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Research Report

Conflict adjustment through domain-specific multiple cognitive control mechanisms

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ABSTRACT

Cognitive control is required to regulate conflict between relevant and irrelevant information. Although previous neuroimaging studies have focused on response conflict, recent studies suggested that distinct neural networks are recruited in regulating perceptual conflict. The aim of the current study was to distinguish between brain areas involved in detecting and regulating perceptual conflict using a conflict adjustment paradigm. The Stroop color-matching task was combined with an arrow version of the Stroop task in order to independently manipulate perceptual and response conflicts. Behavioral results showed that post-conflict adjustment for perceptual and response conflicts were independent from each other. Imaging results demonstrated that the caudal portion of the dorsal cingulate cortex (cdACC) was selectively associated with the occurrence of perceptual conflict, whereas the left dorsal portion of the premotor cortex (pre-PMd) was selectively associated with both preceding and current perceptual conflict trials. Furthermore, the rostral portion of the dorsal cingulate cortex (rdACC) was selectively linked with response conflict, whereas the left dorsolateral prefrontal cortex (DLPFC) was selectively involved in both preceding and current response conflict trials. We suggest that cdACC is involved in detecting perceptual conflict and left pre-PMd is involved in regulating perceptual conflict, which is analogous to the recruitment of rdACC and left DLPFC in control processes for response conflict. Our findings provide support for the hypothesis that multiple independent monitor-controller loops are implemented in the frontal cognitive control system.

1. Introduction

Goal-directed behavior requires a control system to integrate thought and action in accordance with internal goals. This ability is referred to as cognitive control (Miller and Cohen, 2001). Numerous functional neuroimaging studies have sought to reveal the underlying neural mechanisms of cognitive control by employing various cognitive tasks that evoke conflict in information processing. According to the conflict monitoring theory, an influential theory of cognitive control, the dorsal anterior cingulate cortex (dACC) detects response conflict, and subsequently triggers the dorsolateral prefrontal cortex (DLPFC) to regulate conflict through the attentional biasing of perceptual processes in a top-down manner (Botvinick et al., 2001; Botvinick et al., 2004). This type of conflict can be seen in many cognitive tasks. For example, in the

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Stroop color-naming task, response conflict is greater in incongruent trials (i.e., the word RED printed in blue ink) than in congruent trials (i.e., the word RED printed in red ink).

Previous studies have employed the conflict adjustment paradigm in an effort to distinguish neural correlates of conflict detection and resolution (Botvinick et al., 1999; Egner and Hirsch, 2005a; Egner and Hirsch, 2005b; Egner et al., 2007; Kerns, 2006; Kerns et al., 2004). The conflict adjustment paradigm has been employed to show dynamic behavioral adjustments following conflict, such as an increase or decrease in reaction time (Gratton et al., 1992). This is referred to as the conflict adjustment (or adaptation) effect. For example, in the Stroop color-naming task, reaction times (RTs) are faster for incongruent trials that are preceded by incongruent trials (II) when compared to those that are preceded by congruent trials (CI). Furthermore, RTs are slower for congruent trials preceded by incongruent trials (IC) than those preceded by congruent trials (CC). Using the conflict adjustment paradigm, functional neuroimaging studies found that dACC showed decrease in neural activity for II trials compared to CI trials, suggesting that dACC plays an important role in detecting response conflict (Botvinick et al., 1999). In addition, DLPFC has been found to be more activated for II than CI, indicating that DLPFC plays a critical role in regulating response conflict (Egner and Hirsch, 2005a; Egner and Hirsch, 2005b).

Although the conflict monitoring theory focuses on conflict at the response level, behavioral studies have found that there exist multiple types of conflict, such as perceptual and response conflict (Kornblum et al., 1990; Sugg and McDonald, 1994). Moreover, recent neuroimaging studies proposed that distinct brain regions are recruited in perceptual and response conflict processes (Kim et al., 2010; Kim et al., 2011b; Orr and Weissman, 2009). A common finding of these studies is that the rostral dACC (rdACC) is activated only by response conflict, whereas the caudal dACC (cdACC) is recruited during perceptual conflict processing. Anatomically, these two regions correspond to the anterior rostral cingulate zone (i.e., rdACC) and posterior rostral cingulate zone (i.e., cdACC), originally distinguished by Picard and Strick (1996). Another common finding of these studies is that DLPFC is associated only with response conflict processing. Furthermore, one of our previous studies found that cdACC and the rostral portion of the dorsal premotor cortex (pre-PMd) were recruited during perceptual conflict processing, whereas response conflict processing recruited the rdACC/DLPFC network (Kim et al., 2010).

According to the "multiple conflict-control loops" hypothesis proposed by Egner (2008), multiple domain-specific control systems involve multiple sets of conflict monitor-controller loops. An important expectation of this hypothesis is that at least two monitor-controller loops operate at perceptual and response levels independently. It appears to be evident that response conflict processing recruit the rdACC and DLPFC (a monitor and controller, respectively) loop. However, it remains unknown whether there exists another cognitive control system (i.e., a monitor-controller loop) associated with perceptual conflict in the brain. Although we have suggested that cdACC and pre-PMd appear to play important roles in perceptual conflict processing (Kim et al., 2010), the task design employed in the previous study did not allow us to specify their functional roles in the context of the monitor-controller loop. Specifically, the previous study was designed to test whether neural correlates of perceptual and response conflict processes are independent from each other using a two way (perceptual congruency × response congruency) factorial design. However, this task was not designed to separately gauge detection and regulation of perceptual conflict using a conflict adjustment (Kerns et al., 2004) or a cuing paradigm (MacDonald et al., 2000). Thus, the current study aimed at distinguishing between cortical regions involved in detecting and resolving perceptual conflict using a conflict adjustment paradigm.

