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The neural correlates and functional integration of cognitive control in a Stroop task

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It is well known that performance on a given trial of a cognitive task is affected by the nature of previous trials. For example, conflict effects on interference tasks, such as the Stroop task, are reduced subsequent to high-conflict trials relative to low-conflict trials. This interaction effect between previous and current trial types is called "conflict adaptation" and thought to be due to processing adjustments in cognitive control. The current study aimed to identify the neural substrates of cognitive control during conflict adaptation by isolating neural correlates of reduced conflict from those of increased cognitive control. We expected cognitive control to be implemented by prefrontal cortex through context-specific modulation of posterior regions involved in sensory and motor aspects of task performance. We collected event-related fMRI data on a color-word naming Stroop task and found distinct fronto-parietal networks of current trial conflict detection and conflict adaptation through cognitive control. Conflict adaptation was associated with increased activity in left middle frontal gyrus (GFm) and superior frontal gyrus (GFs), consistent with increased cognitive control, and with decreased activity in bilateral prefrontal and parietal cortices, consistent with reduced response conflict. Psychophysiological interaction analysis (PPI) revealed that cognitive control activation in GFs and GFm was accompanied by increased functional integration with bilateral inferior frontal, right temporal and parietal areas, and the anterior cerebellum. These data suggest that cognitive control is implemented by medial and lateral prefrontal cortices that bias processes in regions that have been implicated in high-level perceptual and motor processes.

Keywords: Conflict adaptation; Cognitive control; Stroop task; Psychophysiological interaction

Introduction

The study of the neural bases of executive attention processes has featured prominently in the cognitive neurosciences. Executive or supervisory control refers to the collection of processes that allow us to react flexibly to changing or novel task requirements, by adaptively integrating changes in contextual information and, if necessary, inhibiting and overriding responses that may have previously been associated with successful task performance but are no longer appropriate (e.g., Norman and Shallice, 1986). In recent years, research has focused on dissociating supposed subcomponents of executive processes and their neural substrates, particularly with respect to an emerging model of complementary response conflict monitoring and cognitive control functions of executive attention (Botvinick et al., 1999; Carter et al., 1998, 2000; Casey et al., 2000; Kerns et al., 2004; MacDonald et al., 2000).

According to this prominent model, a response conflict monitoring system continuously parses ongoing information processing for potential response conflict due to interference or "crosstalk" between different processing streams, and this evaluative function is implemented by the (dorsal) anterior cingulate cortex (ACC). When conflict is detected, this model suggests that a cognitive control system, situated in dorsolateral prefrontal cortices (DLPFC), is alerted and subsequently engaged in reducing conflict by biasing information processing in posterior brain regions towards the criteria most relevant to successful task completion (Botvinick et al., 2001).

The behavioral and neuroimaging data on which the conflict monitoring/cognitive control model is based have primarily been derived from the Stroop task (MacLeod, 1991; Stroop, 1935) and the Eriksen Flanker task (Eriksen and Eriksen, 1974), where task-relevant and task-irrelevant stimulus properties are either in conflict with each other or not. For instance, in a typical Stroop paradigm, subjects are required to name the ink color in which a word stimulus is printed, and level of conflict is manipulated by varying the task-irrelevant property of the stimuli (in this case the word-meaning), from conflicting or "incongruent" (e.g., the word RED printed in green ink) to nonconflicting neutral, or "congruent" properties (e.g., the word RED printed in red ink). The Eriksen Flanker task, on the other hand, requires subjects to identify the nature of a central stimulus in a stimulus array (e.g., to indicate the direction of an arrow stimulus pointing left "<"or right ">"), and conflict is manipulated by displaying either incongruent (e.g., >><>>) or congruent flanker stimuli (<<<<<). The interference

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effects of these conflict manipulations are evident in behavioral measures of reaction times (RT) and error rates, with incongruent trials leading to longer RTs and higher error rates.

Crucially, performance on any given trial is influenced by the context of this trial with respect to conflict levels of preceding trials. The crossing of previous trial type (congruent/incongruent) with current trial type (congruent/incongruent), giving congruent–congruent (CC), congruent–incongruent (CI), incongruent–congruent (IC), and incongruent–incongruent (II) trial pairs, results in an interaction effect. Conflict effects (i.e., differential incongruent versus congruent trial responses) are reduced subsequent to high-conflict (incongruent) trials compared to low-conflict (congruent) trials, the so-called conflict adaptation effect (Gratton et al., 1992). This reduction in conflict stems from the fact that a preceding incongruent trial has opposing effects on responses to incongruent and congruent trials in comparison to responses following congruent trials: Responses to incongruent trials are faster and more accurate, interpreted as reflecting conflict reduction due to cognitive control, whereas congruent trial responses are slower and less accurate, interpreted as reflecting the elimination of a facilitation effect due to cognitive control (Botvinick et al., 1999, 2001). It is this interaction between previous and current trial type ("conflict adaptation" or the "Gratton effect") on which the conflict monitoring/cognitive control model rests (Botvinick et al., 1999, 2001; Kerns et al., 2004; Mayr et al., 2003).

