

Flexible neural mechanisms of cognitive control within human prefrontal cortex

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Edited by Edward E. Smith, Columbia University, New York, NY, and approved March 2, 2009 (received for review August 26, 2008)

A major challenge in research on executive control is to reveal its functional decomposition into underlying neural mechanisms. A typical assumption is that this decomposition occurs solely through anatomically based dissociations. Here we tested an alternative hypothesis that different cognitive control processes may be implemented within the same brain regions, with fractionation and dissociation occurring on the basis of temporal dynamics. Regions within lateral prefrontal cortex (PFC) were examined that, in a prior study, exhibited contrasting temporal dynamics between older and younger adults during performance of the AX-CPT cognitive control task. The temporal dynamics in younger adults fit a proactive control pattern (primarily cue-based activation), whereas in older adults a reactive control pattern was found (primarily probe-based activation). In the current study, we found that following a period of task-strategy training, these older adults exhibited a proactive shift within a subset of the PFC regions, normalizing their activity dynamics toward young adult patterns. Conversely, under conditions of penalty-based monetary incentives, the younger adults exhibited a reactive shift some of the same regions, altering their temporal dynamics toward the older adult baseline pattern. These experimentally induced crossover patterns of temporal dynamics provide strong support for dual modes of cognitive control that can be flexibly shifted within PFC regions, via modulation of neural responses to changing task conditions or behavioral goals.

dorsolateral PFC | event-related fMRI | inhibition | interference control | working memory

A hallmark of human cognition is its flexible nature: We are able to rapidly adapt thoughts and behaviors to changing internal states and evolving external environments. The flexibility of human cognition is thought to depend on specialized cognitive control mechanisms, which facilitate goal-directed actions and suppress inappropriate ones. Although it is appreciated that cognitive control mechanisms enable flexibility, it is still not well understood how such flexibility is achieved (1).

One possibility that has been frequently explored in cognitive neuroscience is the idea of functional specialization and flexible selection of the neural mechanisms that subserve cognitive control (2). That is, there may be a variety of different cognitive control mechanisms housed within *anatomically* distinct brain regions, and a subset of these mechanisms are dynamically selected according to the specific cognitive demands of the task situation. Here, we explore an alternative possibility, that cognitive flexibility can also be achieved by modulating the manner in which a particular control mechanism is deployed in response to changing task demands or internal goal states. Specifically, we examine the hypothesis that flexibility in the deployment of a cognitive control mechanism might occur through modulation of the temporal dynamics of its engagement (i.e., the time period and duration over which a region is activated).

We have recently developed a theoretical account of how flexibility in cognitive control might be achieved in such a manner. In this theory, termed dual mechanisms of control (DMC), we postulate a distinction between proactive and reactive modes of cognitive control (3). The proactive control mode can be conceptualized as a form of “early selection,” in which

goal-relevant information is actively maintained in a sustained/anticipatory manner, before the occurrence of cognitively demanding events, to optimally bias attention, perception, and action systems in a goal-driven manner (4). In contrast, in the reactive mode, attentional control is recruited as a “late correction” mechanism that is mobilized only as needed, such as after a high-interference event is detected (5). Thus, proactive control relies on the anticipation and prevention of interference before it occurs, whereas reactive control relies on the detection and resolution of interference after its onset.

Critically, the DMC theory provides a strong prediction about the dynamics and location of brain activity under proactive versus reactive control. Proactive control should be associated with sustained and/or anticipatory activation of lateral PFC, which reflects the active maintenance of task goals. This goal-maintenance activity serves as a source of top-down bias that can facilitate processing of expected upcoming events that have a high cognitive demand. In contrast, reactive control should be reflected in transient activation of lateral PFC, along with a wider network of additional brain regions. This transient activity might reflect the bottom-up reactivation of task goals, mediated either via the detection of interference (e.g., through the engagement of conflict-monitoring regions such as anterior cingulate cortex; ACC) (6) or via associative connections (as might occur through posterior cortical regions). Thus, the DMC theory suggests that proactive and reactive control can be distinguished in terms of a dissociation between an anticipatory/sustained mode of lateral PFC activity and one that is more transient and interference sensitive.