In this study, we sought to directly test whether the functions of cdACC and pre-PMd are analogous to those of rdACC and DLPFC (i.e., monitor vs. controller), and whether these two cognitive control loops (rdACC/DLPFC and cdACC/pre-PMd) are independent and distinguishable from each other. If the two monitor-controller loops are independent, a preceding perceptual incongruent trial would not affect a subsequent response conflict adjustment, and a preceding response incongruent trial would not be associated with a subsequent perceptual conflict adjustment. Based on these assumptions, we expected that behavioral adjustment for each perceptual or response conflict would be observed only in the same subsequent incongruent trials. We also expected that the monitor-controller loop associated with response or perceptual conflict operates independently. In detail, we hypothesized that rdACC activation would be increased by current response conflict and decreased by previous response conflict if rdACC is involved in monitoring response conflict (response conflict monitor). In addition, DLPFC activation would be increased by previous as well as current response conflict and would be higher in the response incongruent trials following response conflict trials than those following congruent or perceptual conflict trials if DLPFC is engaged in regulation of response conflict (response conflict controller). We also hypothesized that cdACC activation would be increased by current perceptual conflict and decreased by previous perceptual conflict if cdACC is involved in monitoring perceptual conflict (perceptual conflict monitor). Finally, we hypothesized that pre-PMd activation would be increased by both current and previous perceptual conflict and would be higher in the perceptual incongruent trials following perceptual conflict trials than those following congruent or response conflict trials if pre-PMd is involved in regulation of perceptual conflict (perceptual conflict controller).

In order to test these hypotheses, we employed a combined version of the Stroop color-matching task and an arrow version of the Stroop task (see Fig. 1), in which two types of conflict (i.e., perceptual and response) were independently manipulated. The task included congruent, perceptual–incongruent and response–incongruent trials and these three trial types were pseudo-randomly intermixed in order to measure brain activation specific to conflict adjustment at either perceptual or response level.

2. Results

2.1. *Behavioral results*

Mean error rates and RTs for the task conditions are presented in Fig. 2. Error rates and RTs were analyzed using 3×3

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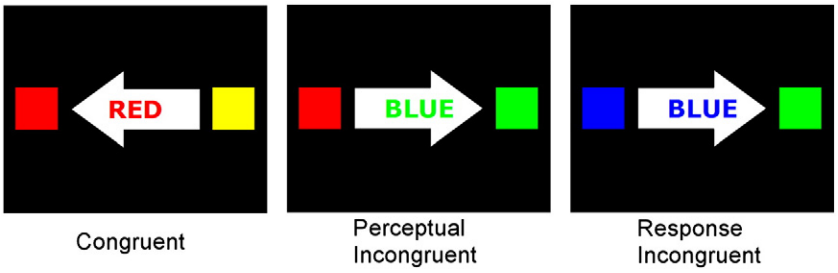

Fig. 1 – Task stimuli and conditions used in the experiment. Three task conditions were included: congruent (C), perceptual incongruent (I_P), and response incongruent (I_R) conditions. The C stimulus included a congruent sample and arrow. The I_P stimulus included an incongruent sample and a congruent arrow. The I_R stimulus included a congruent sample and an incongruent arrow. During the experiment, these three stimulus types were pseudo-randomly intermixed, which results in 9 trial-to-trial transitions. See Experimental procedure for details.

(previous trial type×current trial type) repeated measures ANOVAs to test whether conflict adjustment effects are selectively observed according to the type of conflict. For error rates, the main effect of the current trial type was significant ($F(2,28)=5.03$, $p=0.014$), due to the fact that the current C condition showed lower error rates (mean=2.0%, SD=0.4) than I_P (mean=4.6%, SD=0.8) and I_R (mean=3.5%, SD=0.9) conditions ($F(1,14)=15.53$, $p=0.001$). In contrast, the main effect of the previous trial type and the interaction effect between previous trial type and current trial type were not significant ($F(2,28)=0.35$, $p=0.709$; $F(4,56)=0.538$, $p=0.708$).

For RTs, the main effect of the current trial type was significant ($F(2,28)=12.51$, $p<0.001$), reflecting the fact that behavioral performance was faster in the current C condition (mean=623 ms, SD=163) than I_P (mean=671 ms, SD=170) and I_R (mean=646 ms, SD=159) conditions ($F(1,14)=25.46$, $p<0.001$). In other words, both perceptual (48 ms) and response conflict (23 ms) effects were observed. In contrast, the main effect of the previous trial type was not significant ($F(2,28)=0.43$, $p=0.656$). The interaction effect between previous trial type and current trial type was also significant ($F(4,56)=8.86$, $p<0.001$). Specifically, the RTs for the I_PI_P trials (mean=656 ms, SD=167) were faster than CI_P (mean=676 ms, SD=178) and I_RI_P (mean=680 ms, SD=172) trials ($F(1,14)=16.12$, $p=0.001$). Also, RTs were faster in I_RI_R trials (mean=632 ms, SD=161) than CI_R (mean=653 ms, SD=161) and I_PI_R (mean=654 ms, SD=156) trials ($F(1,14)=22.58$, $p<0.001$). In short, the RT for the current I_R trial was decreased when there was a preceding I_R trial compared to a preceding I_P or C trial. On the other hand, the RT for the current I_P trial was faster when there was a preceding I_P trial than when there was a preceding I_R or C trial. These results confirmed the hypothesis that behavioral adjustment effects at perceptual and response levels would be independent from each other.

Although behavioral results demonstrate that behavioral adjustment effects at perceptual and response levels are independent, it is important to test whether the amount of the two conflict effects (48 ms vs. 23 ms) are different because the two conflict adaptation effects might be associated with the difference in difficulty between the two tasks. Thus, we tested this possibility in RTs as well as error rates. The results showed that the RTs between the two conflict effects (i.e., between I_P and I_R) were not significantly different ($F(1,14)=3.46$, $p=0.085$). Additionally, error rates were not significantly different between I_P and I_R conditions ($F(1,14)=1.28$, $p=0.277$).

2.2. *Imaging results*

Functional imaging data were analyzed using 3×3 (previous trial type×current trial type) repeated measures ANOVAs to test whether BOLD signal changes within a priori ROIs showed different conflict adjustment effects depending on the type of conflict being processed. Peak BOLD signal changes extracted from the ROIs are presented in Fig. 3. First, three ROIs (rdACC and left/right DLPFC) were analyzed to test whether these regions are selectively involved in response conflict in the context of the monitor-controller loop. First of all, BOLD signal changes within rdACC were analyzed to test whether

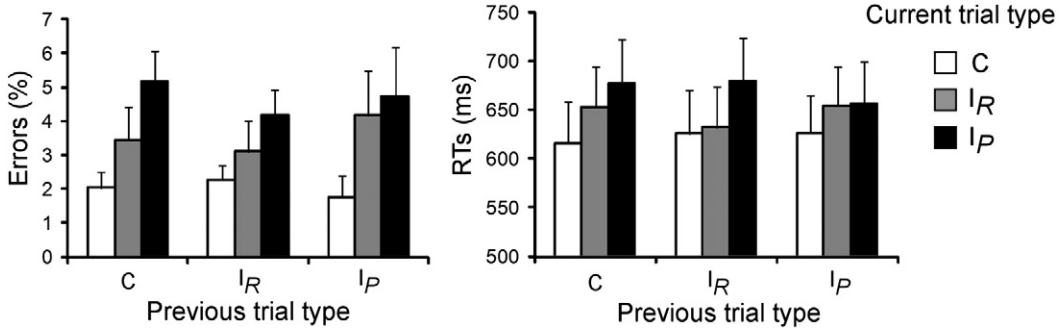

Fig. 2 – Mean error rates (left) and mean RTs (right) for each task condition. Error bars represent the standard errors of the means. Note: C, congruent; I_P, perceptual incongruent; I_R, response incongruent.

