Dorsal Anterior Cingulate Cortex Resolves Conflict from Distracting Stimuli by Boosting Attention toward Relevant Events

D.H. Weissman, A. Gopalakrishnan, C.J. Hazlett and M.G. Woldorff

Center for Cognitive Neuroscience, Duke University, Durham, NC 27708, USA

In everyday life, we often focus greater attention on behaviorally relevant stimuli to limit the processing of distracting events. For example, when distracting voices intrude upon a conversation at a noisy social gathering, we concentrate more attention on the speaker of interest to better comprehend his or her speech. In the present study, we investigated whether dorsal/caudal regions of the anterior cingulate cortex (dACC), thought to make a major contribution to cognitive control, boost attentional resources toward behaviorally relevant stimuli as a means for limiting the processing of distracting events. Sixteen healthy participants performed a cued global/local selective attention task while brain activity was recorded with event-related functional magnetic resonance imaging. Consistent with our hypotheses, greater dACC activity during distracting events predicted reduced behavioral measures of interference from those same events. dACC activity also differed for cues to attend to global versus local features of upcoming visual objects, further indicating a role in directing attention toward task-relevant stimuli. Our findings indicate a role for dACC in focusing attention on behaviorally relevant stimuli, especially when the achievement of our behavioral goals is threatened by distracting events.

Keywords: anterior cingulate cortex, attention, fMRI, response conflict

Introduction

Prior investigations of cognitive control suggest that increasing attention toward task-relevant items is one way to resolve conflict from distracting events (Cohen *et al.*, 1990; Banich *et al.*, 2000b; Botvinick *et al.*, 2001; Weissman *et al.*, 2002a). For example, when multiple stimuli fall within a visual cortical neuron's receptive field, attention to one of the stimuli results in an effective 'narrowing' of the neuron's receptive field such that its activity is driven mainly by the attended stimulus (Desimone, 1998; Kastner *et al.*, 1999). As another example, increasing the perceptual load of a task such that greater attention is necessary to identify target stimuli, reduces both behavioral and neural effects of distracting events (Lavie, 1995; Rees *et al.*, 1997). Finally, brain regions activated by cues to orient attention are also frequently activated by conflict from distracting events (Banich *et al.*, 2000b; Weissman *et al.*, 2002a). These include regions of dorsolateral prefrontal cortex (DLPFC) that increase attention toward task-relevant representations (Banich *et al.*, 2000b; MacDonald *et al.*, 2000; Kerns *et al.*, 2004), parietal regions that allocate attentional resources to target stimuli (Casey *et al.*, 2000; Sylvester *et al.*, 2003) and sensory regions that receive inputs from frontoparietal regions that bias sensory processing in favor of target versus distracter stimuli (Desimone, 1998; Kastner *et al.*, 1998, 1999; Weissman *et al.*, 2002a). All of these findings suggest that focusing greater attention on task-relevant items helps to resolve conflict from distracting events, even when participants are not biased to do so by other experimental manipulations.

Several sources of data suggest that dorsal/caudal regions of the anterior cingulate cortex (dACC), widely believed to make a major contribution to cognitive control (Botvinick *et al.*, 2001), help to resolve conflict from distracting events by increasing processing resources towards task-relevant stimuli (Posner and DiGirolamo, 1998). First, numerous studies have suggested a role for dACC in focusing attention on task-relevant stimuli by indicating dACC activity during anticipation (Murtha *et al.*, 1996) and voluntary attentional orienting (Hopfinger *et al.*, 2000; Weissman *et al.*, 2002a; Woldorff *et al.*, 2004). Secondly, dACC activity is robustly observed under conditions of distraction (Posner and DiGirolamo, 1998; Botvinick *et al.*, 1999; Banich *et al.*, 2000b; Carter *et al.*, 2000). These results are consistent with the view that dACC helps to resolve conflict from distracting events by increasing attention toward task-relevant stimuli (Posner and DiGirolamo, 1998).

Nonetheless, findings from numerous functional magnetic resonance imaging (fMRI) studies have been interpreted as indicating a dACC role in detecting conflict rather than in focusing attention to resolve that conflict (Carter *et al.*, 1999, 2000; MacDonald *et al.*, 2000; Milham *et al.*, 2002). Although some of these studies used paradigms in which neural activity associated with focusing attention, detecting conflict and resolving conflict could not be dissociated unequivocally (Carter *et al.*, 1999, 2000; Milham *et al.*, 2002), one in particular clearly separated cue-triggered neural activity due to focusing attention from target-related activity associated with distracting events (MacDonald *et al.*, 2000). In this experiment, participants were cued in each trial to attend to and identify either the ink color or word identity of an upcoming Stroop color word. The authors reasoned that brain regions involved in focusing attention on task-relevant stimuli should exhibit greater activity for ink color than for word identity task cues. They made this argument because it is more demanding to focus attention on ink color than on word identity in this task (MacLeod, 1991). Importantly, this contrast also provided a natural control for any possible effects of sensory, semantic or motor processes on dACC activity, since ink color and word identity cues should have placed roughly equal demands on these processes. On the other hand, the authors argued that brain areas involved in conflict detection should be activated more by incongruent Stroop stimuli (e.g. the word RED printed in blue ink) than by congruent stimuli (e.g. the word RED printed in red ink). They adopted this reasoning because only incongruent stimuli evoke response conflict (MacLeod, 1991). The results indicated a double dissociation, which provided key evidence for the

conflict monitoring view of dACC. Specifically, the dACC was selectively activated by response conflict from distracting events while the DLPFC was selectively activated by focusing attention on task-relevant stimuli.

While consistent with the conflict detection view of dACC, several key limitations of the study above preclude a strong conclusion that dACC does not help to focus attention on task-relevant stimuli. First, the investigators employed extremely long (12.5 s) cue-target intervals, reducing the likelihood that participants oriented their attention at the time of cue presentation. If participants did wait several seconds before orienting their attention, then both overall levels of cue activity and the probability of observing differential cue activity would have been reduced in brain regions that focus attention. From this perspective, the conflict-related dACC activity observed by MacDonald *et al.* (2000) still reflected processes that focus attention on task-relevant stimuli. However, the differential cue activity needed to confirm this hypothesis was difficult to observe because the authors used a long cue-target interval. Secondly, the investigators did not consider the effects of practice on cue-related activity, which has recently been shown to decrease rapidly in frontal, parietal, and sensory regions during the performance of conflict tasks analogous to those studied by MacDonald *et al.* (2000), but using much shorter cue-target intervals (Weissman *et al.*, 2002b). Such practice effects are consistent with models in which practice reduces the degree to which cognitive control mechanisms are necessary to maintain acceptable levels of task performance (Norman and Shallice, 1986). However, if such models are correct, then practice might have diminished the probability of observing greater dACC activity for ink color versus word identity cues. For these reasons, there has not yet been a clear verdict on the longstanding issue of whether dACC helps to resolve conflict from distracting events by increasing attention towards task-relevant stimuli.