A task paradigm that has been frequently used to examine the underlying mechanisms of cognitive control is the AX version of the Continuous Performance Test, or AX-CPT (7–15). This task is thought to measure goal representation, maintenance, and updating. Contextual cues serve as task goals regarding the appropriate actions to make in response to ambiguous probes. Active maintenance of this frequently updated task goal information is required to bridge the delay between cue and probe presentation. In a series of behavioral studies, it has been shown that the AX-CPT task provides sensitive and specific indices of cognitive control function (7–9). Likewise, neuroimaging studies have reliably demonstrated the presence of lateral PFC activity related to the active maintenance of task goals during AX-CPT performance (10–15).

We recently conducted 2 related functional magnetic resonance imaging (fMRI) studies of the AX-CPT, which both demonstrated variability in the temporal dynamics of lateral PFC activity observed during task performance. In one study (15), participants performed the AX-CPT under both baseline con-

Author contributions: T.S.B. and D.M.B. designed research; J.L.P. and H.S.L. performed research; J.L.P. analyzed data; and T.S.B. and J.L.P. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

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This article contains supporting information online at www.pnas.org/cgi/content/full/0808187106/DCSupplemental.

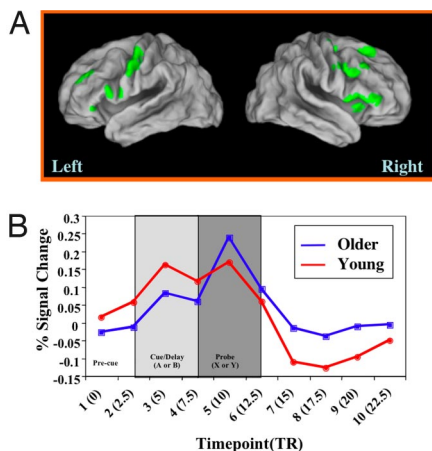


Fig. 1. (A) The set of 17 age-related crossover ROIs originally reported in ref. 10. (B) Activation dynamics during trial for younger and older adults (averaged across all ROIs). Older adults show reduced cue-related but increased probe-related activity, associated with a reactive control mode.

ditions and conditions of reward-based monetary incentives (for good performance). We found that activity shifted from a primarily event-related dynamics to one in which activation was sustained across trials. In the other study (10), we contrasted activity dynamics of younger and older adults. We found a significant age-related shift in lateral PFC regions, such that older adults showed both reduced cue-related activation and increased probe-related activation relative to younger adults (Fig. 1). These imaging-based age differences are consistent with prior behavioral studies, in which older adults exhibited smaller cue-based expectancy effects but also larger probe-related interference effects than younger adults (7–9).

Critically, the patterns in both studies are consistent with the DMC framework. Specifically, the DMC framework predicts that a shift toward proactive control will be associated with increased anticipatory activation dynamics in lateral PFC, which can emerge at the time of contextual cues, when these are available, such as in tasks like the AX-CPT. Proactive control is also hypothesized to be associated with sustained or tonic activation, which may reflect a more persistent or extreme form of preparation that reduces control demands at the time when contextual cues are presented in tasks such as the AX-CPT (or it may be required for active goal maintenance in tasks where trial-based contextual cues are not available, such as in the Stroop) (3). In contrast, reactive control is predicted to be associated with reduced cue-related (or sustained) activity, but increased activation during probe periods (especially when probes have the potential to produce interference). Thus, according to the DMC framework, younger adults were more able than older adults to engage in proactive control strategies during the AX-CPT, and their utilization of proactive control further increased under reward incentive conditions. Conversely, older adults may have been less able to engage in proactive control, and thus more dependent on a reactive control strategy for task performance.