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this region was involved in monitoring response conflict. The results showed that the main effect of the current trial type was significant ($F(2,28)=26.14$, $p<0.05$, corrected), due to higher activity for current I_R trials (mean=0.31%, SD=0.09) than both C (mean=0.09%, SD=0.14) and I_P (mean=0.11%, SD=0.08) trials ($F(1,14)=91.74$, $p<0.05$, corrected). In contrast, the main effect of the previous trial type was not significant ($F(2,28)=1.87$, $p=0.173$). The interaction effect between previous trial type and current trial type was significant ($F(4,56)=4.16$, $p<0.05$, corrected), due to lower signal changes in I_RI_R trials (mean=0.19%, SD=0.18) than both CI_R (mean=0.40%, SD=0.17) and I_PI_R (mean=0.34%, SD=0.11) trials ($F(1,14)=13.47$, $p<0.05$, corrected). In sum, the data showed that rdACC activation was selectively increased by current response conflict and selectively decreased by previous response conflict, which confirmed our hypothesis on the rdACC's role in monitoring response conflict.

For the signal changes within left DLPFC, the main effect of the previous trial type was significant ($F(2,28)=8.72$, $p<0.05$, corrected), attributable to higher signal changes for previous

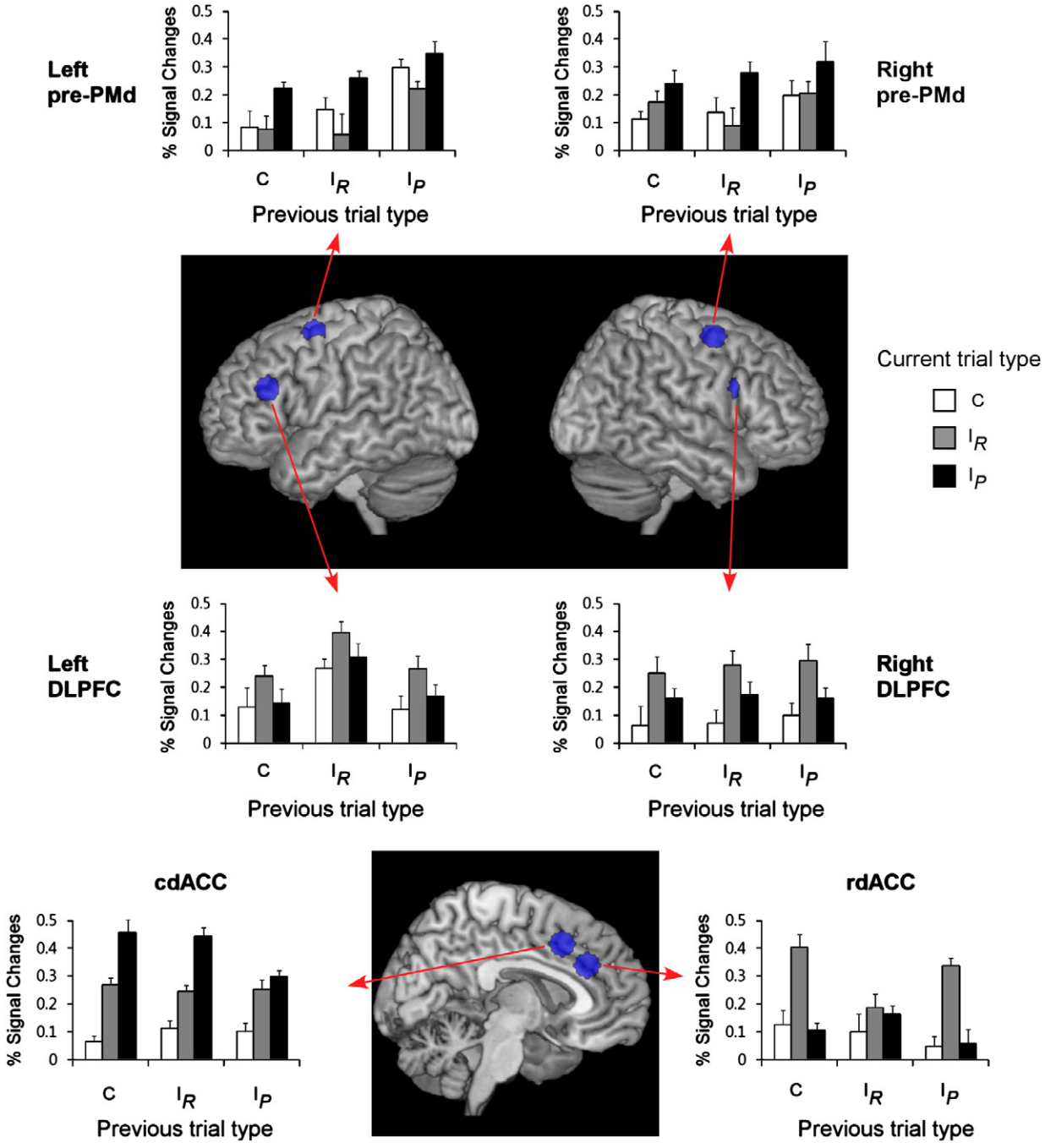

Fig. 3 – BOLD signal changes specific to task conditions within a priori regions of interest (ROIs). Note that the ROIs represent the locations on the MNI-normalized brain, not activation maps. Error bars represent the standard errors of the means. Note: C, congruent; I_P, perceptual incongruent; I_R, response incongruent.