To determine whether dACC helps to resolve conflict from distracting events by boosting attention toward task-relevant stimuli, we used a cued attention task that featured short cue-target intervals (1.25 s) and a low percentage of congruent trials (33%). Both of these task parameters were used to encourage participants to promptly and fully orient their attention toward the cued stimulus dimension at the time of cue presentation (MacLeod, 1991). We also investigated how cue activity changed with practice to determine whether the pattern of differential cue activity we predicted would be more evident relatively early in performance, before practice reduces demands on executive orienting mechanisms triggered by attention-directing cues (Weissman *et al.*, 2002b).

In our task, participants were cued on a trial-by-trial basis to identify either the global or the local form of a possible upcoming hierarchical stimulus (e.g. a large, global H made up of small, local Ss; Navon, 1977) (Fig. 1*a*). In cue-plus-target trials (75%), a hierarchical stimulus appeared 1.25 s after cue onset. Participants pressed one response key if the cued letter was either an H or an S and a different response key if the cued letter was either an X or an O, while ignoring the letter at the irrelevant stimulus dimension. These stimulus–response mappings allowed us to manipulate the relationship between responses engendered by the relevant versus the irrelevant letter in each trial, while ensuring the global and local letters within each hierarchical stimulus were distinct. For example, in the local task (Fig. 1*b*), the irrelevant global letter could be
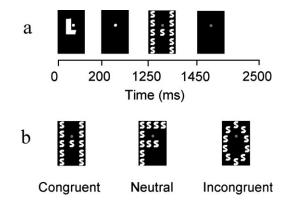

Figure 1. The experimental task used in the present study. (*a*) The sequence and timing of events in cue-plus-target trials. In each trial, participants were cued to attend to and identify either the global 'G' or the local 'L' letter of an upcoming hierarchical stimulus, by pressing one response key if the cued letter was either H or S and another if it was either X or O. Pictured is a sample local cue-plus-target trial. In the actual experiment, cues were sized midway between the size of the global and local letters to prevent reflexive orienting to either level (see Materials and Methods). (*b*) Sample congruent, neutral, and incongruent hierarchical stimuli for the local task. Given the stimulus–response mappings described above, we were able to vary the relationship between responses primed by the relevant and irrelevant letters in each trial, while holding constant the fact that these letters were always perceptually distinct. For example, in the local task, the irrelevant global letter could be mapped to the same response as the relevant local letter (e.g. a large, global H made up of small local Ss; congruent trials), to no response (e.g. a global F made up of local Ss; neutral trials), or to a conflicting response (e.g. a global O made up of local Ss; incongruent trials).

mapped to the same response as the relevant local letter (e.g. a large, global H made up of small, local Ss; congruent trials), to no response (e.g. a global F made up of local Ss; neutral trials), or to a conflicting response (e.g. a global O made up of local Ss; incongruent trials). Contrasting neural activity for incongruent versus congruent hierarchical target stimuli allowed isolation of neural activity due to distracting events (Weissman *et al.*, 2002a). In cue-only trials (25%), no target followed cue presentation, which allowed isolation of neural activity due to focusing attention on task-relevant stimuli (Shulman *et al.*, 1999).

Several predictions arise from the view that dACC resolves conflict by increasing attention to task-relevant stimuli. First, this view predicts that local cues should be associated with greater dACC activity than global cues, since demands on processes that increase attention to task-relevant stimuli are greater when participants attend to local versus global stimulus features (Navon, 1977; Stoffer, 1993, 1994). Secondly, because practice reduces the degree to which executive attention mechanisms are necessary to sustain adequate levels of task performance, this view also predicts that greater dACC activity for local versus global cues should be especially pronounced early in performance, before cue-triggered executive orienting activity decreases (Norman and Shallice, 1986; Weissman *et al.*, 2002b). Given that the greatest reduction of cue activity occurred after three blocks of trials in our prior study (Weissman *et al.*, 2002b), each participant completed six functional runs, and we analyzed runs 1–3 separately from runs 4–6. Thirdly, this view predicts that regions of dACC involved in increasing attention to task-relevant stimuli will be additionally recruited by distracting events, such as incongruent versus congruent target stimuli (Posner and DiGirolamo, 1998; Weissman *et al.*, 2002a). Finally, this view predicts that participants who exhibit relatively large amounts of dACC activity in response to

distracting events should exhibit relatively small amounts of behavioral interference from those same events.

Materials and Methods

Subjects
Sixteen participants were recruited from the Duke University community in accordance with the rules of the local human subjects committee. All (6 male, 10 female; aged 18–29 years) were right-handed, had normal or corrected-to-normal vision, and had no history of serious neurological trauma or disorders. Informed consent was obtained from each participant prior to the experiment. Before the MR session, each participant practiced one or two blocks of the experimental task. Participants were paid $20/h for being in the study, which lasted ~2 h.

Apparatus
A PC was used for stimulus presentation and the recording of response data. Stimuli were projected onto a screen at the back of the magnet's bore. Participants viewed stimuli through a mirror. Responses were recorded with an MR-compatible response box.

Event-related fMRI Paradigm
We used a cued version of the global/local paradigm in combination with a recently developed event-related fMRI approach (Shulman *et al.*, 1999; Weissman *et al.*, 2002a; Woldorff *et al.*, 2004). At the beginning of each 2.5 s trial, participants viewed a cue ('G' or 'L'; 1.6° × 1.0° of visual angle; duration = 200 ms), which instructed them to identify either the global ('G') or the local ('L') aspect of an upcoming hierarchical stimulus (e.g. a global H made of local Ss, which we will abbreviate here as 'Hs'). Cue stimuli were sized midway between the global and local forms to prevent reflexive orienting to either stimulus dimension. In cue-plus-target trials (75%; Fig. 1*a*), a hierarchical target stimulus appeared 1250 ms after cue onset (global form 3.3° × 2.1°; local form 0.6° × 0.4°; target duration = 200 ms). Target stimuli were congruent (Hs, Sh, Xo, Ox), incongruent (Hx, Os, Xh, Oh) or neutral (global task: Hd, Sf, Od, Xf; local task: Dh, Fs, Do, Fx) in equal numbers of trials (Fig. 1*b*). Participants were told to press one button if the cued target letter was either an H or an S and a different button if the cued target letter was either an X or an O, using the index and middle fingers of their right hand. In cue-only trials (25%), no target stimulus followed cue presentation.

