Published in final edited form as:

Cortex. 2014 January ; 50: . doi:10.1016/j.cortex.2013.08.011.

Conflict Adaptation in Prefrontal Cortex: Now You See It, Now You Don't

Chobok Kim^{a,b}, Nathan F. Johnson^b, and Brian T. Gold^{b,c}

^aDepartment of Psychology, Kyungpook National University, Daegu, 702-701, South Korea

^bDepartment of Anatomy and Neurobiology, University of Kentucky, Lexington, KY 40536, USA

^cMagnetic Resonance Imaging and Spectroscopy Center, University of Kentucky, Lexington, KY 40536, USA

Abstract

Daily life requires people to monitor and resolve conflict arising from distracting information irrelevant to current goals. The highly influential conflict monitoring theory (CMT) holds that the anterior cingulate cortex (ACC) detects conflict and subsequently triggers the dorsolateral prefrontal cortex (DLPFC) to regulate that conflict. Multiple lines of evidence have provided support for CMT. For example, performance is faster on incongruent trials that follow other incongruent trials (ii), and is accompanied by reduced ACC and increased DLPFC activation (the conflict adaptation effect). In this fMRI study, we explored whether ACC-DLPFC conflict signaling can result in behavioral adjustments beyond on-line contexts. Participants completed a modified version of the Stroop conflict adaptation paradigm which tested for conflict adaptation effects on the current (N) trial associated with not only by the immediately preceding (N-1) trial, but also 2-back (N-2) trials. Results demonstrated evidence for direct relationships between ACC activity on N-2 trials and both N trial DLPFC activity and behavioral adjustment when intervening trials were congruent (i.e., iI). In contrast, when N-1 trials were incongruent (i.e., iiI), ACC-DLPFC signaling failed and conflict adaptation was absent. These results provide new evidence demonstrating that the conflict monitor-controller maintains previously experienced conflict in the service of subsequent behavioral adjustment. However, the processing of multiple, temporally proximal conflict signals takes a toll on the working memory system, which appears to require re-setting in order to adapt our behavior to frequently changing environmental demands.

Keywords

Prefrontal cortex; Cognitive control; Conflict adaptation; fMRI

1. INTRODUCTION

Cognitive control refers to a set of functions allowing humans to integrate thought and action in accord with internal goals in order to adjust our behavior to environmental

© 2013 Elsevier Masson Italy. All rights reserved.

Correspondence: Chobok Kim, Ph.D., Assistant Professor, Department of Psychology, Kyungpook National University, Daegu, 702-701, South Korea, Phone: +82-53-950-5250, Fax: +82-53-950-5243, ckim@knu.ac.kr.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

demands (Miller and Cohen, 2001). Fundamental to successful behavioral adjustment are the abilities to detect and resolve conflict arising from simultaneous, incompatible representations. According to the conflict monitoring theory (CMT), the predominant account of cognitive control, these functions are served by a dedicated neural conflict-monitor controller loop. Specifically, CMT holds that the anterior cingulate cortex (ACC) detects conflict in information processing, and subsequently triggers the dorsolateral prefrontal cortex (DLPFC) to regulate the conflict through top-down attentional biasing processes in-line with the current task set (Botvinick, Braver et al., 2001; Botvinick, Cohen et al., 2004; MacDonald, Cohen et al., 2000).

The CMT has been successful in explaining how humans can dynamically adjust behavior in variety of conflicting situations (Egner, 2007). For example, in the Stroop color-naming task (Stroop, 1935), conflict is greater on incongruent trials (e.g., “RED” printed in blue ink) than on congruent trials (e.g., “BLUE” printed in blue ink), resulting in slower reaction times (RTs). Interestingly, however, RTs are faster for incongruent trials that follow N-1 incongruent trials (iI) than those following N-1 congruent trials (cI) (Gratton, Coles et al., 1992; Mayr, Awh et al., 2003). According to the CMT, this ‘conflict adaptation effect’ is the result of enhanced cognitive control that follows the presentation of a stimulus with incompatible representations. Neuroimaging studies have linked this behavioral adjustment with decreased ACC activity and increased DLPFC activity on iI trials compared to cI trials (Kerns, Cohen et al., 2004; Botvinick, Nystrom et al., 1999).

The ACC-DLPFC loop is assumed to function as an on-line conflict monitor-controller system. The ACC detects conflict and signals the DLPFC to increase the level of cognitive control. However, the established role of the DLPFC and ACC in active maintenance of information (Cohen, Perlstein et al., 1997; Fuster and Alexander, 1971; D’Esposito, Ballard et al., 2000; D’Esposito, Postle et al., 2000; Goldman-Rakic, 1987; Petit, Courtney et al., 1998; Owen, McMillan et al., 2005) call for a greater understanding of whether conflict signals can be maintained in the face of intervening, incompatible representations (i.e., iCI trials). In addition, the fate of the ACC conflict signal following successful behavioral adjustment remains unknown. That is, does the conflict signal decay immediately following initial behavioral adjustment (i.e., on iI), or is maintained in the service of subsequent behavioral adjustment (i.e., iII trial)?

To address these questions, we manipulated the classic Stroop conflict adaptation paradigm to enable analysis of N-2 trials in addition to N-1 trials. If the up-regulation of conflict is transient (i.e., occurs only at a trial-to-trial level) then current-trial behavioral performance should not be influenced by N-2 trial type. In contrast, if the up-regulation of conflict is maintained in working memory (WM), we would expect current-trial behavioral adjustment in response to N-2 conflict, despite interference from an intervening congruent trial (faster RTs on iCI trials than on cCI trials). Furthermore, if conflict adaptation is carried out through interface with the limited capacity WM system, then current-trial behavioral adjustment may be disrupted by an interaction between N-1 and N-2 trial types, associated with interference between those trials (Baddeley, 1992).