Employing Stroop and Eriksen paradigms and contrasting neural responses between conditions of high and low conflict, a number of studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have documented the ACC's susceptibility to conflict (Barch et al., 2001; Bench et al., 1993; Botvinick et al., 1999; Carter et al., 1995, 2000; Casey et al., 2000; Durston et al., 2003; Fan et al., 2003; Hazeltine et al., 2003; Kerns et al., 2004; Leung et al., 2000; MacDonald et al., 2000; Milham et al., 2001, 2003; Pardo et al., 1990; Ullsperger and von Cramon, 2001; vanVeen et al., 2001), and the DLPFC's purported role in the implementation of cognitive control (Durston et al., 2003; Kerns et al., 2004; MacDonald et al., 2000; Milham et al., 2001, 2003). However, parsing brain responses related to conflict detection from those related to conflict resolution through cognitive control has not been addressed by the majority of these studies. In view of the conflict adaptation effect, it is evident that to ignore the interaction between previous and current trial types introduces error into the interpretation of current trial interference effects, but only few investigations into the neural bases of conflict detection and resolution have explicitly taken this effect into account (Botvinick et al., 1999; Carter et al., 2000; Casey et al., 2000; Durston et al., 2003; Kerns et al., 2004).

The studies that have addressed the conflict adaptation effect, on the other hand, have focused exclusively on identifying neural correlates of response conflict reduction, i.e., brain regions in which activity decreases parallel to behavioral conflict effects (Botvinick et al., 1999; Carter et al., 2000; Casey et al., 2000; Durston et al., 2003; Kerns et al., 2004). This emphasis derived from efforts to resolve whether the role of ACC function in interference tasks is one of response conflict monitoring (e.g., Botvinick et al., 1999; Carter et al., 2000) or selection for action (e.g., Posner and DiGirolamo, 1998). Attempts at identifying brain regions implicated in cognitive control have consisted of examining neural effects of preparing for high- versus low-conflict trials in a cued Stroop paradigm (MacDonald et al., 2000), and of median-split analyses of Stroop trials subsequent to high conflict, associated with either low or high behavioral adjustments in terms of reaction times (Kerns et al., 2004). However, no previous study has specifically investigated the flip-side of conflict reduction in conflict adaptation, namely brain regions that display increased activity with the conflict adaptation interaction effect, paralleling a presumed increase in cognitive control. Furthermore, although it has frequently been suggested that cognitive control is likely implemented by PFC regions affecting the processing in posterior (particularly parietal) brain regions (e.g., Durston et al., 2003), only one previous fMRI study has attempted to assess connectivity measures related to Stroop task performance (Peterson et al., 1999). This study, however, conducted principal components analysis on data from a blocked Stroop paradigm and thus could not measure changes in functional connectivity related to component processes of Stroop performance, such as phasic adjustments in cognitive control.

The current study aimed to further our understanding of executive control mechanisms by identifying neural correlates of conflict adaptation, in particular cortical areas displaying increased activation with reduced conflict, reflecting enhanced cognitive control. In addition, a psychophysiological interaction (PPI) (Friston, 2004; Friston et al., 1997) analysis was employed to reveal changes in the functional interaction between brain regions implementing cognitive control during conflict adaptation. It was hypothesized that neural correlates of cognitive control would be detected in DLPFC, and that these activation foci would display increased functional integration with posterior cortical regions responsible for implementing changes in the focus of sensory and motor processing during conflict adaptation. We designed a simple Stroop paradigm variant that allowed us to examine conflict adaptation effects related to stimulus congruency in the absence of stimulus probability and repetition priming effects. Repetition priming here refers to direct stimulus repetitions that have been shown to be a major potential confounding variable in the interpretation of conflict adaptation effects in the Eriksen flanker task (Mayr et al., 2003) but have not been controlled for in previous studies (for an exception, see Kerns et al., 2004). Our Stroop task entailed equal proportions of CC, CI, IC, and II trial sequences, and none of the CC and II trial pairs contained stimulus repetitions. By excluding error and post-error trials[1] from the assessment of behavioral interference effects, and separately modeling the neural correlates of these trials, we furthermore

[1] The confounding influence of error trials on behavioral interference effects and in the interpretation of neuronal activity, particularly with reference to probing ACC function (e.g., Braver et al., 2001; Carter et al., 1998; Garavan et al., 2002, 2003; Kiehl et al., 2000; Ullsperger and von Cramon, 2001), have long been recognized and error trials are typically excluded from analyses in event-related fMRI paradigms. It has also long been noted that a special status must be conferred to trials following error trials, so-called post-error trials (e.g., Rabbitt, 1966), characterized behaviorally by a marked and reliable slowing of RT (e.g., Kleiter and Schwarzenbacher, 1989; Rabbitt, 1966; Rabbitt and Rogers, 1977), referred to as post-error slowing. Thus, post-error trials are clearly not comparable to other correct responses, nor to trials occurring subsequent to high-conflict trials, as post-error slowing occurs irrespective of current or previous trial type. Even though the phenomenon of post-error slowing forms an integral part of the model of conflict adaptation through cognitive control (Botvinick et al., 2001), such trials have previously not been excluded or modeled separately from other correct trials in the analyses of behavioral and neural interference effects, introducing a serious potential confound.