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I_R trials (mean=0.33%, SD=0.12) than both C (mean=0.17%, SD=0.13) and I_P (mean=0.19%, SD=0.10) trials ($F(1,14)=22.43$, $p<0.05$, corrected). Also, the main effect of the current trial type was significant ($F(2,28)=7.12$, $p<0.05$, corrected), as current I_R trials (mean=0.30%, SD=0.12) showed higher signal changes than current C (mean=0.17%, SD=0.10) and I_P (mean=0.21%, SD=0.11) trials ($F(1,14)=13.59$, $p<0.05$, corrected). In addition, planned comparisons between I_RI_R and CI_R and between I_PI_R and CI_R were performed in order to test whether only I_RI_R shows increased activation compared to CI_R. The results showed that the signal changes of I_RI_R was significantly higher than CI_R ($t(15)=3.77$, $p<0.05$, corrected), whereas I_PI_R was not higher than CI_R ($t(15)=0.391$, $p=0.702$). On the other hand, the interaction effect between previous trial type and current trial type was not significant ($F(4,56)=0.05$, $p=0.994$). These data demonstrated that left DLPFC activation was selectively increased by both previous and current response conflict, confirming our hypothesis on the DLPFC's role in regulation of response conflict.

Right DLPFC showed that the main effect of the current trial type was significant ($F(2,28)=11.98$, $p<0.05$, corrected), attributable to the fact that signal changes in I_R trials (mean=0.28%, SD=0.13) were higher than those in I_P (mean=0.17%, SD=0.09) and C (mean=0.08%, SD=0.13) trials ($F(1,14)=20.62$, $p<0.05$, corrected). In contrast, the main effect of the previous trial type ($F(2,28)=0.18$, $p=0.839$) and the interaction effect between previous trial type and current trial type ($F(4,56)=0.09$, $p=0.984$) were not significant. The right DLPFC results showed different activation patterns (i.e., increased activation only for current response conflict) than left DLPFC and did not support our hypothesis.

In sum, rdACC activation was increased for current response conflict but decreased for previous response conflict, which supported our hypothesis that rdACC would be involved in monitoring response conflict. In addition, left DLPFC showed increased activation for both previous and current response conflict, which supported the hypothesis that this region would be engaged in regulation of response conflict. In contrast, right DLPFC showed increased activation only for current response conflict but was not linked with previous response conflict, which was contrary to our expectation.

The next analyses focused on the other three ROIs (cdACC and left/right pre-PMd) to specify their roles in perceptual conflict processing. For the analysis of cdACC, the main effect of the current trial type was significant ($F(2,28)=57.52$, $p<0.05$, corrected). Specifically, cdACC activity for current I_P trials (mean=0.40%, SD=0.09) was higher than both current C (mean=0.09%, SD=0.07) and I_R (mean=0.26%, SD=0.08) trials ($F(1,14)=48.67$, $p<0.05$, corrected). Additionally, activity for current I_R trials was also higher than current C trials ($F(1,14)=108.01$, $p<0.05$, corrected). In contrast, the main effect of the previous trial type was not significant ($F(2,28)=2.65$, $p=0.089$). The analysis also showed a significant interaction effect ($F(4,56)=4.99$, $p<0.05$, corrected), due to the fact that cdACC activity was lower in I_PI_P trials (mean=0.30%, SD=0.08) than both CI_P (mean=0.46%, SD=0.18) and I_RI_P (mean=0.44%, SD=0.12) trials ($F(1,14)=20.36$, $p<0.05$, corrected) whereas it was not different between CI_P and I_RI_P ($F(1,14)=0.14$, $p=0.716$). These data demonstrated that cdACC activation was selectively increased by current perceptual conflict and selectively decreased by previous perceptual conflict, which supported our hypothesis on the cdACC's role in monitoring perceptual conflict.

The analysis for left pre-PMd showed that the main effect of the previous trial type was significant ($F(2,28)=11.97$, $p<0.05$, corrected), reflecting increased signal changes for previous I_P (mean=0.29%, SD=0.04) relative to previous C (mean=0.13%, SD=0.12) and I_R (mean=0.16%, SD=0.14) trials ($F(1,14)=23.83$, $p<0.05$, corrected). Also, the main effect of the current trial type was significant ($F(2,28)=10.79$, $p<0.05$, corrected), demonstrating that current I_P trials (mean=0.28%, SD=0.07) showed stronger signal changes than current C (mean=0.18%, SD=0.09) and I_R (mean=0.12%, SD=0.15) trials ($F(1,14)=23.64$, $p<0.05$, corrected). Additionally, planned comparisons between I_PI_P and CI_P and between I_RI_P and CI_P were conducted in order to test whether I_PI_P shows selective increase in activation compared to CI_P. The results showed that I_PI_P was significantly higher in signal changes than CI_P ($t(15)=4.84$, $p<0.05$, corrected), whereas I_RI_P and CI_P were not different ($t(15)=0.329$, $p=0.747$). The interaction effect between previous trial type and current trial type was not significant ($F(4,56)=0.51$, $p=0.731$). These data showed that left pre-PMd activation was selectively increased by both previous and current perceptual conflict, which supported the hypothesis that pre-PMd would be involved in regulation of perceptual conflict.

Right pre-PMd showed different activation patterns than left pre-PMd. Specifically, the main effect of the current trial type was significant ($F(2,28)=7.66$, $p<0.05$, corrected), with greater signal changes in I_P (mean=0.28%, SD=0.13) than I_R (mean=0.16%, SD=0.12) and C (mean=0.15%, SD=0.14) trials ($F(1,14)=15.63$, $p<0.05$, corrected). In contrast, the main effect of the previous trial type ($F(2,28)=1.73$, $p=0.196$) and the interaction effect between previous trial type and current trial type ($F(4,56)=0.55$, $p=0.697$) were not significant. The right pre-PMd analysis showed that this region was selectively activated by current perceptual conflict but was not associated with previous perceptual conflict, which did not support our hypothesis.

In sum, cdACC demonstrated increased activation for current perceptual conflict but decreased activation for previous perceptual conflict, supporting our hypothesis that cdACC would be involved in monitoring perceptual conflict. On the other hand, left pre-PMd showed increased activation for both previous and current perceptual conflict, supporting our hypothesis that pre-PMd would be involved in regulation of perceptual conflict. However, right pre-PMd was not associated with previous perceptual conflict although it was more active for current perceptual conflict than current response conflict, which did not support our hypothesis.