2. METHODS

2.1. Subjects

A total of 18 young volunteers (mean age 25.3 years, SD = 3.6, range 19–34 years, 8 females) participated in this study. All subjects were right-handed and native English speakers who reported no history of head injury, psychiatric or neurological problems. Subjects had normal or corrected-to-normal vision without color blindness. Subjects

provided written informed consent in a manner approved by the University of Kentucky Institutional Review Board and were compensated for their participation.

2.2. Materials and procedure

The experiment was programmed via E-Prime v1.2 and back-projected onto a screen, sitting outside the magnet, which was viewed by the subjects through a mirror attached to the head coil. Reaction times and accuracies for the subjects' responses on each trial were recorded by the stimulus program. A variation of the Stroop color-word task was employed for the fMRI experiment. The stimuli consisted of visual words presented in one of six different potential colors (red, green, blue, yellow, purple, and orange). Each trial included a sample word and two response probes, presented on a black background (Figure 1). The color of the sample was either congruent with its spelling (e.g., "RED" printed in red ink) or incongruent with its spelling (e.g., "BLUE" printed in yellow ink). One of the response probes was the name of the sample word's color (correct probe) and the other was an incorrect probe. For the congruent condition, the incorrect probe was randomly selected from the five colors which were not assigned to the sample. For example, for the congruent sample "RED" printed in red ink the correct response probe was "RED" and the incorrect probe was one of the other colors. For the incongruent condition, the incorrect probe had the same spelling as the sample word. For example, for an incongruent sample "BLUE" printed in yellow ink, the correct probe was "YELLOW" and the incorrect probe was "BLUE").

The task required subjects to identify the color of the sample and select the response probe word that spelled that color by pressing either the left or right button (either left or right thumb). Subjects were not asked to remember the preceding trial or to anticipate the next trial type. The order of congruent and incongruent trials was pseudo-randomly intermixed in order to measure brain activation associated with post-conflict adaptation. Task conditions were manipulated according to three trial types: the current (N) trial type (congruent or incongruent), the preceding (N-1) trial type (congruent or incongruent), and the 2-back (N-2) trial type (congruent or incongruent). Accordingly, the task involved 8 trial-type transitions: congruent-congruent-congruent (ccC), congruent-incongruent-congruent (ciC), incongruent-congruent-congruent (icC), and incongruent-incongruent-congruent (iiC) for the congruent conditions; congruent-congruent-incongruent (ccI), congruent-incongruent-incongruent (ciI), incongruent-congruent-incongruent (icI), and incongruent-incongruent-incongruent (iiI) for the incongruent conditions. In order to control for the effect of preceding trial types (i.e., N-3 trial types), we counterbalanced the probability of N-3 trial types (i.e., there were 50% ciiI trials and 50% iiiI).

As described in previous studies (Egner, Etkin et al., 2008; Monti, Weintraub et al., 2010), it is important to control for factors that could confound conflict adaptation effects, such as repetition priming effects (Mayr, Awh et al., 2003). In doing so, the stimuli for the sample and response cues were always changed from trial to trial. Additionally, in the half of the trials for each condition, responses were repeated (e.g., left followed by left) and in the other half, those were changed (e.g., left followed by right).

An event-related design was employed in order to measure trial-specific neural activity. Stimuli were presented for 1.2 sec, followed by an inter-stimulus-interval ranging from 2.2 to 5.6 sec (average 3.3 sec). Across the experiment there were a total of 120 trials in each of the congruent and incongruent conditions. The experiment was divided into three runs, each lasting 388 sec.

2.3. Imaging acquisition

Imaging data were acquired on a 3-T Siemens TIM scanner at the Magnetic Resonance Imaging and Spectroscopy Center at University of Kentucky. T2*-weighted functional images were collected using a gradient-echo (EPI) sequence (33 interleaved slices, repetition time (TR) = 2000 ms, echo time (TE) = 30 ms, flip angle = 77°, field of view (FOV) = 224 mm², matrix = 64×64, isotropic 3.5 mm voxels). To correct inhomogeneity of the B₀ field, field maps were created from a double-echo gradient-echo sequence (TE1 = 5.19 ms, TE2 = 7.65 ms) with slice position and spatial resolution matching those of the EPI acquisition. T1-weighted structural images were collected using the magnetization-prepared rapid gradient-echo (MPRAGE) sequence (TR = 2100ms, TE = 2.93ms, TI = 1100ms, flip angle = 12°, FOV = 224×256×192 mm, resolution=1 mm³, sagittal partitions).

2.4. Image preprocessing and voxel-wise analyses

Statistical Parametric Mapping (SPM5; Wellcome Department of Cognitive Neurology, UCL, London, UK) was used in preprocessing and statistical analyses of fMRI data. The first five functional volumes of each run were discarded prior to preprocessing. Sinc interpolation was used to correct differences in timing between slices (Henson, Buchel et al., 1999), and the corrected images were spatially realigned to the first volume of the first run using a six-parameter rigid body transformation to correct for head motion. These realigned images were then unwarped via B₀ field maps to reduce magnetic field distortions, coregistered with the structural image (MPRAGE), and then normalized into the standard the Montreal Neurological Institute (MNI) T1 template, using unified segmentation-based normalization with 12-parameter affine and non-linear transformations (2mm cubic voxels). Finally, the normalized images were smoothed with an 8 mm full-width at half-maximum (FWHM) Gaussian kernel and high-pass filtered with a 128 sec cutoff period.