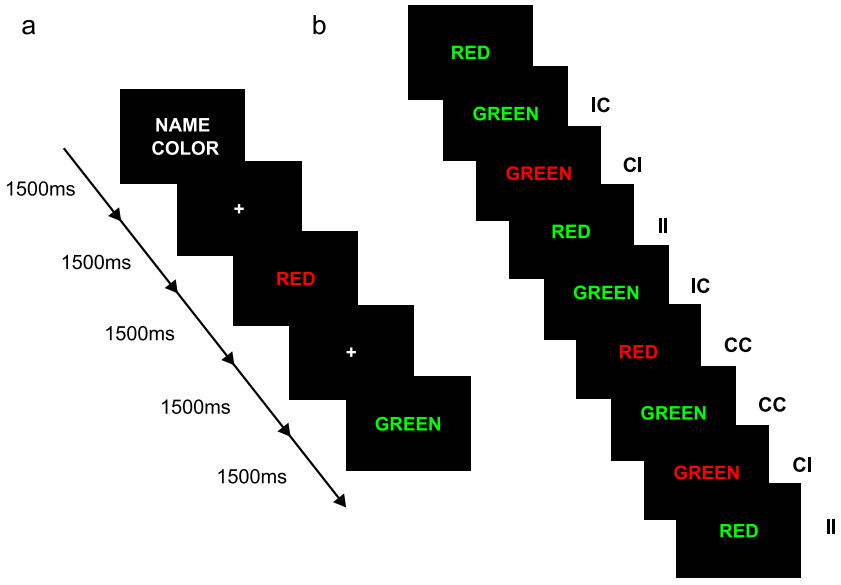

Fig. 1. Schematic depiction of the Stroop paradigm, showing (a) representative timing parameters for two trials at the beginning of a new block, and (b) a representative block (instruction and fixation screens not shown) of nine trials resulting in equal proportions of congruent–congruent (CC), congruent–incongruent (CI), incongruent–congruent (IC), and incongruent–incongruent (II) trial sequences.

isolated conflict adaptation-related processes from error-related processes.

Methods

Subjects

Participants were 14 right-handed native or highly proficient English-speaking volunteers (mean age = 27.4 years, age range = 21–40 years, eight females) with normal or corrected-to-normal vision, who had been screened to exclude participants with previous or current neurological or psychiatric conditions, current medication use, colorblindness, or dyslexia. Participants gave written informed consent in accordance with institutional guidelines.

Paradigm

The Stroop variant employed in this study was a two word color- and word-naming task previously found to reliably induce significant interference effects (Egner et al., 2004). The two color–word stimuli employed were the words RED and GREEN, presented either in red or green hue on a black background. Stimuli were presented for 1500 ms with an interstimulus interval (ISI) of 3000 ms in alternating blocks of color-naming and word-naming instructions (Fig. 1a). No jittering of ISI was applied so as to not introduce an additional variable to interact in an unpredictable manner with the conflict adaptation process, and in a recent comparable study the identical ISI has been shown to bear out equivalent efficiency for detecting trial-type differences as slow event-related or fast jittered designs (Kerns et al., 2004). Each block started with a "name color" or "name word" instruction presented for 1500 ms and contained a pseudorandom sequence of 9 stimuli (Fig. 1b). There were 20 blocks, resulting in 180 trials and a task length of 11 min and 40 s. The stimuli were sequenced in a way as to result in equal proportion of CC, CI, IC, and II trials (n = 45). Furthermore, none of the CC and II trial sequences contained exact stimulus repetitions to avoid potential repetition priming effects[2] (Fig. 1b). Subjects were instructed to respond through button presses with their right-hand index finger (left button, indicating "green") and middle finger (right button, indicating "red") as fast as possible whilst maintaining accuracy, and a brief training period of four blocks of the task was administered outside the scanner before the fMRI session. For the purpose of this study, that factor of instruction (word-naming versus color-naming) was not considered in the analyses. Presentation software (Neurobehavioral Systems, http://nbs.neuro-bs.com) was used to create and deliver the paradigm and record subject responses. The task was presented to the subjects via a back projection onto a screen that could be viewed through a mirror attached to the head-coil of the scanner.

fMRI data acquisition

Images were acquired with a GE Signa 1.5-T scanner. Functional data were acquired along the AC–PC line with a T2*-weighted EPI sequence of 25 contiguous axial slices (TR = 4000, TE = 60, flip angle = 60, FoV = 190) of 4.5-mm thickness and 1.5 × 1.5 mm in-plane resolution, providing whole-brain coverage. The functional data on the Stroop paradigm were recorded in a single run of 188 acquisitions (20 blocks, 180 trials, see Paradigm section). Structural data were acquired with a high-

[2] It should be noted that II sequences on a two color–word task that do not contain stimulus repetitions invariably may incur negative priming effects, where the to-be-ignored dimension on the previous trial (e.g., the word GREEN in red hue) slows down responses to the current trial relevant dimension (e.g., the word RED in green hue) if the two are related (Dalrymple-Alford and Budayr, 1966; for reviews, see Fox, 1995; May et al., 1995). These effects are not being controlled for in the current paradigm. However, negative Stroop priming effects are typically in the range of 20 ms (considerably smaller than conflict adaptation effects) and here would therefore only slightly mitigate against obtaining a conflict adaptation effect when comparing CI with II trial RTs.

resolution T1*-weighted SPGR scan (TR = 19, TE = 5, flip angle = 20, FoV = 220) recording 124 slices at a slice thickness of 1.5 mm and in-plane resolution of 0.86 × 0.86 mm.