In all trials, the fixation dot changed from white to red 1250 ms after cue-onset, with the instruction being that if a target did not appear at this time, the participant should cease attending. This procedure helped to ensure that demands on cue-triggered processes were of roughly equal duration for cue-plus-target and cue-only trials (Corbetta *et al.*, 2000). Thus, contrasting these trial types isolated neural activity specific to the different types of target stimuli (Shulman *et al.*, 1999) and, subsequently, to distracting events (i.e. incongruent versus congruent targets separately for the global and local tasks).

All eight trial types (two cue-only and six cue-plus-target) were included within each run. They were presented equally often and in a counterbalanced order such that, on average, each trial type was preceded equally often by every trial type in the design. The inter-trial interval (ITI) ranged from 0 to 5 T_Rs, following a nearly exponential distribution that favored short ITIs. Such jittering of the ITI increases the efficiency with which response estimates for distinct trial types are made when brain responses to different stimuli overlap (Woldorff, 1993) and is therefore highly advantageous within a multiple regression framework (Ollinger *et al.*, 2001a,b).

FMRI Data Acquisition and Analysis
A spiral imaging sequence was used to measure the blood oxygenation level-dependent (BOLD) signal (T_R = 1.25 s, T_E = 40 ms, flip angle = 90°) during the collection of functional images on a 1.5 T GE whole-body scanner. Every participant completed six runs, each of which lasted ~5 min. During each run, 276 brain volumes were collected, each of which contained 17 contiguous, 7.5-mm-thick slices (in-plane resolution: 3.75 mm × 3.75 mm). Structural images were collected using a T1-weighted spin echo sequence (T_R = 500 ms, T_E = 14 ms, flip angle = 90°). The first six functional images of each run contained no trials and were discarded prior to analysis of the functional data. The software analysis package SPM'99 (Friston *et al.*, 1995) was used to correct functional images for head motion, normalize functional images to MNI (Montreal Neurological Institute) standard space, and spatially smooth the functional data with a Gaussian filter (full-width half maximum = 8 mm in the *x*, *y* and *z* dimensions).

Event-related Analyses
The time series for each functional run was modeled using a finite impulse response version of the general linear model, which makes no assumptions about the shape of the BOLD response. This version of the general linear model reliably distinguishes BOLD responses to different types of cue-only and cue-plus-target trials in fast-rate paradigms (Ollinger *et al.*, 2001a,b; Shulman *et al.*, 1999). For each of the eight trial types, we modeled the first 12 T_Rs (i.e. 16 s) of the hemodynamic response, beginning with the T_R of stimulus onset. Thus, there were 12 regressors for each trial type in the design. Within the design matrix, we also included six motion regressors (i.e. SPM'99 estimates of head translation and rotation around the *x*, *y* and *z* axes for each time point in the run) and two regressors for the linear trend and *y*-intercept term. The parameter estimates from each run were converted to units of percent change from baseline (i.e. the *y*-intercept term for that run). Next, for every participant, the average regression-estimated hemodynamic response for each of the eight trial types in the design was generated by averaging the appropriate parameter estimates across (i) all six runs; (ii) runs 1–3 only; and (iii) runs 4–6 only.

The responses to global cue-only and local cue-only trials, in which no target stimuli were presented, were used to estimate the BOLD responses to our global and local cue stimuli. One might wonder whether the absence of a target in cue-only trials constitutes a rare event that evokes a 'surprise' response over and above the part of the cue response that reflects orienting of attention. Although this is a possibility, estimates of cue activity derived using cue-only trials do not differ much from estimates of cue activity derived using cue information from both cue-plus-target trials, in which a rare event does not occur, and cue-only trials (Shulman *et al.*, 1999). This fact suggests that any response due to a rare event in cue-only trials must be quite small. More important, however, any contribution to the total cue-only response made by 'surprise' at an absent target should be equal for global cue-only and local cue-only trials. Therefore, when contrasting the activity for global cue-only and local cue-only trials, any 'surprise' response should subtract out, leaving only the true difference in activity produced by local versus global cues. Importantly, our conclusions about dACC functioning are based on comparisons of global and local cue activity, in which any activity due to 'surprise' should subtract out.

Due to the fast-rate nature of our paradigm, several processing steps were necessary to isolate conflict-related activity for each task. First, we contrasted the regression-estimated response to each of the cue-plus-target trial types with the regression-estimated response to its corresponding cue-only trial type to isolate neural activity specific to the different types of target stimuli (Shulman *et al.*, 1999). For example, in the global task we contrasted neural activity in global cue-plus-congruent-target trials with that in global cue-only trials containing no target. Contrasting these two trial types allowed us to isolate the average BOLD response for congruent targets during the global task. Indeed, because the same global cue was presented in both of these trial types, activity due to the global cue canceled in the subtraction leaving only the activity due to the congruent target stimulus. A similar procedure involving cue-plus-incongruent-target trials and cue-only trials isolated the average BOLD response to incongruent targets in the global task. Contrasting peak activity evoked by the extracted incongruent and congruent target responses above provided a measure of conflict-related activity during the global task (Weissman *et al.*, 2002a,b, 2003). An analogous multi-step procedure was used to isolate conflict-related activity for the local task.

A region of interest (ROI) in dACC was defined by averaging the regression-derived hemodynamic response estimates for global and local cue-only trials at every voxel and entering this average into a voxelwise one-way, repeated-measures, random effects analysis of variance (ANOVA). We thresholded the resulting *F*-map at a value [$F(11,165) = 2.5$, $P < 0.007$] that allowed us to identify an ROI that encompassed the dACC as well as the adjacent medial frontal gyrus [63

voxels; center of mass Talairach (Talairach and Tournoux, 1988) coordinates: $x = -2$, $y = 5$, $z = 43$], both of which are consistently activated by response conflict (Banich *et al.*, 2000a; Weissman *et al.*, 2002a). Within this ROI, we computed the average (across all voxels) regression-derived time courses for global cue-only trials and for local cue-only trials within each participant. Next, we performed random effects ROI analyses on peak activity separately for cues and for targets, as described in the Results section. We selected the fourth time point of the evoked BOLD response, representing neural activity 3.75–5 seconds after stimulus onset, as our measure of peak activity because it was the time point at which neural activity peaked in the average response to global and local cue-only trials. Importantly, all of the statistical contrasts conducted in the ROI analyses were orthogonal to the contrast used to create the ROIs (i.e. average cue activity across both cue types versus baseline). Thus, the ROI analyses were unbiased, and *P*-values < 0.05 were considered to be significant. Conversion from MNI to Talairach coordinates (to facilitate comparisons of activated loci with other studies) was implemented with two non-linear transformations (http://www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html).