Statistical analyses at the subject-level were conducted in the context of the general linear (GLM) model using a canonical hemodynamic response function (HRF) with temporal and dispersion derivatives. Eight different conditions (4 congruent conditions including ccC, ciC, icC, and iiC; 4 incongruent conditions including ccI, ciI, icI, and iiI) were separately submitted into the GLM model. Error trials and post-error trials were modeled separately as a regressor of non-interest in order to exclude error-related neural activity. Additionally, head movement parameters in six dimensions were included in the model as covariates of non-interest. This resulted in 8 regressor images of interest for each subject.

The goal of the study was to explore and compare activation patterns of three regions known to be critically involved in conflict monitoring and adaptation processes: the ACC and bilateral DLPFC. In order to identify peak ACC and DLPFC regions in our subjects in a manner unbiased by any specific condition, these regions were identified based on the results of a group analysis comparing all incongruent conditions (ccI, ciI, icI, and iiI) to all congruent conditions (ccC, ciC, icC, and iiC). Regressors for all incongruent and congruent trials constructed a design matrix. Accordingly, a paired-sample t-test was used to identify and determine ACC and DLPFC regions for ROI analyses. This activation map was corrected for multiple comparisons at p<0.05 family-wise error (FWE).

2.5. Region-wise analyses

Based on the voxel-wise group analysis, signal changes in ACC and bilateral DLPFC were extracted for the further analyses. ROIs were defined as 5 mm radius spheres centered on the peak coordinates of ACC and bilateral DLPFC activated by the voxel-wise comparison described above (all incongruent conditions > all congruent conditions). Marsbar software (<http://marsbar.sourceforge.net>) was used to generate these ROIs and to extract % signal changes based on beta-parameters estimated from the subject-level analyses. For the first

ROI analyses, the signal changes of these ROIs for the all incongruent conditions (i.e., ccI, ciI, icI, and iiI) were extracted and analyzed in the context of the analyses of variance (ANOVA) to test whether the current signal changes in these ROIs differed as a function of N-2 and N-1 trial types. We also tested whether the conflict adaptation effects for ciI, icI, and iiI (i.e., ccI vs. ciI, ccI vs. icI, and ccI vs. iiI, respectively) were significantly observed using paired-sample t-tests.

For the next ROI analyses, signal changes within ACC on the previous (N-1 and N-2) incongruent trials were extracted and were correlated with the current DLPFC activity. For these analyses, individual data were separately modeled two times for N-1 and N-2 trials in order to extract ACC signal changes on the N-1 (for ciI and iiI conditions) and N-2 (for icI and iiI conditions) incongruent trials. These data were then correlated with the current DLPFC activity to test whether ACC activity on the previous (N-1 and N-2) incongruent trials predicts increases in DLPFC activity on the current ciI, icI and iiI trials.

Finally, signal changes of ACC on the previous (N-1 and N-2) incongruent trials were correlated with behavioral adaptation effects in order to test whether ACC activity on the previous (N-2 and N-1) incongruent trials predicts conflict adaptation effects. These analyses were restricted only to the incongruent conditions showing significant behavioral adaptation effects (i.e., ciI and icI; see behavioral data).

3. RESULTS

3.1. Behavioral data

Mean accuracy and reaction times (RTs) are presented in Figure 2. These data were analyzed in the context of a $2 \times 2 \times 2$ repeated measures ANOVA with N-2, N-1 and N trial types (congruent vs. incongruent for each trial type). For accuracy, the main effect of the N trial type was significant ($F(1,17)=23.13$, $p<0.001$). Specifically, the accuracy for the current congruent trials ($M=0.99$, $SD=0.01$) was higher than the current incongruent trials ($M=0.94$, $SD=0.04$). In contrast, the main effects of N-2 and N-1, and all two-way and a three-way interaction effects were not significant ($ps>0.05$).

For RTs, the main effect of the N trial type was significant ($F(1,17)=244.70$, $p<0.001$), due to slower RTs for the current incongruent trials ($M=880.6$ ms, $SD=107.3$) than the current congruent trials ($M=674.8$ ms, $SD=97.2$). The main effect of N-2 trial type was also significant ($F(1,17)=6.46$, $p<0.05$), due to slower RTs for the incongruent N-2 trials ($M=829.5$ ms, $SD=100.0$) than the congruent N-2 trials ($M=816.0$ ms, $SD=103.7$). In contrast, the main effect of the N-1 trial type was not significant ($F(1,17)=0.01$, $p>0.05$).

The interaction between N-1 and N trial types was significant ($F(1,17)=31.91$, $p<0.001$). Specifically, RTs for the current congruent trials were faster when preceded by congruent trials ($M=754.3$ ms, $SD=92.3$) than when preceded by incongruent trials ($M=775.4$ ms, $SD=104.6$). In contrast, this pattern was reversed for the current incongruent trials, in that RTs for the current incongruent trials were slower when preceded by congruent trials ($M=890.5$ ms, $SD=111.3$) than when preceded by incongruent trials ($M=870.7$ ms, $SD=106.4$). The interaction effect between N-2 and N-1 was also significant ($F(1,17)=18.16$, $p<0.001$). Specifically, when N-2 was congruent, RTs were slower when N-1 was congruent ($M=827.7$ ms, $SD=110.0$) than when it was incongruent ($M=804.2$ ms, $SD=100.3$). In contrast, this was reversed when N-2 was incongruent; RTs were faster when N-1 was congruent ($M=817.1$ ms, $SD=92.8$) than when it was incongruent ($M=841.9$ ms, $SD=110.7$). However, the interaction between N-2 and N trial types was not significant ($F(1,17)=0.89$, $p>0.05$).

