera-
tures below the 20°C threshold for neuronal deactivation
(Adey, 1974). Even after months or years of daily cooling
deactivations, there is no alteration to either the structure
or function of underlying cortex (Yang, Kennedy, Lomber,
Schmidt, & Rothman, 2006). Each experimental session
lasted between 60 and 70 min to ensure consistent moti-
vation of the animals and task performance. We did not
observe any indications of discomfort from the animals
during any of the cooling sessions. On average, monkeys
performed 50 task switches during each session. Postses-
sion, monkeys received liquid until satiation, after which
they were returned to their home cages. Daily records
of the weight and health status of the monkeys were
kept, and additional fruit was provided.

Data Analysis

Data analysis was performed using custom-designed soft-
ware running in Matlab (Mathworks, Natick, MA). Saccade
onset was defined as the time at which eye velocity ex-
ceeded 30°/sec and saccade end as the time at which radial
velocity fell below 30°/sec. Trials with broken or incorrect
fixation were excluded from further analyses as were trials

Figure 1. Placement of cryoloops and experimental paradigm.
(A) Photo of right PFC of Monkey B during cryoloop surgery. One
cryoloop was implanted in the principal sulcus (idlPFC), and the
other one was placed over the cortex dorsal to the principal sulcus
(sdlPFC). (B) Depiction of estimated area of deactivated cortex,
shown in relation to PFC cytoarchitecture as proposed by Petrides
(C) Schematic diagram of the switch task. Monkeys had to alternate
between blocks of prosaccades (saccade toward a visual stimulus)
and blocks of antisaccades (saccade away from the stimulus). Visual
stimuli were presented randomly to the left or right side. In the
cued condition, the color of the central fixation point instructed
the animals which task to perform. In the uncued condition,
monkeys had to acquire and maintain the current task rule by
reward feedback that was given at the end of the trial.
with RTs <80 msec (anticipations) or >1000 msec (no response trials). For each experimental session, the average time course of pro- and antisaccade performance before and after a task switch was calculated, and the time course across sessions was computed by averaging the individual sessions from both subjects. Because there was no effect of the task switch on RTs of pro- and antisaccades, with the exception of the first trial after a switch, which was associated with longer RTs, the mean RT of all correct pro- and antisaccades was computed for each session and then averaged across sessions.

**RESULTS**

**Effects of DLPFC Deactivation on Uncued Task Performance**

Figure 2A shows the monkeys’ performance on the trial immediately preceding and on the 15 trials following a switch from anti- to prosaccades in the uncued condition. The black line depicts mean percentage of correct trials on control days when no cooling was performed (n = 17). In these sessions, monkeys performed antisaccades at ∼75% before the task switch. On the first trial postswitch, performance dropped to ∼25%, a finding which was expected as the animals received no warning of the impending switch. Performance then recovered quickly, reaching ∼50% on the second postswitch trial and ∼90% after six trials. This pattern of behavior is consistent with previous studies using this task (Johnston et al., 2007; Everling & Desouza, 2005). When the idlPFC was cooled bilaterally (red line, n = 17), prosaccade performance improved only to ∼70%. When we bilaterally deactivated the sdlPFC (blue line, n = 17) or the idlPFC together with the sdlPFC (purple line, n = 17), prosaccade recovery after the task switch showed a similar time course to that on control days. Figure 2B shows the animals’ performance for task switches from pro- to antisaccades. On control days (black lines), the monkeys’ performance dropped from ∼85% on the last trial of the prosaccade block to 15% on the switch trial and then reached ∼75% correct performance after five trials. Following deactivation of the idlPFC, monkeys retained the ability to switch to the antisaccade task, but their performance reached a plateau at ∼60%. Cooling of the sdlPFC produced no effects, whereas combined cooling of the idlPFC and sdlPFC showed a similar deficit to that observed when cooling the idlPFC alone.