Thus, the prior fMRI results suggest prominent differences in the cognitive control strategies used by younger (more proactive) and older adults (more reactive). Yet a key hypothesis of the DMC model is that cognitive control strategies are flexible and can be significantly impacted by specific experimental manipulations as well as stable individual and group differences. Thus, in the current study we asked a key question: Can the default cognitive control strategies used by younger and older adults change as a result of theoretically focused experimental manipulations?

To answer this question, we tested each group of participants while they performed an additional AX-CPT session that was designed to independently target and shift cognitive control strategy. Different experimental manipulations were used for each group. For older adults, we attempted to promote proactive control by providing focused cognitive training in the AX-CPT task, using an instructional protocol that was successful in a prior behavioral study (9). Conversely, in younger adults, we tested whether we could promote reactive control through a penalty incentive manipulation that increased attention to the probe (potentially at the expense of the cue). For both groups, we hypothesized that the experimental manipulations would selectively impact the activation dynamics in specific lateral PFC regions that mediate such cognitive control strategies.

To test the DMC model, we adopted a region-of-interest (ROI)-based approach, focusing exclusively on the PFC regions showing age-related changes in activity dynamics from our prior study (Fig. 1). In older adults, we predicted that cognitive training would shift activation from primarily probe related to primarily cue related in these ROIs. Conversely, in younger adults, we predicted that the incentive manipulation would cause a reverse trend (i.e., a shift from primarily cue-related to primarily probe-related activation). Note that our use of an exclusively ROI-based analysis approach provides an especially strong test of the DMC hypothesis that reactive and proactive control effects can occur within the same PFC regions.

Results

Older Adults. The 16 older adults that formed the sample reported in ref. 10 participated in a second session involving instructional strategy training, immediately followed by a posttraining scan in which the AX-CPT was performed again. Based on our previous behavioral results with this training procedure (9), we hypothesized that performance after AX-CPT training should show evidence of increased proactive control. We developed behavioral indices of proactive control that combine performance across the different trials types that are theoretically predicted to be most sensitive to changes in cognitive control strategy (see [supporting information \(SI\) Methods](#) for details). Separate indices were used for error rate and reaction time (as both of these measures have been found to be useful indicators in prior aging studies with the AX-CPT) (7–9) as well as an index that summed both measures. In all of the indices, a higher value indicates higher proactive control. Following training, we observed increases in both the RT and error rate indices relative to pretraining performance (see [Table S1](#)). When both of these measures were summed together, the effect was statistically significant, $t(15) = -2.22, P < 0.05$. Thus, we found behavioral evidence of a training-related proactive shift. These behavioral effects were also confirmed via 2 additional convergent analyses (see [SI Results and Fig. S1](#)).

Each of the 17 age-related crossover ROIs described in Fig. 1 (taken from our previous study; see ref. 10) was examined for a shift in activation dynamics in the posttraining session relative to baseline. Specifically, we determined whether the dynamics shifted from a primarily probe-based to primarily cue-based pattern, termed a “training-related proactive shift” in activation. The criterion for such a shift was the presence of a statistically significant session (baseline/posttraining) by event (cue/probe) crossover interaction, such that cue activity increased and probe activity decreased in posttraining session relative to pretraining baseline. Nine of the 17 ROIs met this criterion (indicated with a 1 in Table 1), including regions within right inferior frontal junction (IFJ), left dorsolateral PFC (DLPFC), and left superior frontal cortex (Fig. 2B illustrates the activation dynamics averaged across the regions, indicated in bold in Table 1).

It is noteworthy that, although the behavioral effect of training on proactive control was statistically significant, there was

Table 1. Frontal age-related crossover regions [modified from Paxton et al. (10)]