The three-way interaction between N-2, N-1 and N trial types was also significant ($F(1,17)=13.06$, $p<0.01$). To explore this interaction pattern, we performed two separate 2×2 repeated measures ANOVAs with N-2 and N-1 trial types for each of the current congruent and current incongruent trial types. The results demonstrated that there was no interaction between N-2 and N-1 for the current congruent trials ($F(1,17)=0.64$, $p>0.05$). In contrast, the interaction effect was significant for the current incongruent trials ($F(1,17)=20.31$, $p<0.001$). Specifically, for the N-2 congruent trials, RTs for the current incongruent trials were slower when preceded by congruent N-1 (ccI; $M=907.0$ ms, $SD=126.5$) trials than when preceded by incongruent N-1 (ciI; $M=843.3$ ms, $SD=97.4$) trials ($t(17)=4.89$, $p<0.001$). In contrast, for the N-2 incongruent trials, the current incongruent trials showed a trend toward faster RTs when N-1 was congruent (icI trials; $M=874.0$ ms, $SD=103.1$) than when N-1 was incongruent (iiI trials; $M=898.1$ ms, $SD=118.3$) ($t(17)=1.89$, $p=0.08$).

Finally, we tested whether the conflict adaptation effects for ciI, icI, and iiI (i.e., ccI-ciI, ccI-icI, and ccI-iiI, respectively) were significantly observed using paired-sample t-tests. The results showed that the conflict adaptation effect for ciI (i.e., ccI-ciI; $M=63.7$ ms, $SD=55.3$) and icI (i.e., ccI-icI; $M=33.0$ ms, $SD=60.8$) were significant ($t(17)=4.89$, $p<0.001$; $t(17)=2.30$, $p<0.05$). In contrast, the adaptation effect for iiI (i.e., ccI-iiI; $M=8.9$ ms, $SD=14.4$) was not significant ($t(17)=0.62$, $p>0.05$).

3.2. Imaging data

Functional imaging data were analyzed in the context of a flexible factorial design. In order to identify brain regions associated with the Stroop interference effect, all incongruent conditions (ccI, ciI, icI, and iiI) were compared to all congruent conditions (ccC, ciC, icC, and iiC). These results are shown in Figure 3A and listed in Table 1. Compared to the congruent conditions, the incongruent conditions resulted in prominent activation of bilateral DLPFC (BA 9), ACC (BA 32), ventrolateral prefrontal cortex (BA 47), bilateral supramarginal gyrus (BA 40), and cerebellum (not shown).

Signal changes in ACC and bilateral DLPFC regions during incongruent trials (i.e., ccI, ciI, icI, and iiI) were extracted in order to test whether conflict adaptation effects were affected by the types of the N-2 and N-1 trials in the context of 2×2 ANOVA (Figure 3B). For the signal changes of ACC, both the main effects of N-2 and N-1 trial types were not significant ($F(1,17)=0.25$, $p>0.05$; $F(1,17)=0.49$, $p>0.05$). In contrast, the interaction between N-2 and N-1 was significant ($F(1,17)=18.35$, $p<0.001$), due to the fact that the signal changes of ccI ($M=0.34$ %, $SD=0.21$) were higher than those of ciI ($M=0.19$ %, $SD=0.15$) trials ($t(17)=2.62$, $p<0.05$) whereas the signal changes of icI ($M=0.23$ %, $SD=0.12$) were lower than those of iiI ($M=0.33$ %, $SD=0.11$) trials ($t(17)=2.86$, $p<0.05$). We also tested whether the conflict adaptation effects for ciI, icI, and iiI (i.e., ccI-ciI, ccI-icI, and ccI-iiI, respectively) within ACC were significant using paired-sample t-tests. The results showed that the conflict adaptation effects for ciI (i.e., ccI-ciI; $M=0.15$ %, $SD=0.24$) and icI (i.e., ccI-icI; $M=0.11$ %, $SD=0.21$) trials ($t(17)=2.62$, $p<0.05$; $t(17)=2.13$, $p<0.05$) were significant. In contrast, the conflict adaptation effect for iiI (i.e., ccI-iiI; $M=0.01$ %, $SD=0.22$) was not significant ($t(17)=0.22$, $p>0.05$).

In summary, the results showed that ACC activations for ciI and icI trials were lower when compared to ccI trials whereas the activations for iiI trials were not different from ccI trials. In other words, ACC activity was decreased when either N-1 or N-2 trial was incongruent (i.e., only one trial between N-1 and N-2 was incongruent) whereas it was not affected when both N-1 and N-2 trials were incongruent.