fMRI data analysis

Spatial pre-processing and statistical inference testing were carried out with SPM2 software (Wellcome Department of Cognitive Neurology, University College London, UK, http://www.fil.ion.ucl.ac.uk/spm/spm2.html). Functional T2* images were spatially realigned to the first volume scanned in the run using a six-parameter rigid-body transformation. The structural T1* scan was co-registered to a mean image of the realigned functional scans. Normalization parameters were determined from warping the co-registered SPGR scan to a template T1* brain complying with the Montreal Neurological Institute (MNI) stereotactic coordinate system and subsequently applying those parameters to the functional scans. Finally, the functional images were spatially smoothed with a Gaussian kernel of 4.5 × 4.5 × 13.5 mm FWHM (i.e., three times the voxel dimensions as originally acquired). The first four functional scans were discarded from the analyses. Within the general linear model (GLM) framework, regressors of events, modeled by the canonical hemodynamic response function (hrf) and its first temporal derivative, were created for each trial type (CC, CI, IC, II) as well as for error and post-error trials. A 128-s temporal highpass filter was applied to the data to exclude low-frequency artifacts such as scanner drift. Temporal autocorrelation within the data was estimated via an autoregressive function.

Voxel-wise statistical parametric maps (SPM) were calculated for main and interaction effects of previous and current trial type, and results of these *t*-contrasts from each subject were then entered into random-effects analysis at the group level. Based on the most frequently reported activation sites in the literature, the analyses were conducted within a priori regions of interest (ROI) limited to Brodmann areas (BA) 24 and 32 in the medial prefrontal cortex, BA 8, 9, and 46 in the DLPFC, and BA7 and 40 in the parietal cortex, employing a mask created with the WFU Pick Atlas toolbox (Maldjian et al., 2003; see http://www.rad.wfubmc.edu/fmri). Within these ROIs we accepted statistical significance at *Z*-scores of >3.50 (corresponding to a *t*-score of >4.70 and $P < 0.001$) with a cluster threshold of ≥5 voxels.

Psychophysiological interaction (PPI) analysis

To assess the hypothesis that prefrontal regions involved in cognitive control interact with posterior brain regions to effect response conflict reduction, we estimated the functional integration of cognitive control in conflict adaptation in a psychophysiological interaction (PPI) analysis. PPI analysis allows the detection of regionally specific responses in one brain area in terms of the interaction between input from another brain region and a cognitive/sensory process (Friston, 2004; Friston et al., 1997). Although the PPI analysis approach has been described as constituting a measure of *effective connectivity* (the direct influence of one region on another) rather than mere *functional connectivity* (a correlation between activity in different regions), this definition strictly speaking applies only to cases where an exhaustive number of input/modulatory sources to a particular region are assessed (see Friston et al., 1997, p. 227). In the instance of assessing the input from a single ROI, as is the case in the current study, PPI analysis cannot provide definitive evidence for effective connectivity (Friston, 2004; Friston et al., 1997). In interpreting PPI results, we will therefore use the terminology of these analyses providing a measure of context-specific *functional integration* or *functional interaction* (Friston et al., 1997).

PPI analysis employs one regressor representing the (deconvolved) activation time course in a given volume of interest (the physiological variable), one regressor representing the psychological variable of interest, and a third regressor representing the cross-product of the previous two (the psychophysiological interaction term). An SPM is computed that reveals areas where activation is predicted by the psychophysiological interaction term, and the physiological and psychological regressors are treated as confound variables. Accordingly, using SPM2, we extracted the deconvolved time course of activity in the ROIs identified as reflecting cognitive control activation (see Results section) (a 10-mm radius sphere centered at the GFm and GFs voxels displaying peak activity in the group analysis, see Table 3). We then calculated the product of this activation time course with the interaction term of previous × current trial congruency factors to create the psychophysiological interaction term. PPI analyses were carried out for each ROI in each subject, and then entered into a random effects group analysis (thresholded at $P < 0.001$ and a cluster size of >10 voxels).

Results

Behavioral results

Dependent measures of RT and percent accuracy rates were analyzed in 2 × 2 previous trial type (incongruent vs. congruent) × current trial type (incongruent vs. congruent) factorial mixed-effects ANOVAs. Within each subject, error and post-error trial RTs were excluded from the mean RT estimates, as were RT outlier values (>3 SDs from the mean), resulting in the exclusion of approximately 1.5% of RT data points. Post-error slowing was found to be significant (correct responses RT = 818 ms, SD = 185; post-error RT = 1041 ms, SD = 341; t [13] = 3.75, $P < 0.005$). Descriptive statistics are presented in Table 1. In the RT data, a significant previous × current trial interaction effect (F [1, 13] = 18.90, $P = 0.001$) was accompanied by a main effect of current trial type (F [1, 13] = 31.78, $P < 0.001$), the latter due to higher RTs on incongruent than congruent trials (mean congruent RT = 784 ms, mean incongruent RT = 869 ms; interference effect = 85 ms, corresponding to a 10.8% increase in RT). As can be seen in Fig. 2a, this interaction effect was due to a significant conflict effect following congruent trials (t [13] = 6.23, $P < 0.001$) that was not present following incongruent trials (t [13] = 0.03, n.s.), as II trials

Table 1
Mean Reaction Time (RT) and percentage of accurate responses (% accuracy) and respective standard deviation (SD) values for all trial types

Trial	RT (ms)	SD	% Accuracy	SD
CC	723	167	99.1	2.1
CI	852	193	91.4	7.2
IC	804	197	97.9	2.5
II	804	177	95.1	6.1

Note. Trial types are previous followed by current trial congruency, CC = congruent–congruent, CI = congruent–incongruent, IC=incongruent–congruent, II = incongruent–incongruent.