Results

Behavior

Reaction Time
Mean reaction times (RTs) were analyzed within a repeated measures ANOVA with three factors: Block (runs 1–3, runs 4–6), Task (global, local) and Distracter Type (congruent, neutral, incongruent). As expected (Navon, 1977), there was a significant main effect of Task because RTs were significantly faster for global (671 ms) than for local (733 ms) trials, $F(2,15) = 32.996$, $P < 0.001$. Also as expected (Kimchi, 1992), there was a significant main effect of Distracter Type, $F(1,15) = 15.848$, $P < 0.001$, since RTs increased with the degree of conflict engendered by distracter stimuli. Planned comparisons revealed that mean RTs were significantly faster for congruent trials (683 ms) than for neutral trials (704 ms), $t(15) = 3.77$, $P < 0.001$, significantly faster for neutral than for incongruent trials (718 ms), $t(15) = 2.31$, $P < 0.02$, and significantly faster for congruent than for incongruent trials, $t(15) = 4.94$, $P < 0.0001$.

Notably, when analyses were restricted to the difference in reaction time between congruent and incongruent trials (our measure of behavioral interference from distracting events), there was a significant interaction between Block and Task, $F(1,15) = 5.418$, $P < 0.035$. During the local task, interference from global distracters did not vary significantly between runs 1–3 (48 ms) and runs 4–6 (43 ms), $P > 0.35$. In contrast, during the global task, interference from local distracters was significantly greater in runs 4–6 (43 ms) than in runs 1–3 (5 ms), $t(15) = 3.31$, $P < 0.001$. This result in the global task is consistent with previous findings that practice strengthens associations between stimuli and their responses, thereby enabling those stimuli to engender greater conflict when they serve as distracters in a selective attention task (MacLeod and Dunbar, 1988). During the local task, such practice effects may have been less pronounced because global distracters usually evoke relatively large amounts of conflict (Navon, 1977) that may have reached a ceiling relatively early in practice. No other reaction time effects were significant.

Error Rate
An analogous ANOVA with percent error rate as the dependent measure replicated the main effects found in the analysis of RT. As expected based on the RT analysis, there was a significant

main effect of Task on error rate, $F(1,15) = 17.621$, $P < 0.002$, which revealed that error rates were lower for the global task (3.94%) than for the local task (6.34%). Also expected, there was a significant main effect of Distracter Type, $F(2,15) = 21.069$, $P < 0.001$, since error rates increased with the degree of conflict evoked by distracter stimuli. Planned contrasts revealed that error rates were significantly higher for incongruent trials (6.77%) than for either congruent trials (3.91%), $t(15) = 4.47$, $P < 0.001$, or neutral trials (4.25%), $t(15) = 3.17$, $P < 0.005$, but mean error rates did not significantly differ between congruent and neutral trials, $t(15) = 0.52$, $P > 0.30$. Finally, there was a significant interaction between Block and Task, $F(1,15) = 5.37$, $P < 0.04$. While error rates for the global task were significantly higher in runs 4–6 (4.52%) than in runs 1–3 (3.36%), $t(15) = 1.90$, $P < 0.04$, error rates for the local task did not differ significantly between runs 4–6 (6.08%) and runs 1–3 (6.60%), $t(15) < 1$. Although this interaction was unexpected, there was no evidence of a speed-accuracy tradeoff. No other error rate effects were significant.

Imaging

Dorsal/Caudal Anterior Cingulate Cortex

Cue-related Activity. We predicted that local cues would produce significantly greater dACC activity than global cues and that this effect would be most pronounced early in practice. To test these hypotheses, we identified a dACC region of interest (ROI) [63 voxels; geographic center of mass in Talairach space, $x = -2$, $y = 5$, $z = 43$, Brodmann area 32 (BA32)] activated by the average response to global and local cue-only trials (Fig. 2*a*). Consistent with prior findings (MacDonald *et al.*, 2000), an ROI analysis revealed no significant difference in peak activity associated with local versus global cues when the data were collapsed across all six functional runs (Fig. 2*b*, top). However, a finer-grained examination of peak activity using repeated-measures analysis of variance (ANOVA) revealed a significant interaction between Block (runs 1–3, runs 4–6) and Task (global, local), $F(1,15) = 8.508$, $P < 0.02$. In line with predictions, local cues produced significantly greater peak activity than global cues early in performance during runs 1–3, $t(15) = 1.97$, $P < 0.04$ (Fig. 2*b*, middle).

Also as predicted, greater dACC activity for local versus global cue-only trials was observed only in runs 1–3. This result occurred because peak neural activity associated with local cues decreased sizably from runs 1–3 to runs 4–6, $t(15) = 3.53$, $P < 0.002$, whereas peak activity for global cues did not change significantly across the experiment, $P > 0.3$ (Fig. 2*c*). Thus, local cues produced significantly less dACC activity than global cues in runs 4–6, $t(15) = 2.51$, $P < 0.05$ (two-tailed test; Fig. 2*b*, bottom).