For the signal changes within left DLPFC, both the main effects of N-2 and N-1 types were not significant ($F(1,17)=0.02$, $p>0.05$; $F(1,17)=0.14$, $p>0.05$). In contrast, the interaction

between N-2 and N-1 was significant ($F(1,17)=8.79$, $p<0.01$). Specifically, the signal changes of ciI ($M=0.30\%$, $SD=0.23$) were higher than those of ccI ($M=0.16\%$, $SD=0.23$) trials ($t(17)=2.42$, $p<0.05$) whereas the signal changes of icI ($M=0.29\%$, $SD=0.17$) showed a trend toward being higher than those of iiI ($M=0.18\%$, $SD=0.28$) trials ($t(17)=1.83$, $p=0.08$). Additionally, we tested whether the conflict adaptation effects for ciI, icI, and iiI (i.e., ciI-ccI, icI-ccI, and iiI-ccI, respectively) within left DLPFC were significant. The results showed significant conflict adaptation effects for ciI (i.e., ciI-ccI; $M=0.15\%$, $SD=0.26$) and icI (i.e., icI-ccI; $M=0.14\%$, $SD=0.24$) trials ($t(17)=2.42$, $p<0.05$; $t(17)=2.37$, $p<0.05$). In contrast, the conflict adaptation effect for iiI (i.e., iiI-ccI; $M=0.02\%$, $SD=0.25$) was not significant ($t(17)=0.36$, $p>0.05$).

In summary, left DLPFC showed increased activations for ciI and icI trials, but not for iiI trials, when compared to ccI trials. In other words, these data demonstrated that left DLPFC activity was increased when either N-1 or N-2 was incongruent whereas it was not affected when the both previous trials were incongruent.

For the signal changes within right DLPFC, on the other hand, both the main effects of N-2 and N-1 types ($F(1,17)=0.56$, $p>0.05$; $F(1,17)=1.91$, $p>0.05$), and the interaction between N-2 and N-1 ($F(1,17)=0.15$, $p>0.05$) were not significant. Furthermore, the conflict adaptation effects for ciI, icI, and iiI (i.e., ciI-ccI, icI-ccI, and iiI-ccI, respectively) within right DLPFC were not significant ($ps>0.05$).

The next analyses focused on whether ACC activity on the previous (N-1 and N-2) incongruent trials predicts DLPFC activity on the current ciI, icI and iiI trials (Figure 4). Although the whole brain analysis revealed that bilateral DLPFC regions were more activated in incongruent trials than congruent trials, these analyses were restricted within left DLPFC because right DLPFC activity on the current incongruent trials was not affected by the N-2 or N-1 trial type as described above. First of all, ACC activity on the N-1 trials was correlated with DLPFC activity on the current trials for both ciI and iiI conditions. Figure 4A and 4B present the results of the correlations between ACC activity on the N-1 trials and DLPFC activity on the current trials for ciI and iiI conditions. For the ciI condition, a significant positive correlation was observed between N-1 ACC activity and current DLPFC activity ($r=0.74$, $p<0.001$) whereas it was not significant between N-1 ACC activity and current DLPFC activity for the iiI condition ($r=0.30$, $p>0.05$). The same pattern was observed in the results of correlations between ACC activity on the N-2 trials and DLPFC activity on the current trials for icI and iiI conditions (Figure 4C and 4D). For the icI condition, there was a significant positive correlation between N-2 ACC activity and current DLPFC activity ($r=0.64$, $p<0.005$) whereas it was not significant between N-2 ACC activity and current DLPFC activity for the iiI condition ($r=0.20$, $p>0.05$).

Finally, we tested whether ACC activations on the N-2 and N-1 incongruent trials were correlated with behavioral adaptation effects for ciI and icI conditions. These analyses were restricted to the ciI and icI conditions because behavioral adaptation effects were observed only in these two conditions (see behavioral data). As shown in Figure 5, the correlation between N-1 ACC activity and the behavioral adaptation effect for the ciI condition was significant ($r=0.74$, $p<0.001$). A significant positive correlation was also observed between N-2 ACC activity and the behavioral adaptation effect for the icI condition ($r=0.60$, $p<0.01$).

4. DISCUSSION

We manipulated the classic Stroop conflict adaptation paradigm to enable analyses of N-2 trials in addition to N-1 trials. Results demonstrated that adaptation effects related to N-2 depend critically on whether the intervening trial is congruent or incongruent. For icI trials,

up-regulation of control through ACC-DLPFC (i.e., the monitor-controller loop), and related behavioral adaptation, are maintained. However, for iil trials, ACC-DLPFC up-regulation of control fails and behavioral adaptation is absent. Below we discuss these novel findings in detail and their implications suggesting that the monitor-controller system (ACC and DLPFC) can flexibly maintain or reset previously experienced conflict signals in the service of successful performance.

Our behavioral findings on N-1 trials provide support for conflict monitoring theory (CMT). According to CMT, the level of cognitive control is higher for trials that follow an incongruent trial (e.g., iI) than for trials that follow a congruent trial (e.g., cI) (Botvinick, Braver et al., 2001). This is because the high conflict encountered on incongruent trials leads to the recruitment of greater cognitive control on subsequent trials. The temporary up-regulation of cognitive control following incongruent trials thus results in faster RTs on iI trials than for cI trials. Consistent with this account, our behavioral results demonstrated that responses on the current incongruent trials were faster when N-1 trials were incongruent than when they were congruent, replicating the well-established conflict adaptation effect (i.e., faster RTs for iI trials than for cI trials).