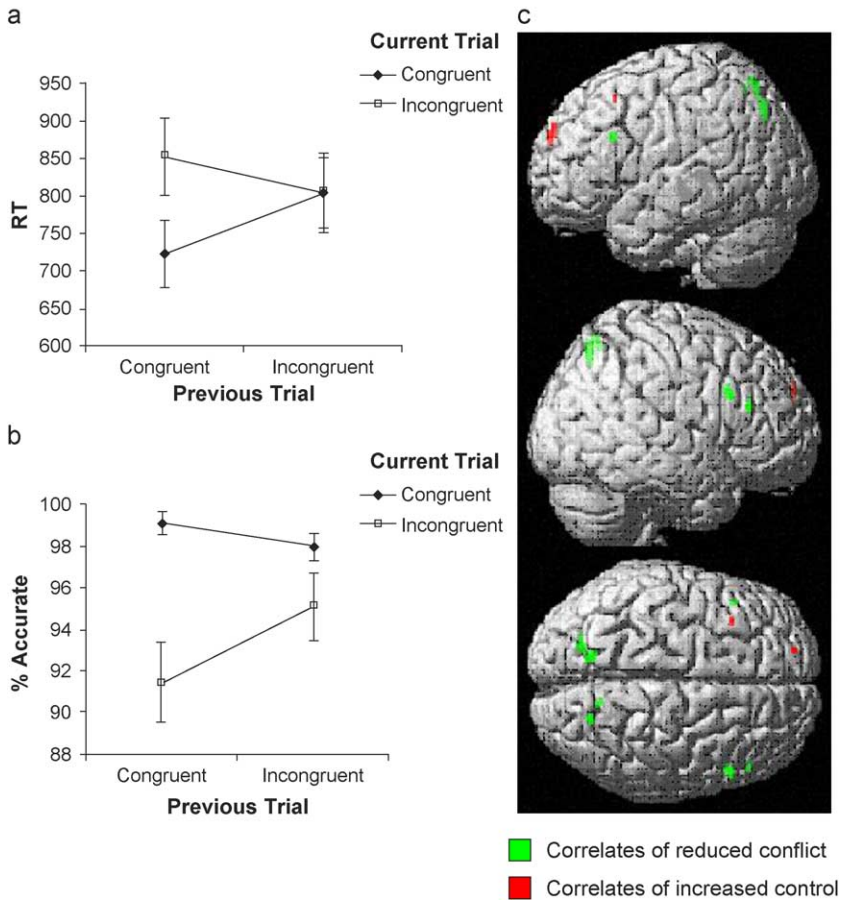

Fig. 2. Conflict adaptation previous trial × current trial interaction effects on (a) reaction time in ms, (b) accuracy rates (% correct responses), and (c) BOLD responses (projected onto rendered single subject MNI brain). Activation foci showing increased activity with conflict adaptation are displayed in red, foci showing decreased activity with conflict adaptation are displayed in green.

had faster responses than CI trials (t [13] = 2.30, $P < 0.05$), and IC trials had slower responses than CC trials (t [13] = 5.06, $P < 0.001$), the classic Gratton effect (reduction of interference = 129 ms).

Similar to the RT data, the accuracy data displayed a previous × current trial interaction effect (F [1, 13] = 17.52, P = 0.001), accompanied by main effects of previous (F [1, 13] = 7.05, $P <$ 0.05) and current trial type (F [1, 13] = 17.37, P = 0.001), the latter two due to higher accuracy following incongruent than congruent trials, and lower accuracy on current incongruent than congruent trials (Fig. 2b). The conflict adaptation interaction was characterized by a significant reduction in current trial conflict following incongruent trials compared to congruent files (t [13] = 4.19, P =

Table 2
Brain regions susceptible to main effects of current trial type and/or previous trial type

Talairach label	Side	BA	Talairach (x, y, z)	Z-score	Inc> Con
Effect of current trial type					
Superior parietal lobule	L	7	−24, −53, 58	3.94	↑
Superior frontal gyrus	L	8	−8, 37, 46	3.79	↑
Cingulate gyrus	R	24	18, 8, 46	3.69	↑
Superior parietal lobule	L	7	−30, −68, 50	3.60	↑
Superior parietal lobule	R	7	24, −53, 60	3.58	↑
Effect of previous trial type					
Superior parietal lobule	R	7	18, −63, 53	3.97	↓

Note. BA = Brodmann area, R = right, L = left, ↑ = increases activation in incongruent > congruent contrast, ↓ = decreases activation in incongruent > congruent contrast.

Table 3
Brain regions susceptible to previous × current trial type conflict adaptation interaction effect

Talairach label	Side	BA	Talairach (x, y, z)	Z score	Activation
Middle frontal gyrus	L	8	−36, 20, 47	3.56	↑
Superior frontal gyrus	L	9	−18, 56, 27	3.55	↑
Precuneus	L	7	−14, −65, 51	3.80	↓
Precuneus	L	7	−20, −70, 42	3.75	↓
Precuneus	R	7	22, −64, 51	3.70	↓
Inferior frontal gyrus	R	9	54, 19, 23	3.67	↓
Middle frontal gyrus	L	46	−46, 21, 25	3.62	↓
Middle frontal gyrus	R	46	50, 30, 19	3.58	↓

Note. BA = Brodmann area, R = right, L = left, ↑ = increases in activation with conflict adaptation, ↓ = decreases in activation with conflict adaptation.