3. Discussion

The purpose of the current study was to reveal neural mechanisms involved in detecting and resolving perceptual conflict using a conflict adjustment paradigm and to test whether multiple independent conflict-driven monitor-controller systems are implemented in the prefrontal cortex. Importantly, behavioral data demonstrated that the conflict adjustment effect for each perceptual or response conflict was independent from each other. In detail, participants' performance for the

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current response conflict trial was faster when there was a preceding response conflict trial than a preceding perceptual conflict or congruent trial. In the same vein, participants' performance for the current perceptual conflict trial was faster when there was a preceding perceptual conflict trial than a preceding response conflict or congruent trial. These domain-specific behavioral adjustment effects support the "multiple conflict-control loops" hypothesis (Egner, 2008), and suggest that control processes involved in the two types of conflict are independent and distinguishable.

3.1. *Selective recruitment of the rdACC/DLPFC network for response conflict processing*

Our results demonstrated that rdACC and left DLPFC were selectively associated with both previous and current response conflict trials, suggesting that these two regions play important roles in response conflict processing. Specifically, rdACC activation was selectively increased when there was response conflict in the current trial whereas it was decreased by preceding response conflict. On the other hand, left DLPFC activity was selectively increased by previous response conflict as well as current response conflict. Furthermore, preceding response conflict resulted in increased DLPFC activation in the current response conflict trials whereas preceding perceptual conflict did not affect DLPFC activation in the current response conflict trials. According to the conflict monitoring theory, detection of response conflict in the previous trial results in a strengthening of regulation processing which reduces the influence of current response conflict. Thus, our results support the conflict monitoring theory that rdACC is selectively associated with detecting (monitoring) the occurrence of response conflict in information processing and that DLPFC is engaged in cognitive control through resolving response conflict (Aarts et al., 2008; Botvinick et al., 1999; Kerns, 2006; Kerns et al., 2004; MacDonald et al., 2000). Importantly, rdACC and left DLPFC activations were not associated with perceptual conflict, but were affected only by response conflict, suggesting that the monitor-controller network for response conflict processing is independent from that for perceptual conflict processing (Egner, 2008; Kim et al., 2010).

Our finding that left DLPFC was selectively involved in resolving response conflict is consistent with previous studies demonstrating that left DLPFC plays a critical role in resolving response conflict (Aarts et al., 2008; MacDonald et al., 2000). However, in addition to left DLPFC, other studies have shown that right DLPFC was also involved in the resolution of response conflict (Egner and Hirsch, 2005b; Kerns, 2006; Kerns et al., 2004). If right DLPFC were also involved in regulation of response conflict, it should be increased by preceding response conflict as in left DLPFC. Our data, however, showed that right DLPFC was not affected by preceding response conflict although it was more activated by current response conflict than by current perceptual conflict. A potential explanation for the finding of this lateralization is that it might be due to functional dissociation between left and right DLPFC in cognitive control processes, such as sustained vs. transient nature of control processes. In other words, left DLPFC may be involved in cognitive control for resolving response conflict in a transient manner, whereas right DLPFC may operate in a sustained manner throughout the task (Braver et al., 2003; Jimura and Braver, 2010; Savine and Braver, 2010). Furthermore, a recent review proposed that left DLPFC appears to be involved in rapid regulation processing based on sequential control processes whereas right DLPFC is related to regulation processing at the global and macro level (Vanderhasselt et al., 2009).

Another explanation is that right DLPFC may play a role in domain-general cognitive control processes (e.g., Fassbender et al., 2006). However, the opposite lateralization pattern has also been reported. For example, a recent study found that left DLPFC is involved in domain-general control processes whereas right DLPFC is engaged in domain-specific processes (Rajah et al., 2008). Thus, future research will be required to test whether right DLPFC operates in a domain-general or domain-specific manner or whether it operates in a sustained manner.

3.2. *Selective recruitment of the cdACC/pre-PMd network for perceptual conflict processing*

One of the main aims of the current study was to test whether there is dissociation between cdACC and pre-PMd in terms of the detection and resolution of perceptual conflict, which is analogous to the recruitment of rdACC and DLPFC during response conflict. Our data clearly demonstrated that cdACC was associated with the detection of perceptual conflict, while left pre-PMd responded more to the resolution of perceptual conflict. Specifically, cdACC showed increased activity for current perceptual conflict and decreased activity for preceding perceptual conflict. The cdACC activation for perceptual conflict showed the same pattern as rdACC for response conflict. On the other hand, left pre-PMd showed increased activation for both preceding and current perceptual conflicts. Also, only preceding perceptual conflict resulted in increased activation in the current perceptual conflict trials. These activation patterns were the same as DLPFC activations for response conflict. These results suggest that cdACC plays a critical role in detecting perceptual conflict whereas left pre-PMd is involved in regulation of perceptual conflict.

Importantly, cdACC and left pre-PMd were not associated with previous or current response conflict, but were selectively linked with perceptual conflict. These results provide strong evidence that the cdACC/pre-PMd network, involved in perceptual conflict, is independent from the rdACC/DLPFC network recruited in response conflict processing. Thus, we suggest that multiple independent monitor-controller loops are implemented in the cognitive control system, which supports the multiple conflict-driven cognitive control hypothesis (Egner, 2008; Kim et al., 2010).

The specific role of dACC in cognitive control has been under debate. Some propose that dACC increases attention to relevant stimuli (Dreher and Berman, 2002; Weissman et al., 2005), whereas others suggest that it detects response conflict and subsequently signals DLPFC to resolve conflict (Botvinick et al., 1999; Kerns et al., 2004). With regard to this issue, functional neuroimaging studies have found that rdACC plays a role in response conflict processing and cdACC is involved in attending to relevant stimuli (Kim et al., 2011b; Milham and Banich, 2005; Weissman et al., 2004). Specifically, Milham and

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Banich (2005) found that rdACC showed response conflict-related activity whereas cdACC was associated with perceptual competition between stimulus features (i.e., color information). In another study (Kim et al., 2011b), we also observed a functional dissociation between the two subregions of dACC, in that cdACC was involved in perceptual conflict processing whereas rdACC was associated with response conflict. In line with these studies, our data provide direct evidence that cdACC is preferentially involved in detecting perceptual conflict, whereas rdACC is preferentially associated with detecting response conflict. Furthermore, our data suggest that the two sub-regions of dACC appear to be independent from each other in conflict processing despite the fact that they are closely situated within dACC.