The selective effect of practice on local cue activity is highly consistent with prior findings that practice facilitates processing more quickly for task conditions that make relatively large versus relatively small demands on attentional control processes (Meiran, 1996; Kramer *et al.*, 1999). We speculate that given further practice, dACC activity for global cues would also have decreased, consistent with other results from our laboratory (Weissman *et al.*, 2002b). Most important for present purposes, differential cue activity has been argued to reflect processes associated with focusing attention on task-relevant stimuli (MacDonald *et al.*, 2000). Thus, our finding of significant
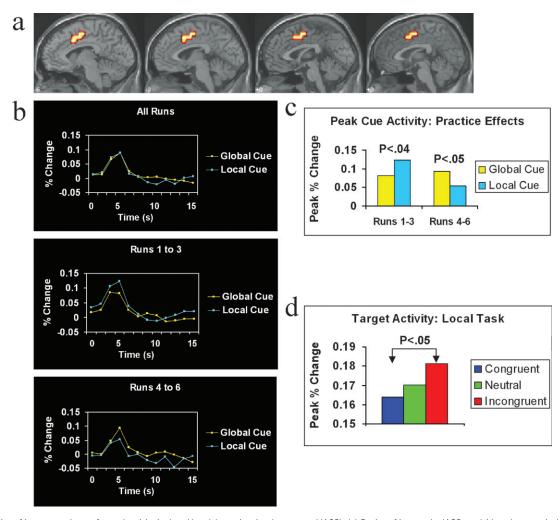
Figure 2. Region of interest analyses of neural activity in dorsal/caudal anterior cingulate cortex (dACC). (*a*) Region of interest in dACC overlaid on the canonical MNI normalized anatomical template provided by SPM'99. This region comprised 63 voxels whose geographic center of mass in Talairach space was located at $x = -2$, $y = 5$, $z = 43$. Anatomical slices range from $x = -6$ mm (top left) to $x = 3$ mm (top right). (*b*) The BOLD response in dACC for global and local attention-directing cues averaged across all six runs of the experiment (top), for runs 1–3 only (middle) and for runs 4–6 only (bottom). There were no differences in peak cue activity when data were averaged across the entire experiment (top), but local cues evoked significantly greater activity than global cues in runs 1–3, $P < 0.04$ (middle), while global cues evoked significantly greater activity than local cues in runs 4–6, $P < 0.05$ (bottom), which resulted in a significant interaction between Block (runs 1–3, runs 4–6) and Task (global, local), $P < 0.05$. (*c*) Peak activity for global and local cues in dACC plotted separately for runs 1–3 and runs 4–6. Practice significantly reduced activity associated with local cues, $P < 0.002$, but did not affect activity evoked by global cues, $P > 0.30$. (*d*) Peak activity for congruent, neutral, and incongruent targets in dACC for the local task, averaged across all six runs of the experiment. Significantly greater activity was observed for incongruent than for congruent targets, $P < 0.05$, in the same region of dACC that exhibited differential cue activity.

differential local versus global cue activity in both runs 1–3 and runs 4–6 provides novel support for the view that dACC contributes to focusing attention on behaviorally relevant stimuli.

Conflict-related Activity. Our next two predictions concerned the nature of brain activity associated with distracting events (i.e. incongruent versus congruent targets). First, we predicted that distracting events would activate the exact same region of dACC identified as playing a role in focusing attention on task-relevant stimuli. Secondly, we predicted that relatively large amounts of conflict-related dACC activity would be associated with relatively small behavioral interference effects. Such findings would support the view that recruiting brain areas involved in focusing attention resolves conflict from distracting events (Botvinick *et al.*, 2001; Weissman *et al.*, 2002a). Both of these predictions were confirmed in the following analyses of conflict-related activity.

Local Task. In agreement with our first prediction for conflict-related activity in dACC, planned *t*-contrasts indicated that incongruent targets produced greater peak activity than congruent targets in dACC during the local task, $t(15) = 1.78$, $P < 0.05$ (Fig. 2*d*), and that this effect was not modulated by Block, $P > 0.6$. Thus, as predicted by our hypothesis, conflict from distracting events activated the exact same region of dACC in which differential cue activity was observed. However, we did not observe a significant correlation between conflict-related dACC activity and behavioral measures of conflict for the local task ($P < 0.05$).

Global Task. In line with our second prediction for conflict-related dACC activity, during the global task participants who exhibited relatively large amounts of conflict-related dACC activity exhibited relatively small differences between incongruent RT and congruent RT, $r(15) = -0.41$, $P = 0.058$ (one-tailed). This negative correlation was highly significant in runs

4–6 when behavioral measures of local interference during the global task were greatest, $r(15) = -0.52$, $P < 0.019$ (one-tailed), but did not achieve significance in runs 1–3 when behavioral measures of local interference were relatively low, $r(15) = 0.13$, $P > 0.30$ (one-tailed). This result supports our hypothesis that conflict-related activity in our region of dACC reflects attention focusing mechanisms that help to resolve conflict from distracting events, particularly when overall levels of conflict are relatively high. Interestingly, the significant negative correlation occurred despite the fact that incongruent targets did not produce significantly greater peak activity than congruent targets, $P > 0.25$, during the global task (no modulation of this effect across Block, $P > 0.10$).

DLPFC

As we discussed in the Introduction, MacDonald *et al.* (2000) used their finding of differential cue activity in DLPFC to support the view that DLPFC plays a role in biasing attention toward task-relevant representations. Given our finding of differential cue activity in dACC, it is of interest to investigate whether a similar pattern of cue activity is present in DLPFC. The presence of similar patterns of differential cue activity in DLPFC and dACC would provide further support for the view that dACC participates in biasing attention toward task-relevant stimuli.

To investigate cue activity in DLPFC, we identified a region of left DLPFC that was activated by the average BOLD response to cue-only trials (i.e. using the same procedure used to identify the dACC region of interest). Importantly, the center of mass of our region of left DLPFC (27 voxels, geographic center of mass at Talairach coordinates: $x = -41$, $y = 18$, $z = 30$) was just 2 mm from the DLPFC region of MacDonald *et al.* (2000) (36 voxels, Talairach coordinates: $x = -41$, $y = 18$, $z = 28$).

Cue-related Activity. ROI analyses of peak activity in left DLPFC revealed a significant interaction between Cue Type (local, global) and Block (runs 1–3, 4–6), $F(1,15) = 5.969$, $P < 0.03$. Of importance, the precise nature of this interaction was highly similar to that observed in dACC. Local cue activity was significantly greater in runs 1–3 than in runs 4–6, $t(15) = 2.34$, $P < 0.02$ (one-tailed). In contrast, global cue activity did not significantly differ in runs 1–3 and runs 4–6, $t(15) = -0.11$, $P > 0.45$ (one-tailed). Also similar to our findings in dACC, local cue activity was marginally greater than global cue activity in runs 1–3, $P = 0.068$, and there was a non-significant trend for global cue activity to be greater than local cue activity in runs 4–6, $P = 0.15$. These results indicate the pattern of differential cue activity across different stages of practice in left DLPFC was virtually identical to that in dACC.

Conflict-related Activity. Analogous to the findings of MacDonald *et al.* (2000), there was a lack of significant conflict-related activity in left DLPFC for both the global ($P > 0.20$) and the local ($P > 0.14$) task.