Regions of interest	Hemisphere	Brodmann area(s)	X [†]	Y [†]	Z [†]	Volume, mm ³ ‡	R [§]
Middle frontal gyrus	Right	8/9	24	27	50	999	
	Right	9/46	42	17	29	243 (1)	0.69**
	Right		43	28	37	243	
	Left		-35	44	32	837 (1, 2)	0.63**
Right inferior frontal gyrus	Right	47	37	20	-6	270 (1)	0.24
	Right		51	21	0	1,485 (1)	0.42*
	Right	47/10	49	39	0	297	
	Left	45/Insula	-24	13	17	945 (2)	
	Left	44	-56	13	12	432 (1)	0.66**
	Left	47	-48	27	-7	459	
Inferior frontal junction	Right	44/6	39	6	33	486 (1, 2)	0.44
	Right		53	6	36	297 (1, 2)	0.47*
Superior frontal	Right	6	29	-10	58	1,269	
	Left		-46	-7	41	1,485 (1, 2)	0.57**
Supplementary and premotor areas	Left	6	-3	-3	65	2,592 (1)	-0.13
	Right	4	15	-14	54	459 (2)	
	Left		-29	-12	52	1,944	

Note: In parentheses, a 1 indicates dynamic shift in activation following training in older adults, and a 2 indicates dynamic shift in activation during penalty condition in young adults. Bold font indicates regions showing both effects. * $P < 0.10$, ** $P < 0.05$, *** $P < 0.001$.

[†]X, Y, and Z are coordinates in Talairach stereotactic space with positive values referring to regions right of (X), anterior to (Y), and superior to (Z) the anterior commissure (AC).

[‡]Volume refers to the number of voxels (converted to mm³) in each region of interest.

[§]Correlations between training-related proactive activation shift and training-related proactive shift in RT.

substantial variability in the effects obtained across participants. Indeed, though 9 of the participants showed strong improvements, 4 participants showed no effect of training, and 3 actually showed behavioral evidence of reduced proactive control following training. Given this between-subjects variability, we

hypothesized that there would be a functional relationship between the magnitude of the behavioral performance effect and a training-related proactive shift in activation dynamics. To test this hypothesis, we derived correlations in which the participants' behavioral shift score was regressed against their corre-