On the other hand, the pre-PMd region, the rostral portion of the dorsal premotor cortex, is heavily interconnected with other prefrontal regions, whereas the caudal portion of the dorsal premotor cortex (PMd proper) is more interconnected with the motor cortex (Barbas and Pandya, 1987). In accord with this anatomical feature, a recent review suggests that pre-PMd is involved in cognitive processes as well as motor planning, while PMd proper is engaged in motor execution (Abe and Hanakawa, 2009). In addition, functional neuroimaging studies suggested that pre-PMd is involved in control processes at the perceptual level (Abe et al., 2007; Badre and D'Esposito, 2007). Specifically, these studies proposed that pre-PMd plays an important role in learning and controlling rule-based associations between perceptual features of stimuli and responses. Moreover, recent meta-analysis and fMRI studies found that pre-PMd was activated by perceptual switching which involves switching between stimulus selection rules or stimulus–stimulus associations, whereas DLPFC was associated with response switching which involves switching between two opposing response rules (Kim et al., 2011a; Kim et al., 2012). Although such convergent evidence suggests that pre-PMd plays a role in control processes at the perceptual level, underlying neural mechanisms have remained unclear. According to our findings, pre-PMd appears to be involved in cognitive control at the perceptual level by regulating perceptual conflict, which is analogous to the role of left DLPFC in the regulation of response conflict.

Although our results clearly demonstrate that pre-PMd is involved in regulation of perceptual conflict, one might claim that this is inconsistent with a previous study which proposed that the posterior parietal cortex is involved in stimulus-based conflict (Egner et al., 2007). However, it is important to note that there is an important difference between perceptual conflict in our study and "stimulus-based conflict" in their study. Specifically, as described in their paper, they employed "stimulus-based" (the Stroop task) and "response-based" (the Simon task) to refer to the origin of conflict. Indeed, in their stimulus-based conflict condition, response buttons were pre-assigned to different colors (i.e., left for green and right for red), in that the stimulus-based conflict condition might include response conflict as well. Moreover, previous behavioral and neuroimaging studies have proposed that the Stroop task involves both perceptual and response conflict (Kim et al., 2010; Kim et al., 2011b; Sugg and McDonald, 1994). In contrast, the current study focuses on "response conflict" (i.e., conflict during the selection of a relevant response between incompatible responses) and "perceptual conflict" (i.e., conflict during the selection of a relevant stimulus between incompatible stimuli).

Despite of the finding that left pre-PMd plays an important role in regulation of perceptual conflict, we observed different activation patterns in right pre-PMd: although right pre-PMd was more activated by current perceptual conflict than by response conflict, it was not associated with preceding perceptual conflict. This suggests that right pre-PMd is also involved in perceptual conflict, but may play a different role than left pre-PMd. In our task design, the perceptual incongruent condition was manipulated by competition between task-related and task-unrelated representations (e.g., word vs. color), which required subjects to deal with more representations as well as more control processes compared to the congruent condition. Thus, a potential explanation for the lateralization of pre-PMd is that left pre-PMd is involved in control processes (i.e., regulation), whereas right pre-PMd is involved in other cognitive processes such as representing stimulus–stimulus associations. There is existing evidence supporting this explanation. Specifically, Hanakawa et al. (2002) found bilateral pre-PMd activations for the presentation of numerical stimuli (i.e., representation of stimulus–stimulus associations) but only left pre-PMd was activated by mathematical operations, namely, control processes. However, the current task design was not manipulated to test this dissociation (i.e., representation vs. regulation). Thus, future research will be required to specify the functional role of right pre-PMd in perceptual conflict processing.

To conclude, behavioral data showed that the conflict adaptation effects at the perceptual and response levels were independent from each other. Neural correlates of these independent adaptation effects were observed in rdACC and left DLPFC for response conflict and in cdACC and left pre-PMd for perceptual conflict. We suggest that cdACC is involved in detecting perceptual conflict and pre-PMd plays a critical role in regulating perceptual conflict, which is analogous to the roles of rdACC and DLPFC in response conflict processing. The current findings provide direct evidence supporting the multiple conflict-driven cognitive control hypothesis (Egner, 2008) which proposes that domain-specific monitor-controller loops operate independently.

4. Experimental procedure

4.1. *Subjects*

Fifteen native Korean-speaking, healthy right-handed volunteers (mean age=22.3, aged between 18 and 28; five females) with normal or corrected-to-normal vision without color blindness participated in this study. All subjects reported no history of head injury, neurological or psychiatric problems. All subjects provided written consent approved by the Brain Science Research Center at KAIST, Daejeon, South Korea.

4.2. *Material and procedure*

Task programming, stimulus presentation, and recording of behavioral responses were carried out through E-Prime

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software 1.2. For behavioral tasks the Stroop color-matching task was combined with an arrow version of the Stroop task (Fig. 1). The stimuli in this study were similar to those used in previous studies, where two types of conflicts at perceptual and response levels were independently manipulated (Kim et al., 2010; Kim et al., 2011b). Task stimuli consisted of a rightward or leftward facing arrow in the center of a black background. A color name printed in an ink color (a sample) was embedded within the arrow. Two colored squares (response cues) were presented on the both sides of the arrow. The task required subjects to 1) identify the color of the sample; 2) select either a left or right response cue corresponding to the color of the sample; and 3) press either the left or right button using their right index or middle finger for each left or right response, respectively. They were asked to respond as quickly and accurately as possible.

One of the four colors (red, green, blue, and violet) and color names were used for the sample. The color of the sample was presented in either a congruent (e.g., BLUE printed in blue ink) or incongruent (e.g., BLUE printed in red ink) manner and was presented in native language (i.e., Korean). One of the response cues was the correct answer and the other was the incorrect answer. For example, for an incongruent sample, the word BLUE printed in green ink was presented with a green square on the right (the correct answer) and a red square on the left. According to the translation model of the Stroop effect, this manipulation evokes interference between the color and the word at the perceptual level when subjects select the color of the stimulus (Sugg and McDonald, 1994). This manipulation was also used in previous studies to evoke perceptual conflict (Kim et al., 2010; Kim et al., 2011b; Milham et al., 2001). It is important to note that the color square for the incorrect response cue was one of the colors which were not assigned to the current sample word. This manipulation allowed us to exclude potential confounds associated with semantic conflict due to the consistency between the meaning of the sample word and the incorrect response cue. For example, if the incorrect response cue is the same as the meaning of the sample word (e.g., when the sample is the word BLUE printed in green ink and green and blue squares are presented as response cues, the correct answer is green and the incorrect answer is blue), this would induce tendency to respond to the incorrect response cue (i.e., semantic conflict).