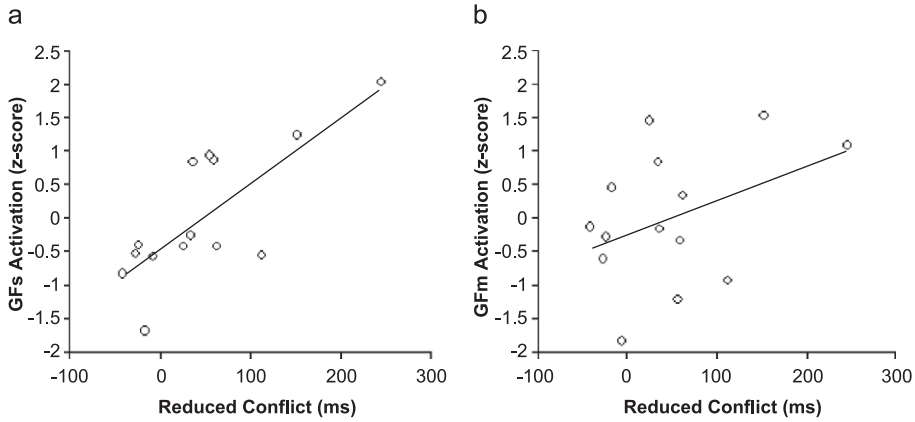

Fig. 3. Correlations between reduced conflict on incongruent trials (RT differences between CI and II trials) and activation in cognitive control ROIs of (a) the medial GFs ($r = 0.77$, $P < 0.001$), and (b) the left GFm ($r = 0.40$, n.s.).

0.001), as II trials had higher accuracy than CI trials (t [13] = 3.85, $P < 0.005$), and IC trials had lower accuracy than CC trials (t [13] = 2.46, $P < 0.05$). Thus, we obtained highly significant conflict adaptation effects on our Stroop paradigm in the absence of repetition priming effects.

Imaging results—conflict adaptation

Random-effects group analyses of the effect of current trial conflict revealed increased activation in voxels in medial frontal areas of the right dorsal cingulate gyrus and left dorsomedial GFs, and parietal activations in left and right superior parietal lobules (LPs) (see Table 2), with no areas showing significantly decreased activity in response to conflict. Voxels displaying a main effect of previous trial type were found in the right medial LPs, where activity was found to be reduced after incongruent compared to congruent trials (see Table 2). Most importantly, a number of clusters within our ROIs displayed significant previous × current trial interaction (conflict adaptation) effects: Voxels in left dorsolateral GFm and left ventromedial GFs were found to display increased activity with conflict adaptation (see Table 3 and Fig. 2c). Bilateral precuneus (PCu) regions, as well as bilateral GFm and right GFi, on the other hand, showed reduced activity with conflict adaptation (see Table 3 and Fig. 2c). Thus, in reference to the behavioral conflict adaptation effect, activity in left GFm and left medial GFs foci mirrored increased cognitive control, while bilateral medial parietal and lateral frontal areas mirrored reduced conflict effects. To confirm the suggested role of the GFm and GFs foci in implementing cognitive control, we directly correlated changes in activation in these ROIs with behavioral interference effects across subjects. As can be seen in Fig. 3, cognitive control effects in the processing of incongruent stimuli (i.e., reduced interference on II relative to CI trials) were highly positively correlated with corresponding changes in GFs activation ($r = 0.77$, $P < 0.001$). These effects also displayed a positive association with changes in GFm activation, albeit not to a statistically significant degree ($r = 0.40$, $P = 0.15$).

Imaging results—functional integration in conflict adaptation

The PPI analysis, as shown in Fig. 4, revealed that cognitive control activity in medial GFs during conflict adaptation was accompanied by increased functional interaction with right lateral GFi ($x = 48$, $y = 31$, $z = 0$), left lateral GFi ($x = -50$, $y = 16$, $z = 1$), left superior temporal gyrus (GTs) ($x = 55$, $y = 0$, $z = 2$), and the medial aspect of the anterior lobe of the cerebellum (the culmen; $x = 6$, $y = -49$, $z = -13$). At the chosen threshold criteria, there was no significant PPI with the left GFm; however, when lowering the cluster threshold (to 3 contiguous voxels), an increased functional interaction during conflict adaptation with the right supramarginal gyrus (Gsm) was detected (see Fig. 4).

Discussion

Employing a Stroop paradigm that incorporated equal proportions of CC, CI, IC, and II trial pairs, we obtained interference and conflict adaptation effects on RT and accuracy measures, presumably in the absence of repetition priming effects, as the task did not

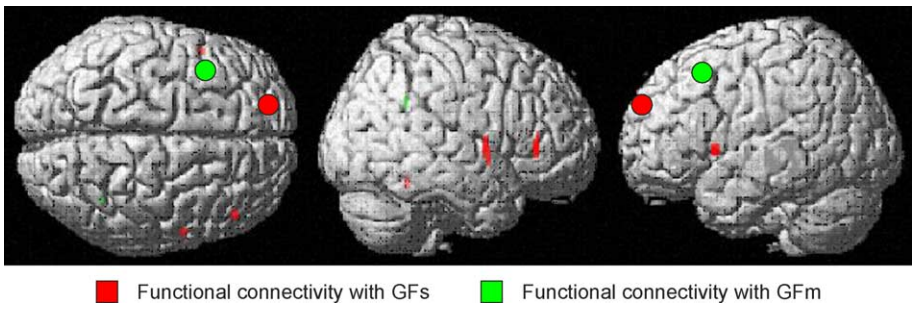

Fig. 4. Increases in functional interaction during conflict adaptation with medial GFs (red circle), displayed in red, and with left GFm (green circle), displayed in green.