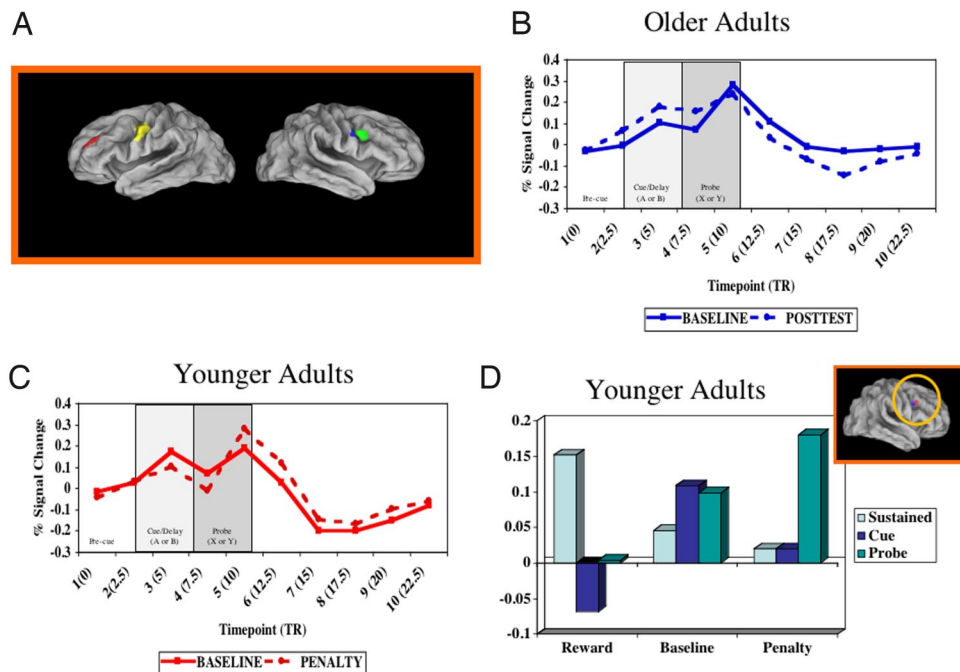


Fig. 2. (A) The set of 4 regions demonstrating training-related proactive shift (increased cue-related activity, decreased probe-related activity) in older adults and penalty-related reactive shift (decreased cue-related activity, increased probe-related activity) in young adults. The right side of the image is the right side of the brain, and the left side of the image is the left side of the brain. The region in red is the left middle frontal gyrus (BA 9/46; $x = -35$, $y = 44$, $z = 32$); yellow is the medial superior frontal gyrus (BA 6; $x = -46$, $y = -7$, $z = 41$). Two right inferior frontal junction regions (BA 44/6) are in green ($x = 39$, $y = 6$, $z = 33$) and blue ($x = 53$, $y = 6$, $z = 36$). (B) Activation dynamics for older adults at baseline and posttest conditions in 4 regions identified in (A). (C) Activation dynamics for young adults at baseline and penalty conditions in 4 regions identified in (A). (D) Shift from sustained to primarily cue-related to primarily probe-related activation dynamics in right IFJ across reward, baseline and penalty AX-CPT conditions, respectively. Cue and probe activation computed by average of time points 3–4 (cue) and 5–6 (probe). Inset shows location of contiguous right IFJ regions showing penalty-related reactive pattern (blue) and reward-related sustained proactive pattern (red).

sponding activation shift score (i.e., posttraining—baseline, with larger scores in both measures indicating more a proactive pattern in the posttraining session compared with baseline). We found that the RT indices were most related to activation measures. Using these measures, significant correlations were found in 6 of the 9 regions that showed changes in activation dynamics across the 2 sessions. These correlations were all positive, such that a greater training-related proactive shift in activation was associated with a larger behavioral shift (Table 1 and Fig. S2).

Younger Adults. The younger adults also performed a second session of the AX-CPT, but under monetary incentive conditions that involved large penalties for poor performance. We again assessed the impact of this experimental manipulation through the composite behavioral indices described previously. In contrast to the proactive shift observed following training in older adults, behavioral performance in younger adults under penalty incentives appeared to shift in the direction of increased reactive control (Table S1). Decreases relative to the no-incentive baseline were observed in all measures, and the effect was statistically reliable in the RT index, [$t(15) = 4.56, P < 0.001$]. To provide more direct evidence that the penalty incentive condition altered cognitive control strategy through a shift in the activation dynamics within lateral PFC, we again interrogated the same 17 age-related crossover ROIs derived from the original testing session. The criterion for a penalty-related reactive shift was the same crossover session (baseline/penalty) \times event (cue/probe) interaction, but in this case with cue activity decreasing and probe activity increasing relative to the baseline session. Six of the 17 ROIs showed such a reactive shift (indicated with a 2 in Table 1). Moreover, 4 of these 6 regions (indicated with bold in Table 1), including left DLPFC and right IFJ, were also among the ROIs that showed a significant training-related proactive shift in activation dynamics in the older adults (Fig. 2C illustrates the activation dynamics averaged across these 4 regions).

We further compared the results obtained in the penalty condition to those observed in our previous report on the effects of reward incentives (15). In that study, the key finding was an increase in sustained activity (i.e., maintained throughout the task, independent of trial-related activation) within lateral PFC during the reward condition relative to baseline. Thus, the combined findings across the reward, baseline (no incentive), and penalty incentive conditions indicate that activation dynamics in cognitive control regions can vary widely from sustained to cue-based to probe-based patterns. A key postulate of the DMC model is that temporal dynamics can vary even within the same brain region. Thus, we asked whether any regions among the lateral PFC ROIs exhibited both the reward-related proactive (sustained) pattern and the penalty-related reactive pattern. In fact, we found that one of the regions showing the reward-related sustained pattern in ref. 15 was directly contiguous with the right IFJ ROI that showed the penalty-related reactive pattern (and which also showed the training-related proactive shift in older adults). Fig. 2D shows the location of these contiguous regions and the shift from sustained to cue-based to probe-based activation dynamics that was observed across reward, standard, and penalty AX-CPT conditions in right IFJ.