Discussion

One of the most enduring questions in attention research concerns how the processing of behaviorally relevant stimuli is enhanced, especially under conditions of distraction. Prior work from electrophysiological studies of animals has indicated that attending to a stimulus gates the processing of irrelevant stimuli by effectively 'narrowing' the receptive fields of sensory neurons to encompass only the attended stimulus (Desimone, 1998). Moreover, behavioral (Lavie, 1995) and functional neuro-imaging (Rees *et al.*, 1997) studies in humans have revealed that biasing participants to increase attention toward task-relevant stimuli reduces the interfering effects of distracting events on performance. In combination with recent findings that focusing attention and distracting events activate common regions of the attentional network (Banich *et al.*, 2000b; Weissman *et al.*, 2002a), these prior data suggest allocating greater attention to task-relevant items might be a useful mechanism for resolving conflict from distracting events, even when participants are not biased to do so.

Our results support this view by indicating a role for dACC in focusing attention on task-relevant stimuli that helps to resolve conflict from distracting events. First, dACC activity varied with the attentional state (global or local) cued in each trial, indicating a role in focusing attention on task-relevant stimuli. Secondly, the pattern of differential cue activity we observed across different stages of practice in dACC was virtually identical to that observed in left DLPFC, a region for which differential cue activity has been argued to reflect processes that bias attention toward task-relevant representations (MacDonald *et al.*, 2000). Thirdly, greater activity in this same dACC area in response to distracting events predicted reduced behavioral interference from those same events, consistent with a role in resolving conflict via greater focusing of attention on task-relevant stimuli. Taken together, these findings support the view that dACC plays a role in focusing attention on task-relevant stimuli that also helps to resolve conflict from distracting events (Posner and DiGirolamo, 1998).

As we hypothesized, analyses of practice effects were crucial for observing differential cue activity within dACC. In particular, the differential cue activity we observed stemmed from a selective effect of practice on local cue activity. Since it is more demanding to orient attention to the local than to the global stimulus dimension (Navon, 1977; Stoffer, 1993, 1994), the selective effect of practice on local cue activity is consistent with data indicating practice facilitates processing more quickly for task conditions that make relatively large versus relatively small demands on processes that focus attention (Meiran, 1996; Kramer *et al.*, 1999). Our finding that practice selectively reduced local cue activity therefore highlights the importance of considering practice effects in fMRI studies of cognitive control.

Analyses of the behavioral data indicated the significant decrease in local cue activity above was not accompanied by a corresponding decrease in reaction times to local targets. Even if the decrease in local cue activity indexed automatic cue processing and a corresponding speed-up in orienting attention to the local stimulus dimension, however, it is not surprising that reaction times to local targets did not decrease. Cueing studies in which the cue-target interval is varied have indicated orienting attention to the local stimulus dimension is accomplished in ~600 ms (Stoffer, 1993, 1994). Therefore, in the present study, participants had sufficient time (i.e. 1.25 s) to fully orient their attention before a target stimulus appeared. If much shorter cue-target intervals were used in future studies, however, a practice-related speed-up in orienting attention to the local stimulus dimension might very well be measured as decreased reaction times to local targets. Our present finding that reaction times to local targets did not reflect the practice-related decrease in local cue activity is therefore

highly consistent with the known time course of orienting attention to the local stimulus dimension (Stoffer, 1993, 1994).

The present results are also consistent with findings indicating that using a low percentage of congruent trials reduces behavioral (MacLeod, 1991) and neural (Carter *et al.*, 2000) measures of conflict. For instance, although we observed significant conflict-related activity for the local task, we did not observe significant conflict-related activity for the global task. Additionally, despite the presence of a significant negative correlation between behavioral and dACC measures of conflict for the global task, there were no significant correlations for the local task. A comparison of the present findings to those from a similar study performed in our laboratory, which used a higher percentage of congruent trials, further supports our view that using a low percentage of congruent trials led to a reduction of conflict-related effects in the present data. First, in our previous study, unlike the present one, we observed robust conflict-related activity in ACC for the global task (Weissman *et al.*, 2003). Secondly, overall levels of behavioral interference in our prior study (47 ms) were 34% higher than in the present study (35 ms). Interestingly, our prior finding that neural measures of conflict are more pronounced during the local than during the global task (Weissman *et al.*, 2003) is mirrored nicely by our present finding that conflict significantly activated dACC during the local but not the global task. We speculate that conflict-related activity during the global task might have been too weak to 'survive' in the context of a low percentage of congruent trials. The effects of conflict that failed to achieve significance in the present study are thus highly consistent with our use of a low percentage of congruent trials (Carter *et al.*, 2000; MacLeod, 1991). At the same time, the more robust effects of conflict that achieved significance clearly support the conclusion that dACC plays a role in focusing attention that helps to resolve conflict from distracting events.

This conclusion is important because dACC's contributions to cognitive control have been a matter of great controversy for over a decade. This brain region has been associated with attentional processing in single-unit (Shima and Tanji, 1998), functional neuroimaging (Bush *et al.*, 1998, 2002; Botvinick *et al.*, 1999; Banich *et al.*, 2000a,b; Carter *et al.*, 2000; Casey *et al.*, 2000; MacDonald *et al.*, 2000; Braver *et al.*, 2001; Weissman *et al.*, 2002a) and patient studies (Carter *et al.*, 1997; Bush *et al.*, 1999) leading to an intense debate as to whether it makes a broad contribution to cognitive control that includes biasing attention toward task-relevant stimuli (Posner and Petersen, 1990; Posner and DiGirolamo, 1998) or a more circumscribed contribution that involves monitoring for response conflict (Cohen *et al.*, 1997; Carter *et al.*, 2000; MacDonald *et al.*, 2000; Botvinick *et al.*, 2001; Braver *et al.*, 2001). Our results clearly support a broad role for dACC in cognitive control that includes boosting attention to task-relevant stimuli (Posner and DiGirolamo, 1998). As discussed in the Introduction, the use of fast rates of stimulus presentation, short cue-target intervals and a low percentage of congruent trials (to encourage participants to orient their attention quickly and fully to the cued stimulus dimension), along with analyses of practice effects (to assess rapid changes in cue-related activity), were likely crucial for revealing the effects we observed.