The analyses of the functional imaging data of N-1 trials also largely support CMT. Using ACC and bilateral DLPFC as regions of interest (ROIs), we found that ACC and left DLPFC (but not right DLPFC) were associated with the well-established neural conflict adaptation effect. Specifically, we found lower activation of ACC and higher activation of left DLPFC for the iI condition than the cI condition (i.e., neural conflict adaptation), replicating previous findings (Egner and Hirsch, 2005a; Kerns, Cohen et al., 2004; Botvinick, Nystrom et al., 1999). CMT also holds that conflict-related activity in ACC should signal an increase in DLPFC activity on the subsequent trial because DLPFC plays a critical role in executing cognitive control (Kerns, Cohen et al., 2004; Botvinick, Braver et al., 2001). Once again, our results on N-1 trials found support for this view, as conflict-related ACC activity on N-1 trials predicted an increase in current-trial DLPFC activity.

Our results concerning N-2 trials serve to support but also to extend CMT. We found that behavioral responses on incongruent trials were faster when N-2 trials were incongruent than when they were congruent (i.e., faster RTs on iI trials than on cI trials). The observed adaptation effects on iI trials provide evidence that N-2 conflict signals do affect current-trial behavioral performance. The persistence of N-2 behavioral adaptation in the face of interference from an intervening congruent trial, suggests that conflict signals may be maintained in working memory (WM) or short-term memory (STM) in the service of successful performance. The view that previously experienced conflict can be maintained in WM or STM over time is not new (Mansouri, Tanaka et al., 2009). In addition, our findings are consistent with a view that many cognitive control operations make use of WM processes (Baddeley, 1992).

Our imaging results concerning N-2 trials provide evidence that the conflict monitor-controller (i.e., ACC and DLPFC) contributes to the up-regulation of cognitive control over a temporal interval despite interference. Firstly, ACC showed lower activity on iI than cI trials and left DLPFC showed the reverse pattern. Secondly, conflict-related ACC activity on N-2 trials predicted an increase in current-trial DLPFC activity. Finally, ACC activity on N-2 trials predicted the strength of current-trial behavioral adaptation effects. These results suggest that ACC and DLPFC contribute to the interface between cognitive control and WM systems, possibly serving to maintain and refresh representation of conflict across trials. This view is consistent with evidence from the primate literature that DLPFC neurons encode and actively maintain conflict experienced on previous trials (Mansouri, Buckley et al., 2007). In addition, our findings are consistent with a body of data showing that DLPFC

and ACC regions function both to maintain/refresh information and perform control operations on that information (Petit, Courtney et al., 1998; Owen, McMillan et al., 2005).

However, our results concerning N-2 trials also provide evidence that the ability of the monitor-controller to successfully up-regulate control over a temporal interval depends critically upon the nature of intervening representations. We observed a complete absence of behavioral adaptation when intervening trials were incongruent (i.e., the absence of adaptation on iiI trials). According to CMT, the iiI condition should show conflict adaptation because the current incongruent trial was preceded by an incongruent trial on N-1, which is supposed to result in faster RTs in iiI trials. A potential explanation for the absence of the conflict adaptation effect on iiI trials could be expectancy effects. However, if this were the case, then expectation effects should also influence ccC trials (i.e., should result in slower RTs for the ccC condition than for the ciC, icC or iiC condition). Based on the behavioral results, this is an inadequate explanation for our findings.

Furthermore, consistent with the lack of behavioral adaptation, our fMRI results demonstrated an absence of neural conflict adaptation effects in both ACC and DLPFC regions associated with iiI trials. These results raised the possibility that ACC may fail to successfully signal to DLPFC when both N-1 and N-2 trials are incongruent. To explore this possibility, we examined the relationship between ACC and DLPFC activation related to the iiI condition. Indeed, results indicated that ACC activation on N-2 incongruent trials failed to predict DLPFC activation on current incongruent trials when the intervening trial was also incongruent.

We interpret our findings as suggestive that the conflict monitor-controller system undergoes 'resetting' following the processing of multiple, temporally proximal conflict signals. This resetting may serve as an adaptive response to a frequently changing external environment such as that encountered in the present randomized inhibitory control design (or related task switching designs (Kim, Cilles et al., 2012; Kim, Johnson et al., 2011). The notion that the monitor-controller system undergoes resetting to promote efficient response is consistent with several neuro-computational modeling studies suggesting that PFC activity returns to a pre-adaptation level following a protracted challenge to promote an adaptive response (Durstewitz, Kelc et al., 1999; Brunel and Wang, 2001; Cohen, Braver et al., 2002). In our experiment, a pre-adaptation level (i.e., as on ciI trials) would relate to reflect a context in which DLPFC response on iiI trials is lower than ciI or ciI trials and is no longer correlated with ACC response.

The present study has several caveats that highlight the need for future work in this field. First, the brain regions identified in the overall Stroop effect are unlikely to be specific to inhibitory control processes and may in part reflect cognitive processes such as task/strategy switching. A related point is that other brain regions identified in the overall Stroop effect beyond ACC and DLPFC (bilateral VLPFC and parietal cortex) may also contribute to conflict adaptation effects, and this should be explored in future studies. Second, previous studies suggest that error-related ACC activity also yields an increase in DLPFC activity and corresponding adjustment in the following trials (Carter, Braver et al., 1998; Kerns, Cohen et al., 2004). However, we were unable to perform meaningful error-related sequential analyses due to the very small percentage of error trials in the present study conditions (average 1% and 6% for congruent and incongruent conditions, respectively). The lack of significant accuracy interaction effects suggests that error-related ACC activity is unlikely to account for the N-2 neural adaptation effects we observed. Nevertheless, future research should test the effect of N-2 error-related ACC activity on the level of cognitive control in the current trial.