Control Analyses. In addition to the primary ROI-based analyses, we also conducted a whole-brain exploratory analysis to identify any additional areas outside of the PFC ROIs showing effects of the experimental manipulations on activation dynamics. Very few regions were identified, and none showed effects in both age groups (see *SI Results*, Tables S2 and S3). Additionally, we tested the specificity of the experimental effects by identifying regions that showed strong task-related activity in both age groups, but no effect of the experimental manipulation. This analysis re-

vealed a widely distributed brain network, including visual sensory and motor regions, along with the classic dorsal frontoparietal attentional circuit (see *SI Results*, Figs. S4 and S5). These findings suggest a high degree of anatomical specificity in the proactive/reactive control effects, as they were observed almost exclusively in lateral PFC. Conversely, the brain regions involved in basic AX-CPT task processing (sensorimotor areas) and visuospatial attention (dorsal frontoparietal areas) did not show the same pattern of flexibility as the lateral PFC regions.

Discussion

These findings provide strong support for DMC theory by demonstrating the flexible nature of activity dynamics within lateral PFC. Critically, we found that the activation dynamics could shift from cue-based to probe-based (and vice versa) within the same lateral PFC regions and within the same individuals as a function of experimental manipulations. Moreover, we found shifting activation dynamics independently in younger and older adult populations, with the shifts occurring in opposite but theoretically predicted directions. Thus, the findings suggest that, at least in some regions of lateral PFC (e.g., DLPFC, IFJ), the activation response can be highly flexible*. This flexibility may not only reflect group differences in the primary means by which cognitive control is deployed, but also a dynamic shift between proactive and reactive control modes that can occur even within individuals as a function of changing task conditions.

The present findings also provide more specific information regarding how dynamic shifts in PFC activation dynamics might achieve flexibility in cognitive control. In particular, in the AX-CPT task, a cue-related pattern of activity in lateral PFC—reflecting proactive control—might represent the active maintenance of context information during the delay period, which would enable top-down biasing of the upcoming ambiguous probe before its onset. A shift in activation to a more tonic, or sustained pattern—as observed in right lateral PFC (IFJ) in younger adults in the reward incentive condition (15)—might reflect a mechanism that maintains task-based expectancies across trials (i.e., that one type of cue occurs far more often than another). This maintenance of expectancies could modulate cue-based responding and thus increase the efficiency of activation dynamics across trials. In contrast, an activation shift to a primarily probe-related pattern, associated with reactive control, might reflect that context information was temporarily encoded but not actively maintained over the delay. Instead, this information may be reactivated at the onset of the probe stimulus due to interference or bottom-up priming. These hypotheses are consistent with the previous literature on lateral PFC. In particular, there is a wealth of data suggesting that DL-PFC regions might be involved in the active maintenance of goals or task set information (4, 16, 17), and more recent work has also suggested that IFJ plays a critical role in cue-based encoding and updating of task sets in task switching and other cognitive control paradigms (18). Our findings extend this previous work by highlighting flexibility in the activation dynamics of these regions that has not been clearly demonstrated by previous work. Other regions, such as anterior PFC have also been shown to exhibit such a wide range in flexibility dynamics, from event related to

*Readers might question the theoretical significance of the fact that only 4 of the 17 ROIs showed flexible activation dynamics in both groups, with the remaining ROIs showing flexibility in either only one group or neither group. It is difficult to speculate regarding the null results in the remaining 13 ROIs, as they may merely reflect a lack of power to detect real flexibility effects in these regions. Nevertheless, it is possible that there may be functional differentiation among the ROIs, and it is also true that the manipulations used in each age group were not identical (e.g., the penalty manipulation may have led to some effects, such as response inhibition, that were not engaged with the training manipulation in older adults). These issues will need to be addressed in future research.

sustained (19), but a question for further research is to determine whether these and other regions can also exhibit this flexibility on a within-subject basis, or instead if there are important anatomical constraints on the range in activity dynamics that might be exhibited in particular PFC region.