To statistically evaluate the effects of cooling on task performance, we computed the mean error rates for Trials 6–15 following a task switch. As shown in Figure 2 (A, B), performance was fairly stable during this period. Figure 2C displays error rates for the control condition (black), idlPFC cooling (red), sdlPFC cooling (blue), and combined cooling of the idlPFC and sdlPFC (purple) on prosaccade blocks. A one-way ANOVA showed a significant effect of cooling on error rates for prosaccade blocks, \( F(3) = 13.99, p < .0001 \). Planned post hoc comparisons (two sample t tests) between the control condition and the deactivations demonstrated that error rates were significantly greater during cooling of idlPFC (\( p < .00001 \)). Error rates during cooling of the sdlPFC and, surprisingly, combined cooling of the idlPFC and sdlPFC did not differ from control (\( p = .83 \) and \( p = .52 \), respectively). Significant effects of cooling on error rates were also observed on antisaccade blocks (Figure 2D), \( F(3) = 13.99, p < .000001 \) (one-way ANOVA). Error rates were elevated significantly during deactivation of the idlPFC (\( p < .0001 \)) and combined deactivation of the idlPFC and sdlPFC (\( p < .0001 \)). These effects were similar for Monkey B and Monkey G (Figure 3).

We also tested whether deactivation impaired the ability to switch between tasks by further investigating the recovery of performance observed following a task switch. As an index of this, we computed the percentage of correctly performed trials following an error on the first postswitch trial. This analysis revealed that cooling had no effects on switching (anti- to prosaccades, \( F(3) = 2.48, p = .07 \); pro- to antisaccades, \( F(3) = 1.72, p = .17 \)). These results demonstrate that cooling of the idlPFC impaired the performance of both pro- and antisaccade task blocks whereas cooling of the sdlPFC did not increase error rates. Combined cooling of these two areas impaired performance on antisaccade blocks but had no effect on prosaccade blocks.

In addition to effects on performance, we tested effects of cooling on the saccadic RTs of correct pro- and antisaccade trials. We found no effects of deactivation on prosaccade trials (Figure 2E), \( F(3) = 2.01, p = .12 \) (one-way ANOVA), but a significant effect on antisaccades (Figure 2F), \( F(3) = 3.8, p = .014 \). A post hoc test (two sample t test) showed that combined cooling of the idlPFC and sdlPFC increased antisaccade RTs (\( p = .002 \)). The effects of cooling were very similar for both subjects (Figure 4).

**Effects of dlPFC Deactivation on Cued Task Performance**

We next investigated the monkeys’ performance when a task instruction was provided throughout each trial by the color of the central fixation spot. This version of the task retained the requirement of switching between pro- and antisaccade task blocks and suppression of prosaccades on antisaccade trials but eliminated the requirement to acquire the task rule by reward-based feedback and maintain it in working memory. Figure 2 (G and H) shows percentage of correct responses on prosaccade and antisaccade blocks, respectively. No effects of cooling were observed on prosaccade trials (Figure 2G, I), \( F(3) = 1.66, p = .20 \) (one-way ANOVA). On antisaccade trials, cooling had a small but significant effect on error rates (Figure 2H, J), \( F(3) = 3.3, p = .03 \). Error rates were significantly increased during combined cooling of the idlPFC and sdlPFC (\( p = .02, t \) test). The effects of cooling on saccadic RTs were similar to those observed in the
Figure 2. Effects of cooling of dorsolateral prefrontal regions on performance and RTs. (A) Performance following task switches from anti- to prosaccades in the uncued condition. The proportion of correct responses is plotted for the trial immediately before the task switch to the 15 trials after a task switch. Data are averaged across sessions from both monkeys. (B) Same as (A) but for task switches fro pro- to antisaccades. (C) Percentage of errors (i.e., responses following the wrong task rule) during the performance of Trials 6–15 following a task switch from anti- to prosaccades in the uncued condition. (D) Same as (C) but for task switches from pro- to antisaccades. (E) RTs of all correct prosaccades in the uncued condition. (F) Same as (E) but for correct antisaccades. (G–L) Same as (A–F) but for the cued condition. *p < .05.
uncued task, with no effect on prosaccade, $F(3) = 2.07$, $p = .13$ (one-way ANOVA), and a significant increase on antisaccade trials, $F(3) = 3.97$, $p < .05$. Post hoc comparisons (two-sample t tests) revealed a significant effect of cooling the idlPFC ($p = .01$) and combined cooling of the idlPFC and sdlPFC ($p < .005$).