The task also included an arrow in the center of the screen, which pointed to either the correct (response-congruent) or incorrect response cue (response-incongruent). The incongruent arrow induced response conflict compared to the congruent arrow because the arrow was not associated with selection of the sample color but associated with response-selection processing. This manipulation for response conflict was also used in previous fMRI studies to evoke response conflict independently (Aarts et al., 2009; Kim et al., 2010).

The two factors (perceptual congruency and response congruency) were combined in a single task paradigm. Accordingly, three conditions were included in the task: congruent (C), perceptual incongruent (I_P), and response incongruent (I_R) conditions. For C trials, both the sample and arrow were congruent. I_R trials involved a congruent sample and an incongruent arrow, whereas I_P trials included an incongruent sample and a congruent arrow. These three trial types were pseudo-randomly intermixed in order to measure brain activation specific to post-conflict adjustment at either perceptual or response level. Accordingly, 9 trial-to-trial transitions were included in the task conditions: congruent–congruent (CC), congruent–response incongruent (CI_R), congruent–perceptual incongruent (CI_P), response incongruent–congruent (I_RC), response incongruent–response incongruent (I_RI_R), response incongruent–perceptual incongruent (I_RI_P), perceptual incongruent–congruent (I_PC), perceptual incongruent–response incongruent (I_PI_R), and perceptual incongruent–perceptual incongruent (I_PI_P). It is also important to note that the same color or word was not presented in two consecutive trials in an effort to avoid potential confounds such as the repetition priming effect (Mayr et al., 2003). Stimuli were presented for 0.9 s followed by jittered inter-stimulus-intervals (ISIs), varied from 2.1 s to 4.1 s (mean ISI = 3.1 s). A total of 48 trials were included in each condition.

4.3. *Image acquisition and analyses*

Images were acquired using a 3-T MRI system (Oxford magnet, Varian console magnet built by ISOL, fMRI center at KAIST, Daejeon, South Korea). For functional scans, T2*-weighted gradient echo planner images (EPI) comprised of 25 interleaved slices were acquired while subjects performed the task (TR = 2 s, TE = 35 ms, FA = 85°, matrix = 64 × 64, in-plane resolution = 3.44 mm^2, thickness = 4.5 mm). Four runs were collected for the fMRI experiment. Each run consisted of 208 volumes comprised of 9 event-related trial types. The first five volumes of each run were collected for signal equilibration and then discarded prior to data analyses. Also, T1-weighted high-resolution anatomical images using the magnetization-prepared rapid gradient-echo (MPRAGE) sequence were collected for all subjects.

Preprocessing and statistical analyses for imaging data were performed using SPM5 (Statistical Parametric Mapping; Wellcome department of Cognitive Neurology, UCL, London, UK). Prior to the statistical analysis, temporal and spatial disparities were corrected. Specifically, temporal disparities between slices were corrected using the sinc interpolation (Henson et al., 1999). Then the corrected images were spatially realigned to the first volume of the first run for motion correction. These images were coregistered with the MPRAGE image and were normalized into the Montreal Neurological Institute (MNI) template, using the 12-parameter affine transformation (2 mm isotropic voxels). Then the images were smoothed with an 8 mm full-width at half-maximum (FWHM) Gaussian kernel. High-pass filtering (a 128 second cutoff) was applied in order to remove cardio-respiratory factors.

All events were included in constructing a general linear model using a canonical hemodynamic function (HRF) with temporal and dispersion derivatives, at the individual level. Nine experimental conditions constructed separate regressors. In addition, the first trial, error trials, and post-error trials were modeled as a separate regressor of non-interest. Statistical analyses were restricted to a priori regions of interest (ROIs) in order to specify their functional roles in monitor-controller loops. Six a priori functional ROIs were selected from our previous studies (Kim et al., 2010; Kim et al., 2011b)

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and defined as 8 mm radius spheres in MNI space. Specifically, two DLPFC ROIs previously shown to be involved in response conflict (x,y,z=−42,30,24 and x,y,z=42,9,24) and two pre-PMd ROIs shown to be associated with perceptual conflict (x,y,z=−27,0,60 and x,y,z=36,0,57) were selected from Kim et al. (2010). In addition, rdACC (x,y,z=4, 32, 27) and cdACC (x,y,z=3, 16, 41) were selected from the meta-analytic results from Kim et al. (2011b). For each subject, BOLD signal changes of particular trial types within each ROI were extracted and then peak activity (the mean of 4 and 6 s after trial onset) was selected to perform statistical tests. These data were analyzed using a 3×3 (previous trial type×current trial type) repeated measures ANOVA to test whether conflict adjustment effects are selectively associated with the type of conflict (i.e., perceptual or response conflict). Since 6 ROIs were tested, the statistical threshold was corrected at $p<0.05$ level using the Bonferroni correction procedure (equivalent to uncorrected $p<0.0083$).

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REFERENCES

Aarts, E., Roelofs, A., van Turennout, M., 2008. Anticipatory activity in anterior cingulate cortex can be independent of conflict and error likelihood. J. Neurosci. 28, 4671–4678.

Aarts, E., Roelofs, A., van Turennout, M., 2009. Attentional control of task and response in lateral and medial frontal cortex: brain activity and reaction time distributions. Neuropsychologia 47, 2089–2099.

Abe, M., Hanakawa, T., 2009. Functional coupling underlying motor and cognitive functions of the dorsal premotor cortex. Behav. Brain Res. 198, 13–23.

Abe, M., Hanakawa, T., Takayama, Y., Kuroki, C., Ogawa, S., Fukuyama, H., 2007. Functional coupling of human prefrontal and premotor areas during cognitive manipulation. J. Neurosci. 27, 3429–3438.

Badre, D., D'Esposito, M., 2007. Functional magnetic resonance imaging evidence for a hierarchical organization of the prefrontal cortex. J. Cogn. Neurosci. 19, 2082–2099.

Barbas, H., Pandya, D.N., 1987. Architecture and frontal cortical connections of the premotor cortex (area 6) in the rhesus monkey. J. Comp. Neurol. 256, 211–228.