The findings from this study extend the literature on cognitive aging. At baseline, older adults exhibited increased PFC activity (specifically during the probe period) relative to younger adults. We interpret this effect similarly to other researchers (20–23)—namely, that an age-related impairment in goal maintenance abilities led to a compensatory shift in cognitive strategy, which we suggest involves reactive control. However, our findings also suggest that such goal maintenance deficits are not fixed and immutable, but might instead be ameliorated by focused training (9). Specifically, we showed that age-related differences in the activation dynamics of lateral PFC during AX-CPT performance can be normalized through direct instruction of cognitive control strategy. Moreover, the degree to which older adults shifted into a younger adult pattern of activation dynamics (i.e., proactive) in lateral PFC predicted the degree of behavioral change. As such, this work provides a striking demonstration that cognitive rehabilitation in older adults might occur via direct changes in the lateral PFC mechanisms that support cognitive control functions in tasks such as the AX-CPT.

The current findings are consistent with other recent studies showing the effects of cognitive training on memory and executive control (24–26) and the associated neural changes that occur as a result (27, 28[†]). However, open questions remain regarding how the type of cognitive training used impacts the nature, magnitude, and generalizability of improvements in performance and brain activity patterns (28, 29). For example, a key question regarding the current study is whether the training-related shifts we observed in lateral PFC activity dynamics among older adults might also be found with just additional task practice, rather than direct proactive strategy instruction. In this respect, an interesting recent paper by Velanova et al. (23) found that giving older adults additional practice (repetition) during episodic encoding led to a shift in activation dynamics within PFC regions, that the authors interpreted as indicating a reduction in the need for control. However, a strong claim of the DMC model, which has not yet been tested, is that simple practice might reduce the need for control, but would not be as effective at shifting activation dynamics towards the proactive pattern (i.e., cue-based, sustained) as focused instruction in training cognitive control strategies.

These findings also inform the small but growing literature on the effects of motivational factors on cognitive control. Consistent with our prior work (15), we observed that changing the incentive value of trials had a striking influence on both behavioral performance and neural activity in lateral PFC. Similar findings have also been observed in prior studies examining working memory (30, 31) and attentional tasks (32). Our findings indicated that reward- and penalty-based incentives had very distinct effects on behavior and brain activity during the AX-CPT. Penalty incentives produced a shift to a more reactive, probe-based pattern of activation. Conversely, reward incentives produced a shift to a more proactive, sustained pattern of activity. This proactive/reactive distinction may have reflected a difference in attentional requirements across the 2 incentive conditions rather than a true valence effect. In particular, rewards were obtained for fast/accurate go responses, which demanded increased attention to the cue and a high state of response readiness. In contrast, penalties were avoided by suppressing nogo responses, which may have divided attention away

from cue processing toward the probe (which is the stimulus that indicated whether a go or nogo response was required) and also increased the emphasis on response suppression processes. Although the current penalty manipulation was designed to produce a shift from proactive to reactive control, a postulate of the DMC model is that, in principle, it should be possible to modulate reactive control without affecting proactive control. Thus, further work will be needed to determine more precisely both the relationship between penalty vs. reward incentive manipulations and the potential independence of proactive vs. reactive control strategy shifts.

The primary theoretical implication of the present findings is that fractionation of cognitive control may occur not only through anatomically based dissociations but also through dissociations based on temporal dynamics. The DMC account suggests one specific form of this dissociation, that between reactive and proactive control modes. According to DMC theory, a shift from reactive to proactive control, and vice versa, could be achieved simply through a shift in the activation dynamics of relevant control regions. Our findings demonstrate that such a shift can occur within the same regions of lateral PFC. As such, they provide an example of a “within-region mechanism” by which flexible cognitive control is achieved. This mechanism of cognitive control flexibility is distinct from those invoked by anatomically based models, which postulate that shifts in control processes require differential selection of anatomically segregated regions as a function of changing task demands (2). Additionally, a major postulate of DMC theory is that a wide range of demanding cognitive tasks might be performed by a pluralistic and fluctuating combination of neural control mechanisms. For example, we have suggested that task periods involving frequent interference, highly predictive contexts, short intertrial intervals, and strong performance incentives are most likely to lead to a shift to a proactive control mode, regardless of whether the task primarily involves context processing, or a related cognitive process such as working memory, attention, or inhibition (3). Thus, to make further progress in understanding these neural mechanisms of cognitive control, it will be necessary to measure the impact of various situational and individual difference (or group) factors that contribute to variability in cognitive control strategy. The present study highlights the utility and potential of such an approach.