It is important to consider whether alternative models might also account for the effects we have observed. First, the local task was more difficult to perform than the global task at all stages of practice as indexed by overall reaction times (or at least equally difficult to perform as the global task if difficulty is defined in terms of behavioral interference effects). Therefore, it is possible that the greater dACC activity observed for local versus global cues in runs 1–3 occurred because participants became more aroused when they expected to perform a relatively difficult task. However, this view cannot explain why significantly less dACC activity was observed for local versus global cues in runs 4–6. Secondly, behavioral measures of conflict were greater for the local task than for the global task in runs 1–3. Therefore, it is possible that the greater dACC activity associated with local versus global cues in runs 1–3 occurred because participants expected greater amounts of conflict. However, this hypothesis does not predict our finding of differential cue activity in runs 4–6 when behavioral measures of conflict were identical for the global and local tasks. Thirdly, our finding that local cue activity was significantly lower in runs 4–6 than in runs 1–3 might indicate that participants started to dual-task (i.e. divide resources between the global and local tasks) rather than switch back and forth between the two tasks as instructed by the cue stimuli. However, the view that participants were dividing resources equally between the global and local tasks in runs 4–6 predicts equal activity for local and global cues, in contrast to our finding of significantly greater activity for global versus local cues. Fourthly, some of the dACC activity we observed may have occurred because our cue stimuli engaged motor preparation processes (Petit *et al.*, 1998). However, it is unlikely that motor-related processes can account for the differential cue activity we observed since both the nature of response requirements and the probability that a target would follow a cue stimulus were equated for the global and the local tasks.

A final alternative account of our results is suggested by our finding that practice reduced cue-related dACC activity without modulating conflict-related activity. This dissociation suggests we may have identified two distinct, yet highly overlapping, regions of dACC that participate in focusing attention and conflict resolution, respectively. Consistent with a single neuroanatomical locus, however, one popular model of cognitive control predicts that practice should have different effects on attention-focusing processes when they are recruited by cued orienting of attention versus conflict resolution (Norman and Shallice, 1986), and recent findings are in line with this prediction (Weissman *et al.*, 2002b). Thus, the most parsimonious explanation of our results is that a single region of dACC implements processes that focus attention on task-relevant stimuli, both during cued orienting of attention and during the resolution of conflict from distracting events.

The present findings do not rule out the possibility that other regions of the ACC make a circumscribed contribution to cognitive control that is limited to monitoring for processing conflict (Cohen *et al.*, 1997; Carter *et al.*, 2000; MacDonald *et al.*, 2000; Botvinick *et al.*, 2001; Braver *et al.*, 2001). Results from previous studies indicate the existence of functional specialization in ACC for distinct cognitive and emotional processes (Bush *et al.*, 2000). Future studies will be necessary to assess whether functional specialization exists in ACC for processes that focus attention versus monitor for processing conflict.

Our results therefore provide new support for views in which dACC plays a general role in focusing attention toward task-relevant stimuli, which is also called upon to resolve conflict from distracting events (Posner and DiGirolamo, 1998). As such, they suggest the dACC may be recruited whenever the need to

increase attention toward task-relevant stimuli increases, consistent with various models of cognitive control (Posner and Petersen, 1990; Posner and DiGirolamo, 1998). Importantly, our findings cannot be easily accounted for by models of cognitive control in which dACC exclusively monitors for response conflict (Cohen *et al.*, 1997; Carter *et al.*, 2000; MacDonald *et al.*, 2000; Botvinick *et al.*, 2001; Braver *et al.*, 2001). Given the importance of understanding the neural bases of cognitive control from both theoretical (Norman and Shallice, 1986; Botvinick *et al.*, 2001) and clinical (Carter *et al.*, 1997; Bush *et al.*, 1999) perspectives, future studies should further investigate the functional role of dACC in cognitive control and how its interactions with other brain areas enables selection. At present, we conclude that dACC helps focus attention on task-relevant stimulus features, both during cued orienting of attention and when the achievement of our behavioral goals is threatened by distracting events.

Notes

Address correspondence to Daniel H. Weissman, Center for Cognitive Neuroscience, Duke University, Box 90999, Durham, NC 27708, USA. Email: weissman@duke.edu.

References

Banich MT, Milham MP, Atchley R, Cohen NJ, Webb A, Wszalek T, Kramer AF, Liang ZP, Wright A, Shenker J, Magin R (2000a) FMRI studies of Stroop tasks reveal unique roles of anterior and posterior brain systems in attentional selection. J Cogn Neurosci 12:988-1000.

Banich MT, Milham MP, Atchley RA, Cohen NJ, Webb A, Wszalek T, Kramer AF, Liang Z, Barad V, Gullett D, Shah C, Brown C (2000b) Prefrontal regions play a predominant role in imposing an attentional 'set': evidence from fMRI. Brain Res Cogn Brain Res 10:1-9.

Botvinick M, Nystrom LE, Fissell K, Carter CS, Cohen JD (1999) Conflict monitoring versus selection-for-action in anterior cingulate cortex. Nature 402:179-181.

Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD (2001) Conflict monitoring and cognitive control. Psychol Bull 108:624-652.

Braver TS, Barch DM, Gray JR, Molfese DL, Snyder A (2001) Anterior cingulate cortex and response conflict: effects of frequency, inhibition and errors. Cereb Cortex 11:825-836.

Bush G, Whalen P, Rosen BR, Jenike MA, McInerney SC, Rauch SL (1998) The counting Stroop: an interference task specialized for functional neuroimaging — validation study with functional MRI. Hum Brain Mapp 6:270-282.

Bush G, Frazier JA, Rauch SL, Seidman LJ, Whalen PJ, Jenike MA, Rosen BR, Biederman J (1999) Anterior cingulate cortex dysfunction in attention-deficit/hyperactivity disorder revealed by fMRI and the Counting Stroop. Biol Psychiatry 45:1542-1552.

Bush G, Phan L, Posner MI (2000) Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn Sci 4:215-222.

Bush G, Vogt BA, Holmes J, Dale AM, Greve D, Jenike MA, Rosen BR (2002) Dorsal anterior cingulate cortex: A role in reward-based decision making. Proc Natl Acad Sci USA 99:523-528.

Carter CS, Mintun M, Nichols T, Cohen JD (1997) Anterior cingulate gyrus dysfunction and selective attention deficits in Schizophrenia: [^{15}O]H$_2$O PET study during single-trial Stroop task performance. Am J Psychiatry 154:1670-1675.

Carter CS, Botvinick MM, Cohen JD (1999) The contribution of the anterior cingulate cortex to executive processes in cognition. Rev Neurosci 10:49-57.

Carter CS, Macdonald AM, Botvinick M, Ross LL, Stenger VA, Noll D, Cohen JD (2000) Parsing executive processes: strategic vs. evaluative functions of the anterior cingulate cortex. Proc Natl Acad Sci USA 97:1944-1948.