**DISCUSSION**

Our results suggest a functional specialization of sub-regions within the dlPFC for rule-guided behavior. We found that deactivation of the cortex lining the caudal principal sulcus impaired monkeys’ performance on both pro- and antisaccade trials in an uncued task variant, which required them to maintain task rules in working memory. Deactivation of the same region when the task rules were fully cued, a task version absent mnemonic demands, led to only minor performance impairments in the antisaccade condition. In contrast, deactivation of the sdlPFC had no effect on error rates in the pro- or antisaccade conditions in either the cued or uncued version of the task. Simultaneous deactivation of both

![Figure 3. Effects of cooling on performance in Monkey B and Monkey G. (A) Percentage of errors (i.e., responses following the wrong task rule) during the performance of Trials 6–15 following a task switch in Monkey B. (B) Same as (A) for Monkey G. *$p < .05$.](http://direct.mit.edu/jocn/article-pdf/26/9/1918/1781688/jocn_a_00608.pdf)
areas produced a selective impairment of antisaccade performance, which was considerably greater when the task rule was uncued. In addition to effects on error rates, dlPFC deactivation caused a selective increase in RTs of antisaccades with the strongest effects elicited by combined cooling of both subregions. These effects were similar for the cued and uncued conditions, suggesting that, unlike the selective cooling-induced impairment of mnemonic processes we observed in the uncued version of our task, other processes underlying antisaccade generation such as vector inversion and motor preparation are generally impaired by deactivation of dlPFC.

Although cooling of the principal sulcus had strong effects on task maintenance, we found no evidence of an effect of deactivation of either dlPFC subregion on the performance recovery observed following a change to a new task rule. This finding is inconsistent with a role of the dlPFC in task switching. Consonant with this, functional imaging studies in humans have reported prefrontal activations during rule maintenance (Crone, Wendelken, Donohue, & Bunge, 2006; Sakai & Passingham, 2003; Passingham et al., 2000) but pre-SMA or anterior cingulate activations during task set reconfigurations (Crone et al., 2006). Moreover, our own previous work has
demonstrated that task rule selectivity of single neurons for uncued pro- and antisaccades was low immediately after a task switch in the DLPFC (caudal areas 9/46d and 46) but high in the ACC in monkeys (Johnston et al., 2007), suggesting that medial, but not lateral, PFC areas are strongly involved in task switching.

Human imaging studies have shown that the ventral PFC is activated for visual conditional tasks (Toni, Rushworth, & Passingham, 2001; Passingham et al., 2000), whereas more dorsal prefrontal regions are active for tasks in which the subjects must represent actions to themselves (Deiber et al., 1991; Frith, Friston, Liddle, & Frackowiak, 1991). Although a number of single neuron recording studies in nonhuman primates have demonstrated rule-related activity in the dIPFC (Tsujimoto et al., 2012; Johnston et al., 2007; Johnston & Everling, 2006b; Everling & Desouza, 2005; Genovesio et al., 2005; Wallis & Miller, 2003; Wallis et al., 2001; Asaad et al., 2000; White & Wise, 1999), the lesion study of Buckley et al. (2009) was the first to demonstrate directly that the cortex in the principal sulcus is essential for the maintenance of task rules in uncued tasks. They proposed that this dIPFC subregion is critical for the selection and maintenance of uncued rules in working memory. Our finding that bilateral cooling of the caudal principal sulcus selectively impaired performance of both pro- and antisaccade blocks in the uncued condition is consistent with this hypothesis. Although it remains unknown whether larger deficits would have been observed had we deactivated the entire principal sulcus, our results demonstrate that deactivation of the caudal principal sulcus by itself leads to significant impairments in the maintenance of task rules in the absence of ongoing instruction.