entail any stimulus repetitions on CC or II trial sequences. Event-related fMRI analyses that controlled for error and post-error trial confounds revealed that main effects of current trial conflict (evident in RT and accuracy data) were reflected by increased activation in dorsal cingulate gyrus, dorsomedial GFs, and bilateral LPs. A main effect of previous trial type (evident in the accuracy data only) was reflected by decreased activation in the right LPs. The main interest of this study, however, lay with identifying brain regions directly susceptible to the conflict adaptation interaction effect. We found that areas in left GFm and left medial GFs showed increased activity with conflict adaptation, mirroring the presumed increase in cognitive control that underpins the conflict adaptation effect. Furthermore, activation in these ROIs (particularly the GFs) correlated directly with reduced behavioral interference effects across subjects. Regions in bilateral PCu, bilateral GFm, and right GFi, on the other hand, showed decreased activation with conflict adaptation, mirroring reduced behavioral interference effects. PPI analyses subsequently disclosed that the left GFm and medial GFs cognitive control effects were accompanied by increased functional interaction between GFs and bilateral GFi, right GTs, and the anterior cerebellum, and between GFm and the Gsm of the right parietal lobe.

A number of important conclusions can be derived from these results. The behavioral data demonstrate that conflict adaptation effects in a Stroop color-naming paradigm are not solely a consequence of repetition priming effects on CC and II trial pairs, as may be the case in instances of the Eriksen flanker task (Mayr et al., 2003), and can thus likely be attributed to cognitive control processes. While repetition priming may well contribute to conflict adaptation effects in Stroop tasks that do involve stimulus repetitions, the current data show that Stroop task variants free of such effects can be successfully employed to investigate mechanisms of conflict adaptation, supplying strong behavioral effects.

When assessing the effects of current trial conflict, increased focal activity in the (right) dorsal cingulate gyrus was observed. While a host of previous studies have reported conflict-related cingulate activation (Barch et al., 2001; Botvinick et al., 1999; Carter et al., 1995; Casey et al., 2000; Durston et al., 2003; Fan et al., 2003; Hazeltine et al., 2003; Kerns et al., 2004; Leung et al., 2000; MacDonald et al., 2000; Milham et al., 2001, 2003; Pardo et al., 1990; Ullsperger and von Cramon, 2001; vanVeen et al., 2001), it may be worthwhile pointing out that these foci display high variability both with respect to their extent well as their precise localization, with the current study's activation being rather focal and lateralized to the far right dorsal cingulate. This variability may be due in large part to the varying nature of interference task parameters and analytical strategies employed across the literature. For instance, the activation detected in the current study may differ from many previous studies in that it neither comprises activation related to error nor to post-error trials, both of which are known to produce strong cingulate activity (Garavan et al., 2002).

In addition to the expected effect in the cingulate gyrus, we also observed effects of current trial conflict on left dorsomedial GFs, and bilateral LPs. Increased activity to response conflict within lateral prefrontal cortex (Casey et al., 2000; Durston et al., 2003; Fan et al., 2003; Hazeltine et al., 2003; Milham et al., 2003; Ullsperger and von Cramon, 2001; vanVeen et al., 2001) and parietal areas (Barch et al., 2001; Botvinick et al., 1999; Carter et al., 1995; Durston et al., 2003; Fan et al., 2003; Hazeltine et al., 2003; Milham et al., 2001; vanVeen et al., 2001) has also been reported in many previous studies, underpinning a general agreement that a cingulate-DLPFC-parietal network underlies conflict detection and resolution.

However, the majority of these studies did not distinguish between conflict and control-related processes in these areas. In contrast, the interaction analysis of brain areas susceptible to previous × current trial effects in the current study allows us to distinguish between the effects of conflict and those of conflict adaptation. The results suggest that brain regions involved in conflict detection differ from those involved in the adaptation process. While frontal conflict-responsive regions were exclusively medial, the reduction in current trial conflict due to increased cognitive control subsequent to high conflict trials was associated with increased activity in left dorsolateral GFm and medial GFs regions. Activation was decreased with current trial conflict reduction due to cognitive control in bilateral PCu, bilateral GFm, and right GFi. These data depict differentially adaptive responses (increased as well as decreased activations) mediating the controlled adjustment in processing following high conflict trials. While these regions were widely distributed, the results also show that areas in relatively close proximity, in this case within the left GFm, can display opposite patterns of interaction, i.e., increased control versus reduced conflict effects.

Notably absent from this conflict adaptation network were the conflict-responsive loci, including the ACC. With respect to the ACC's involvement in conflict adaptation, these data suggest that while this structure may contribute to conflict detection, other brain regions exhibit equivalent susceptibility to conflict effects. Furthermore, the ACC may play a less important role in the adaptation to response conflict than previously assumed (e.g., Botvinick et al., 1999; Carter et al., 2000). Both of these conclusions are supported by data from lesion studies indicating that some patients with extensive ACC damage (e.g., Stuss et al., 2001; Swick and Jovanovic, 2002) and even bilateral anterior cingulotomy (Janer and Pardo, 1991) can exhibit unimpaired Stroop performance.