Casey BJ, Thomas KM, Welsh TF, Badgaiyan RD, Eccard CH, Jennings JR, Crone EA (2000) Dissociation of response conflict, attentional selection, and expectancy with functional magnetic resonance imaging. Proc Natl Acad Sci USA 97:8728-8733.

Cohen JD, Dunbar K, McClelland JL (1990) On the control of automatic processes: a parallel distributed processing account of the Stroop effect. Psychol Rev 97:332-361.

Cohen JD, Perlstein WM, Braver TS, Nystrom LE, Noll DC, Jonides J, Smith EE (1997) Temporal dynamics of brain activation during a working memory task. Nature 386:604-608.

Corbetta M, Kincade JM, Ollinger JM, McAvoy MP, Shulman GL (2000) Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nat Neurosci 3:292-297.

Desimone R (1998) Visual attention mediated by biased competition in extrastriate visual cortex. Philos Trans R Soc Lond B Biol Sci 353:1245-1255.

Friston KJ, Holmes AP, Worsley KJ, Poline JP, Frith CD, Frackowiak RSJ (1995) Statistical parametric maps in functional imaging: a general linear approach. Hum Brain Mapp 2:189-210.

Hopfinger JB, Buonocore MH, Mangun GR (2000) The neural mechanisms of top-down attentional control. Nat Neurosci 3:284-291.

Kastner S, De Weerd P, Desimone R, Ungerleider LG (1998) Mechanisms of directed attention in the human extrastriate cortex as revealed by functional MRI. Science 282:108-111.

Kastner S, Pinsk MA, De Weerd P, Desimone R, Ungerleider LG (1999) Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron 22:751-761.

Kerns JG, Cohen JD, MacDonald III AW, Cho RY, Stenger VA, Carter CS (2004) Anterior cingulate conflict monitoring and adjustments in control. Science 303:1023-1026.

Kimchi R (1992) Primacy of wholistic processing and global/local paradigm: a critical review. Psychol Bull 112:24-38.

Kramer AF, Hahn S, Gopher D (1999) Task coordination and aging: explorations of executive control processes in the task switching paradigm. Acta Psychol 102:339-378.

Lavie N (1995) Perceptual load as a necessary condition for selective attention. J Exp Psychol Hum Percept Perform 21:451-468.

MacDonald AW, Cohen JD, Stenger VA, Carter CS (2000) Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science 288:1835-1838.

MacLeod CM (1991) Half a century of research on the Stroop effect: an integrative review. Psychol Bull 109:163-203.

MacLeod CM, Dunbar K (1988) Training and Stroop-like interference: evidence for a continuum of automaticity. J Exp Pyshcol Learn 14:126-135.

Meiran N (1996) Reconfiguration of processing mode prior to task performance. J Exp Psychol Learn Mem Cogn 22:1423-1442.

Milham MP, Banich MT, Claus E, Cohen NJ (2002) Practice-related effects demonstrate complementary roles of anterior cingulate and prefrontal cortices in attentional control.

Murtha S, Chertkow H, Beauregard M, Dixon R, Evans A (1996) Anticipation causes increased blood flow to the anterior cingulate cortex. Hum Brain Mapp 4:103-112.

Navon D (1977) Forest before trees: the precedence of global features in visual perception. Cognit Psychol 9:353-383.

Norman DA, Shallice T (1986) Attention to action: willed and automatic control of behavior. In: Consciousness and self-regulation (Davidson RJ, Schwartz GE, Shapiro D, eds), pp. 1-18. New York: Plenum Press.

Ollinger JM, Corbetta M, Shulman GL (2001a) Separating processes within a trial in event-related functional MRI. Neuroimage 13:218-229.

Ollinger JM, Shulman GL, Corbetta M (2001b) Separating processes within a trial in event-related functional MRI. Neuroimage 13:210-217.

Petit L, Courtney SM, Ungerleider LG, Haxby JV (1998) Sustained activity in the medial wall during working memory delays. J Neurosci 18:9429-9437.

Posner MI, DiGirolamo GJ (1998) Executive attention: Conflict, target detection, and cognitive control. In: The attentive brain (Parasuraman R, ed.), pp. 401–423. Cambridge, MA: MIT Press.

Posner MI, Petersen SE (1990) The attention system of the human brain. Annu Rev Neurosci 13:25–42.

Rees G, Frith CD, Lavie N (1997) Modulating irrelevant motion perception by varying attentional load in an unrelated task. Science 278:1616–1619.

Shima K, Tanji J (1998) Role for cingulate motor area cells in voluntary movement selection based on reward. Science 282:1335–1338.

Shulman GL, Ollinger JM, Akbudak E, Conturo TE, Snyder AZ, Petersen SE, Corbetta M (1999) Areas involved in encoding and applying directional expectations to moving objects. J Neurosci 19:9480–9496.

Stoffer TH (1993) The time course of attentional zooming: a comparison of voluntary and involuntary allocation of attention to the levels of compound stimuli. Psychol Res 56:14–25.

Stoffer TH (1994) Attentional zooming and the global-dominance phenomenon: effects of level-specific cueing and abrupt visual onset. Psychol Res 56:83–98.

Sylvester CC, Wager TD, Lacey SC, Hernandez L, Nichols TE, Smither EE, Jonides J (2003) Switching attention and resolving interference: fMRI measures of executive functions. Neuropsychologia 41:357–370.

Talairach J, Tournoux P (1988) Co-planar stereotactic atlas of the human brain. New York: Thieme.

Weissman DH, Mangun GR, Woldorff MG (2002a) A role for top-down attentional orienting during interference between global and local aspects of hierarchical stimuli. Neuroimage 17:1266–1276.

Weissman DH, Woldorff MG, Hazlett CJ, Mangun GR (2002b) Effects of practice on executive control investigated with fMRI. Brain Res Cogn Brain Res 15:47–60.

Weissman DH, Giesbrecht B, Song AW, Mangun GR, Woldorff MG (2003) Conflict monitoring in the human anterior cingulate cortex during selective attention to global and local object features. Neuroimage 19:1361–1368.

Woldorff MG (1993) Distortion of ERP averages due to overlap from temporally adjacent ERPs: analysis and correction. Psychophysiology 30:98–119.

Woldorff MG, Hazlett CJ, Fichtenholtz HM, Weissman DH, Dale AM, Song AW (2004) Functional parcellation of attentional control regions of the brain. J Cognitive Neurosci 16:149–165.