We observed no increase in error rates during caudal principal sulcus deactivation in prosaccade blocks in the cued condition. This finding is consistent with several lesion studies in the macaque, which have shown that ventral and orbital lesions impair learning and retention of stimulus–response associations (Bussey et al., 2001; Murray et al., 2000; Passingham et al., 2000; Hoshi, Shima, & Tanji, 1998; see, however, Wang, Zhang, & Li, 2000), whereas dorsolateral ablations cause no or only mild deficits (Gaffan & Harrison, 1989; Petrides, 1982). However, we observed small increases in antisaccade error rate in the fully cued condition during idIPFC cooling. This finding is consistent with a recent study of our group (Koval, Lomber, & Everling, 2011) in which we observed increased RTs and increased error rates during bilateral deactivation of the caudal principal sulcus in a task in which monkeys performed cued, randomly interleaved, pro- and antisaccade trials. In that study, we also recorded the activity of saccade-related neurons in a downstream oculomotor structure, the superior colliculus, and found that deactivation caused a suite of changes in their preparatory, visual, and motor responses consistent with these behavioral changes. These cooling-induced effects on the activity of superior colliculus neurons provide a plausible mechanism for the increase in error rates and RTs on antisaccade trials in the cued condition we observed here.

In contrast to the impairments following deactivation of the idIPFC, cooling of the sdlPFC did not impair the maintenance of task rules for pro- or antisaccades. Although this finding is consistent with the study by Buckley et al. (2009), who did not observe any effects following ablation of the cortex immediately dorsal to the principal sulcus to the midline, it is surprising given that many single neuron recording studies have found rule-related or strategy-related activity in this region (i.e., Genovesio et al., 2005; Wallis et al., 2001). In fact, we have found many neurons with task rule selectivity in this region while monkeys performed the uncued pro- and antisaccade tasks (Johnston, De Souza, & Everling, 2009; Johnston et al., 2007; Everling & Desouza, 2005). A potential explanation for this seeming inconsistency has been provided by Passingham et al. (2000), who have theorized that the activity of a given neuron within a frontal region may be derived from its connections with other frontal regions and that only lesion studies can determine whether a particular region is essential for a given behavior. Following this argument, our data speak against a role of the sdlPFC in rule maintenance and in the suppression of automatic responses.

Although deactivation of the sdlPFC had no effect on task rule maintenance in the uncued condition, combined deactivation of this region with the idIPFC impaired the performance of anti- but not prosaccade blocks. Thus, deactivation of the sdlPFC reversed the impairments on prosaccade blocks seen after deactivation of the idIPFC alone. Although the behavioral deficits following combined deactivation of both dIPFC regions are consistent with the hypothesis that the dIPFC is engaged in rule maintenance when subjects must maintain the goal of overriding a strong response tendency (Bunge, 2004), it suggests that two subprocesses, endemic to two anatomically distinct dIPFC subregions, contribute to this function. On the basis of our results, we hypothesize that the idIPFC plays a general role in maintaining uncued task rules whereas the sdIPFC is specifically involved in the deployment of cognitive resources in contexts requiring more control. According to this hypothesis, deactivation of the idIPFC impairs the maintenance of both automatic (i.e., prosaccades) and less practiced tasks requiring more control (i.e., antisaccades), resulting in the increase in errors observed in both tasks. Deactivation of the sdIPFC by itself may not impair maintenance of the antisaccade task rule because this function could be carried out within the intact idIPFC. Combined deactivation of both dIPFC regions would impair antisaccades, but not prosaccades, because it impaired the maintenance of the task rules and shifted the behavior toward the more automatic prosaccade task rule. Further studies combining cryogenic deactivation and single neuron recordings of prefrontal subregions promise to further refine this model and broaden our understanding of the functional relationships within this multifarious region of the brain.
Acknowledgments

This study was supported by the Canadian Institutes of Health Research.

Reprint requests should be sent to Dr. Stefan Everling, Robarts Research Institute, 1151 Richmond Street, London, Ontario N6A 5B7, Canada, or via e-mail: severlin@uwo.ca.

REFERENCES