How do the conflict adaptation loci identified in the current study relate to findings from previous studies? The left DLPFC has previously been explicitly associated with the implementation of cognitive control processes in preparation for high-conflict trials (MacDonald et al., 2000), but this is not a ubiquitous finding, as another study that sought to dissociate control from conflict monitoring processes localized control effects to the right DLPFC (Kerns et al., 2004). These authors have argued that different areas of the DLPFC may be responsible for different control processes in a task-specific manner. The adaptation effects found in bilateral GFm and right GFi, characterized by reduced activity with conflict reduction, correspond to activation patterns previously reported in more inferior and posterior regions of inferior frontal cortex (Carter et al., 2000), and of course within the ACC (Botvinick et al., 1999; Carter et al., 2000).

We found the same type of conflict adaptation effects in the PCu, which has previously been reported as an activation site in studies that did not distinguish between conflict-related and control-related responses (vanVeen et al., 2001; Fan et al., 2003), but has also been described as pertaining to a fronto-parietal control network (Banich et al., 2000). The distinction between current trial conflict and conflict adaptation processes in the current investigation may serve to resolve some of the discrepancies in localization of conflict/control effects in previous research. Parietal conflict/control effects have variably been localized to LPi

(Botvinick et al., 1999; Carter et al., 1995; Fan et al., 2003; Hazeltine et al., 2003), LPs (Barch et al., 2001; Durston et al., 2003; Milham et al., 2001), or the PCu (vanVeen et al., 2001; Fan et al., 2003), respectively. The current data suggest that dorsolateral regions of superior parietal cortex are responsive to current trial conflict levels, while the more medial aspect of the superior parietal lobe, namely the precuneus, is involved in conflict adaptation processes.

How do supposed cognitive control areas implement conflict adaptation? While a correlation between conflict-related activity in the ACC and subsequent control-related activity in DLPFC has recently been documented (Kerns et al., 2004), the functional connectivity between cognitive control loci in prefrontal cortex and other brain regions has hitherto not been addressed. We found that the conflict adaptation effect was characterized by increased context-specific functional interaction between the ventromedial GFs and bilateral GFi, right GTs, and the anterior cerebellum, as well as between the left GFm and the right Gsm. The lateral frontal regions associated with increased integration with the GFs were situated inferior to the ones responsive to conflict adaptation effects. The loci in (particularly right hemisphere) GFm and GTs display considerable similarity with areas activated in response inhibition paradigms (Braver et al., 2001; Garavan et al., 1999, 2002; Menon et al., 2001), and it is tempting to speculate that one aspect of the implementation of cognitive control consists of the readying of response inhibitory processes.

Increased context-specific integration during conflict adaptation between the GFs and the right anterior cerebellum is intriguing considering recent evaluations of cerebellar involvement in high-level cognitive functions (e.g., Hülsmann et al., 2003), even in the absence of motor requirements (Allen et al., 1997). Our data suggest that frontal cognitive control regions modulate activity in the cerebellum in the course of conflict adaptation, perhaps in the pursuit of fine-tuning the acquisition and discrimination of sensory information (Gao et al., 1996). Interestingly, Casey et al. (2000) reported cerebellar activation on incongruent trials following a number of consecutive incongruent trials, and interpreted this pattern of activity as reflecting the workings of a visuospatial attention system that maintained high activation in the presence of persistent interference. The cerebellum's role in the performance of executive attention tasks poses an exciting domain for future investigation.

A further finding of the PPI analysis was that of increased functional integration with cognitive control implementation between the left dorsolateral GFm and the right Gsm, suggesting that in addition to the conflict responsiveness of the LPs and the conflict adaptation response in the PCu, this more lateral, inferior, and anterior aspect of the parietal lobe plays a role in implementing cognitive control. The right Gsm has frequently been implicated in the spatial orienting of visual attention, both in the context of spatial neglect syndrome (e.g., Driver and Mattingley, 1998) and healthy subjects' performance (Perry and Zeki, 2000). Similar to our interpretation of cerebellar recruitment in the service of increased sensitivity of sensory discrimination, the modulation by cognitive control regions of right Gsm during conflict adaptation can perhaps most parsimoniously be interpreted as reflecting an increased effort at directing attention toward the task-relevant stimulus properties. In summary, we speculate that the regions that display increased context-sensitive functional interaction with frontal cognitive control areas are involved in enhancing response inhibitory, sensory discriminatory, and visuospatial attention processes. Evidently, these data and interpretation require future corroboration from similar estimates of the connectivity of conflict adaptation.

To conclude, we obtained strong behavioral conflict adaptation effects on a Stroop paradigm devoid of repetition priming. Neural correlates of previous and current trial main and interaction effects, assessed in the absence of error or post-error confounds, revealed distinct fronto-parietal networks susceptible to conflict detection versus conflict adaptation effects. Within a conflict adaptation network, correlates of cognitive control implementation were found in left dorsolateral GFm and dorsomedial GFs, and correlates of response conflict reduction were detected in bilateral frontal and precuneus areas. Functional integration analyses suggest that cognitive control implementation relies on modulation of bilateral inferior frontal regions and right GTs, putatively involved in response inhibition, right anterior cerebellum, putatively involved in enhancing sensory discriminatory processes, and right Gsm, putatively involved in orienting visuospatial attention.

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