Additionally, in the present study no conceptual distinction was drawn between the monitor-controller and WM/STM systems because cognitive control and maintenance functions may ultimately boil down to a common processing system, which draws critically on common ACC and DLPFC substrates (reviewed in Braver and Cohen, 2001). However, in addition to their shared neural substrates, the monitor-controller and WM systems may also draw upon partially distinct neural substrates. Future research will be required to address this issue. Potentially fruitful approaches to this issue may come from imaging studies of cognitive control adopting a dual-task approach or those in which the delay interval between N-2 and current trials is manipulated parametrically.

Finally, it is worth noting that neural conflict adaptation effects for N-1 or N-2 incongruent trials in the DLPFC were left-lateralized. One possible reason for this laterality effect could relate to the verbal nature of the Stroop task, which typically results in greater left than right DLPFC activation (e.g., Egner and Hirsch, 2005b). In contrast, flanker-like tasks or tasks using other visuospatial stimuli (e.g., Egner and Hirsch, 2005a) and emotional conflict tasks (e.g., Egner, Etkin et al., 2008) result in more bilateral or right DLPFC activation. It is also possible that our results reflect a more general predominance of left DLPFC involvement in the sequential up-regulation of cognitive control, as suggested by a recent systematic review (Vanderhasselt, De Raedt et al., 2009).

In summary, our findings serve to extend CMT accounts of conflict signaling. Specifically, our results provide new evidence demonstrating that the function of the conflict monitor-controller system (ACC and DLPFC) is not limited to on-line conflict processing. Instead, our results show that ACC-DLPFC loop can preserve conflict signaling in the face of interference from an intervening trial, likely through interface with the WM system. However, the processing of multiple, temporally proximal conflict signals takes a toll on the working memory system, which appears to require re-setting in order to adapt our behavior to frequently changing environmental demands. Based on these findings, we propose that conflict monitor-controller system is capable of both preserving and resetting previously experienced conflict-based representations in the service of successful cognitive control.

Acknowledgments

This study was supported by NIA Grant R01 AG033036 and NSF Grant BCS-0814302. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or NSF. We thank Sara Cilles for her assistance in recruiting and testing participants.

REFERENCES

- Baddeley A. Working memory. *Science*. 1992; 255:556–559. [PubMed: 1736359]
- Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD. Conflict monitoring and cognitive control. *Psychological Review*. 2001; 108:624–652. [PubMed: 11488380]
- Botvinick MM, Cohen JD, Carter CS. Conflict monitoring and anterior cingulate cortex: An update. *Trends Cogn Sci*. 2004; 8:539–546. [PubMed: 15556023]
- Botvinick MM, Nystrom LE, Fissell K, Carter CS, Cohen JD. Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature*. 1999; 402:179–181. [PubMed: 10647008]
- Braver TS, Cohen JD. Working memory, cognitive control, and the prefrontal cortex: Computational and empirical studies. *Cogn Processing*. 2001; 2:25–55.
- Brunel N, Wang XJ. Effects of neuromodulation in a cortical network model of object working memory dominated by recurrent inhibition. *J Comput Neurosci*. 2001; 11:63–85. [PubMed: 11524578]
- Carter CS, Braver TS, Barch DM, Botvinick MM, Noll D, Cohen JD. Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science*. 1998; 280:747–749. [PubMed: 9563953]

- Cohen JD, Braver TS, Brown JW. Computational perspectives on dopamine function in prefrontal cortex. *Curr Opin Neurobiol.* 2002; 12:223–229. [PubMed: 12015241]
- Cohen JD, Perlstein WM, Braver TS, Nystrom LE, Noll DC, Jonides J, Smith EE. Temporal dynamics of brain activation during a working memory task. *Nature.* 1997; 386:604–608. [PubMed: 9121583]
- D'Esposito M, Ballard D, Zarahn E, Aguirre GK. The role of prefrontal cortex in sensory memory and motor preparation: An event-related fmri study. *NeuroImage.* 2000; 11:400–408. [PubMed: 10806027]
- D'Esposito M, Postle BR, Rypma B. Prefrontal cortical contributions to working memory: Evidence from event-related fmri studies. *Experimental Brain Research.* 2000; 133:3–11. [PubMed: 10933205]
- Durstewitz D, Kelc M, Gunturkun O. A neurocomputational theory of the dopaminergic modulation of working memory functions. *J Neurosci.* 1999; 19:2807–2822. [PubMed: 10087092]
- Egner T. Congruency sequence effects and cognitive control. *Cogn Affect Behav Neurosci.* 2007; 7:380–390. [PubMed: 18189011]
- Egner T, Etkin A, Gale S, Hirsch J. Dissociable neural systems resolve conflict from emotional versus nonemotional distracters. *Cereb Cortex.* 2008; 18:1475–1484. [PubMed: 17940084]
- Egner T, Hirsch J. Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information. *Nat Neurosci.* 2005a; 8:1784–1790. [PubMed: 16286928]
- Egner T, Hirsch J. The neural correlates and functional integration of cognitive control in a stroop task. *NeuroImage.* 2005b; 24:539–547.
- Fuster JM, Alexander GE. Neuron activity related to short-term memory. *Science.* 1971; 173:652–654. [PubMed: 4998337]
- Goldman-Rakic, PS. Circuitry of primate prefrontal cortex and the regulation of behavior by representational memory. In: Plum, F., editor. *Handbook of physiology.* Bethesda, MD: American Physiological Society; 1987. p. 373–417.
- Gratton G, Coles MG, Donchin E. Optimizing the use of information: Strategic control of activation of responses. *J Exp Psycho/Gen.* 1992; 121:480–506.
- Henson RN, Buchel C, Josephs O, Friston KJ. The slice-timing problem in event-related fmri. *NeuroImage.* 1999; 9:125.
- Hommel B, Proctor RW, Vu KP. A feature-integration account of sequential effects in the simon task. *Psycho/Res.* 2004; 68:1–17.
- Kerns JG, Cohen JD, MacDonald AW III, Cho RY, Stenger VA, Carter CS. Anterior cingulate conflict monitoring and adjustments in control. *Science.* 2004; 303:1023–1026. [PubMed: 14963333]
- Kim C, Cilles SE, Johnson NF, Gold BT. Domain general and domain preferential brain regions associated with different types of task switching: A meta-analysis. *Human Brain Mapping.* 2012; 33:130–142. [PubMed: 21391260]
- Kim C, Johnson NF, Cilles SE, Gold BT. Common and distinct mechanisms of cognitive flexibility in prefrontal cortex. *The Journal of Neuroscience.* 2011; 31:4771–4779. [PubMed: 21451015]
- MacDonald AW, Cohen JD, Stenger VA, Carter CS. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science.* 2000; 288:1835–1838. [PubMed: 10846167]
- Mansouri FA, Buckley MJ, Tanaka K. Mnemonic function of the dorsolateral prefrontal cortex in conflict-induced behavioral adjustment. *Science.* 2007; 318:987–990. [PubMed: 17962523]
- Mansouri FA, Tanaka K, Buckley MJ. Conflict-induced behavioural adjustment: A clue to the executive functions of the prefrontal cortex. *Nat Rev Neurosci.* 2009; 10:141–152. [PubMed: 19153577]
- Mayr U, Awh E, Laurey P. Conflict adaptation effects in the absence of executive control. *Nat Neurosci.* 2003; 6:450–452. [PubMed: 12704394]
- Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci.* 2001; 24:167–202. [PubMed: 11283309]
- Monti JM, Weintraub S, Egner T. Differential age-related decline in conflict-driven task-set shielding from emotional versus non-emotional distracters. *Neuropsychologia.* 2010; 48:1697–1706. [PubMed: 20176042]