Botvinick, M.M., Nystrom, L.E., Fissell, K., Carter, C.S., Cohen, J.D., 1999. Conflict monitoring versus selection-for-action in anterior cingulate cortex. Nature 402, 179–181.

Botvinick, M.M., Braver, T.S., Barch, D.M., Carter, C.S., Cohen, J.D., 2001. Conflict monitoring and cognitive control. Psychol. Rev. 108, 624–652.

Botvinick, M.M., Cohen, J.D., Carter, C.S., 2004. Conflict monitoring and anterior cingulate cortex: an update. Trends Cogn. Sci. 8, 539–546.

Braver, T.S., Reynolds, J.R., Donaldson, D.I., 2003. Neural mechanisms of transient and sustained cognitive control during task switching. Neuron 39, 713–726.

Dreher, J.C., Berman, K.F., 2002. Fractionating the neural substrate of cognitive control processes. Proc. Natl. Acad. Sci. U. S. A. 99, 14595–14600.

Egner, T., 2008. Multiple conflict-driven control mechanisms in the human brain. Trends Cogn. Sci. 12, 374–380.

Egner, T., Hirsch, J., 2005a. The neural correlates and functional integration of cognitive control in a Stroop task. Neuroimage 24, 539–547.

Egner, T., Hirsch, J., 2005b. Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information. Nat. Neurosci. 8, 1784–1790.

Egner, T., Delano, M., Hirsch, J., 2007. Separate conflict-specific cognitive control mechanisms in the human brain. Neuroimage 35, 940–948.

Fassbender, C., Simoes-Franklin, C., Murphy, K., Hester, R., Meaney, J., Robertson, I.H., Garavan, H., 2006. The role of a right fronto-parietal network in cognitive control: common activations for "cues-to-attend" and response inhibition. J. Psychophysiol. 20, 286–296.

Gratton, G., Coles, M.G., Donchin, E., 1992. Optimizing the use of information: strategic control of activation of responses. J. Exp. Psychol. Gen. 121, 480–506.

Hanakawa, T., Honda, M., Sawamoto, N., Okada, T., Yonekura, Y., Fukuyama, H., Shibasaki, H., 2002. The role of rostral Brodmann area 6 in mental-operation tasks: an integrative neuroimaging approach. Cereb. Cortex 12, 1157–1170.

Henson, R.N., Buchel, C., Josephs, O., Friston, K.J., 1999. The slice-timing problem in event-related fMRI. Neuroimage 9, 125.

Jimura, K., Braver, T.S., 2010. Age-related shifts in brain activity dynamics during task switching. Cereb. Cortex 20, 1420–1431.

Kerns, J.G., 2006. Anterior cingulate and prefrontal cortex activity in an FMRI study of trial-to-trial adjustments on the Simon task. Neuroimage 33, 399–405.

Kerns, J.G., Cohen, J.D., MacDonald III, A.W., Cho, R.Y., Stenger, V.A., Carter, C.S., 2004. Anterior cingulate conflict monitoring and adjustments in control. Science 303, 1023–1026.

Kim, C., Chung, C., Kim, J., 2010. Multiple cognitive control mechanisms associated with the nature of conflict. Neurosci. Lett. 496, 156–160.

Kim, C., Johnson, N.F., Cilles, S.E., Gold, B.T., 2011a. Common and distinct mechanisms of cognitive flexibility in prefrontal cortex. J. Neurosci. 31, 4771–4779.

Kim, C., Kroger, J.K., Kim, J., 2011b. A functional dissociation of conflict processing within anterior cingulate cortex. Hum. Brain Mapp. 32, 304–312.

Kim, C., Cilles, S.E., Johnson, N.F., Gold, B.T., 2012. Domain general and domain preferential brain regions associated with different types of task switching: a meta-analysis. Hum. Brain Mapp. 33, 130–142.

Kornblum, S., Hasbroucq, T., Osman, A., 1990. Dimensional overlap: cognitive basis for stimulus–response compatibility—a model and taxonomy. Psychol. Rev. 97, 253–270.

MacDonald, A.W., Cohen, J.D., Stenger, V.A., Carter, C.S., 2000. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science 288, 1835–1838.

Mayr, U., Awh, E., Laurey, P., 2003. Conflict adaptation effects in the absence of executive control. Nat. Neurosci. 6, 450–452.

Milham, M.P., Banich, M.T., 2005. Anterior cingulate cortex: an fMRI analysis of conflict specificity and functional differentiation. Hum. Brain Mapp. 25, 328–335.

Milham, M.P., Banich, M.T., Webb, A., Barad, V., Cohen, N.J., Wszalek, T., Kramer, A.F., 2001. The relative involvement of anterior cingulate and prefrontal cortex in attentional control depends on nature of conflict. Cogn. Brain Res. 12, 467–473.

Miller, E.K., Cohen, J.D., 2001. An integrative theory of prefrontal cortex function. Annu. Rev. Neurosci. 24, 167–202.

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Orr, J.M., Weissman, D.H., 2009. Anterior cingulate cortex makes 2 contributions to minimizing distraction. Cereb. Cortex 19, 703–711.

Picard, N., Strick, P.L., 1996. Motor areas of the medial wall: a review of their location and functional activation. Cereb. Cortex 6, 342–353.

Rajah, M.N., Ames, B., D'Esposito, M., 2008. Prefrontal contributions to domain-general executive control processes during temporal context retrieval. Neuropsychologia 46, 1088–1103.

Savine, A.C., Braver, T.S., 2010. Motivated cognitive control: reward incentives modulate preparatory neural activity during task-switching. J. Neurosci. 30, 10294–10305.

Sugg, M.J., McDonald, J.E., 1994. Time course of inhibition in color-response and word-response versions of the Stroop task. J. Exp. Psychol. Hum. Percept. Perform. 20, 647–675.

Vanderhasselt, M.A., De Raedt, R., Baeken, C., 2009. Dorsolateral prefrontal cortex and Stroop performance: tackling the lateralization. Psychon. Bull. Rev. 16, 609–612.

Weissman, D.H., Warner, L.M., Woldorff, M.G., 2004. The neural mechanisms for minimizing cross-modal distraction. J. Neurosci. 24, 10941–10949.

Weissman, D.H., Gopalakrishnan, A., Hazlett, C.J., Woldorff, M.G., 2005. Dorsal anterior cingulate cortex resolves conflict from distracting stimuli by boosting attention toward relevant events. Cereb. Cortex 15, 229–237.

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