Methods

Procedure. Sixteen younger adults (9 females; mean = 21.56, SD = 3.14, range = 18–28) and 16 older adults (12 females; mean = 72.38, SD = 6.51, range = 65–84) were scanned while performing the AX-CPT task using procedures that closely matched previous studies (10, 15). Both groups performed the task first under standard conditions in an initial baseline scanning session. In this session, across 3 scanning runs, 2 task blocks of 20 trials each were performed, leading to a total of 120 AX-CPT trials in the baseline session.

The older adult participants returned for a second session at least 1 week later. The first component of this session consisted of behavioral strategy training, following a protocol developed in ref. 9. Following the strategy training component (which lasted about 0.5 h), participants took a rest break and then immediately entered the fMRI scanner. The imaging component of the session consisted of 3 scanning runs during which the AX-CPT was performed according to the exact procedure followed in the baseline session.

The younger adult participants performed a second session of the AX-CPT (performed on the same day, without leaving the scanner) under penalty incentive conditions. Specifically, in this condition, monetary penalties were given when errors were committed on certain trial types (low-frequency and unpredictable “nogo” trials, which were introduced selectively in this condition). An additional 3 scanning runs were performed in this condition.

Data Analyses. Behavioral performance was analyzed through direct measures of accuracy and reaction time in various task conditions, as well as through a composite measure of the strength of context processing, that we refer to as a proactive control behavioral index. Functional imaging data were acquired with the identical parameters, procedures, preprocessing, and basic analysis

[†]See also the special section of journal *Psychology & Aging* (Dec. 2008) on cognitive training in older adults, that was published as this article was going to press.

strategies described in prior reports with these data sets (10, 15). Each functional scanning run (237 images) consisted of 2 task blocks (94 images each) alternating with 3 fixation blocks (20 images each). In each task block, trials occurred with a variable intertrial interval (2.5–7.5 s in steps of 2.5 s). This design enabled implementation of mixed blocked/event-related analyses for which sustained and transient activation patterns were separately estimated (33, 34).

The primary analyses focused on a set of 17 regions of interest (ROIs) showing a statistically significant increase in probe activation and decrease in cue activation in older adults compared with young adults during performance of the AX-CPT task. These regions are referred to as age-related crossover ROIs and were described and reported in a previous publication (see table 4 of ref. 10). The goal of the present analyses was to identify the subset of these age-related crossover ROIs that shifted to either a more proactive pattern of activation (i.e., increased cue activation, decreased probe activation) or a more reactive pattern of activation (i.e., decreased cue activation, increased probe activation) following experimental manipulation. Specifically, we tested whether a proactive shift occurred in older adults following strategy training, and whether a reactive shift occurred in younger adults during the penalty incentive condition. These shifts in activity dynamics were

identified through a set of statistical contrasts identifying condition \times event (cue/probe) crossover interactions in both groups.

After identifying that age-related crossover regions showed an increase in proactive activation after training for older adults, we derived summary scores indicating a proactive control activation index. These were computed by subtracting probe activation from cue activation, with a higher score representing more proactive activation. To represent an increase in proactive performance from baseline to posttest, we derived a training-related proactive shift score by calculating the following: [(posttest cue – posttest probe) – (baseline cue – baseline probe)]. These values were used for correlating changes in activation with changes in behavioral performance in older adults.

More detailed description of the methods can be found in *SI Methods*.

Note Added in Proof. See also the special section of the journal *Psychology and Aging* (35) on cognitive training in older adults, which was published as this article was going to press.

ACKNOWLEDGMENT. This work was funded by National Institute of Mental Health Grant ROI MH66078 (to T.S.B.).

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