- Owen AM, McMillan KM, Laird AR, Bullmore E. N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Hum Brain Mapp.* 2005; 25:46–59. [PubMed: 15846822]
- Petit L, Courtney SM, Ungerleider LG, Haxby JV. Sustained activity in the medial wall during working memory delays. *J Neurosci.* 1998; 18:9429–9437. [PubMed: 9801381]
- Stroop JR. Studies of interference in serial verbal reactions. *J Exp Psycho/.* 1935; 28:643–662.
- Vanderhasselt MA, De Raedt R, Baeken C. Dorsolateral prefrontal cortex and stroop performance: Tackling the lateralization. *Psychon Bull Rev.* 2009; 16:609–612. [PubMed: 19451392]

Figure 1.

Examples of task stimuli and conditions used in the fMRI experiment. The task required subjects to identify the color of the sample (e.g., yellow for the word “BLUE”) and to select the response probe word that spelled that color. The current (N) trials are presented in the right column. The left and middle columns indicate N-2 and N-1 trials, respectively. The task condition of the current incongruent trial is determined by the type of both N-2 and N-1 trial types. For example, the upper panel N trial is the ccI condition because both N-2 and N-1 trials are congruent. The lower panel N trial is the iiI condition because both N-2 and N-1 trials are incongruent.

Figure 2. Accuracy (top) and mean RTs (bottom) for the task conditions. Congruent and incongruent conditions with respect to current trial type are presented on the left and right, respectively. Error bars represent the standard errors of the means.

Figure 3.

Significant brain activations associated with the Stroop interference effect and signal changes for the incongruent conditions. (A) Activations in the lateral and medial brain regions for the incongruent conditions compared to the congruent conditions. (B) Signal changes of bilateral DLPFC and ACC regions of interest for the incongruent conditions (i.e., ccI, ciI, icI, and iiI).

Figure 4.

Correlations between previous ACC activity and current DLPFC activity. The top panel displays correlations between ACC activity on the N-1 incongruent trials and current DLPFC activity on ciI trials (A) and iiI trials (B). The bottom panel displays correlations between ACC activity on the N-2 incongruent trials and current DLPFC activity on icI trials (C) and iiI trials (D).

Figure 5. Correlations between previous ACC activity and behavioral conflict adaptation effects. Left: Correlation between ACC activity on the N-1 incongruent trials and the conflict adaptation effect for the ciI condition. Right: Correlation between ACC activity on the N-2 incongruent trials and the conflict adaptation effect for the icI condition.

Significant brain regions of activation for the incongruent conditions compared to the congruent conditions.

Table 1

Region	Hem	X	Y	Z	BA	z-score
Inferior Frontal Gyms (pars triangularis)/Insula	L	-34	16	-6	47	5.98
	R	40	20	-2	47	6.22
Middle/Inferior Frontal Gyms (DLPFC)	L	-48	12	28	9	5.26
	R	48	12	24	9	5.04
Cingulate Gyms (ACC)	R	6	26	34	32	4.95
Supramarginal Gyms	L	-58	-42	36	40	5.7
	R	62	-40	38	40	4.95
Cerebellum (Culmen)	L	-26	-58	-24		4.94

Hem, hemisphere; BA, Brodmann area; L, left; R, right; DLPFC, dorsolateral prefrontal cortex; ACC, anterior cingulate cortex.