Anterior Cingulate Cortex and Response Conflict: Effects of Frequency, Inhibition and Errors

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Anterior cingulate cortex (ACC) may play a key role in cognitive control by monitoring for the occurrence of response conflict (i.e. simultaneous activation of incompatible response tendencies). Low-frequency responding might provide a minimal condition for eliciting such conflict, as a result of the need to overcome a prepotent response tendency. We predicted that ACC would be selectively engaged during low-frequency responding, irrespective of the specific task situation. To test this hypothesis, we examined ACC activity during the performance of simple choice-discrimination tasks, using rapid event-related functional magnetic resonance imaging. Subjects were scanned while performing three tasks thought to tap different cognitive processes: 'Go/No-go' (response inhibition), 'oddball' (target detection), and two-alternative forced-choice (response selection). Separate conditions manipulated the frequency of relevant task events. Consistent with our hypothesis, the same ACC region was equally responsive to low-frequency events across all three tasks, but did not show differential responding when events occurred with equal frequency. Subregions of the ACC were also identified that showed heightened activity during the response inhibition condition, and on trials in which errors were committed. Task-sensitive activity was also found in right prefrontal and parietal cortex (response inhibition), left superior temporal and tempoparietal cortex (target detection), and supplementary motor area (response selection). Taken together, the results are consistent with the hypothesis that the ACC serves as a generic detector of processing conflict arising when low-frequency responses must be executed, but also leave open the possibility that further functional specialization may occur within ACC subregions.

Introduction

Neuroimaging evidence suggests that the anterior cingulate cortex (ACC) plays a key role in cognitive control. In particular, there have been consistent findings of ACC activity in tasks requiring high degrees of control: (i) tasks which are difficult or performed under high-load conditions, such as divided attention or dual tasks (Corbetta *et al.*, 1991; D'Esposito *et al.*, 1995); (ii) tasks for a which a large number of errors of commission are made, such as the Go/No-go and Eriksen task (Casey *et al.*, 1997; Botvinick *et al.*, 1999; Kiehl *et al.*, 2000); (iii) tasks which involve response inhibition or response competition, such as the Stroop (Pardo *et al.*, 1990; Carter *et al.*, 1995, 2000; Barch *et al.*, 2001); and (iv) tasks which require selection of responses in an underdetermined context, such as stem completion or voluntary/random movements (Frith *et al.*, 1991; Buckner *et al.*, 1995; Jueptner *et al.*, 1997). However, from these studies it has not been clear exactly what is the specific role of the ACC in cognitive control.

In previous work, we have proposed a hypothesis as to why the ACC is activated in such a wide range of cognitive tasks (Carter *et al.*, 1998; Botvinick *et al.*, 2001). Specifically, we have hypothesized that the ACC serves to evaluate the demand for cognitive control by monitoring for the occurrence of conflict in information processing. By conflict, we mean interference or interactions between different information processing pathways. In a series of computer simulation studies, we provide a detailed examination the theoretical consequences of this hypothesis (Botvinick *et al.*, 2001). One of the predictions that arises from such a theoretical exploration is that the ACC should be engaged whenever two or more incompatible responses are simultaneously activated. A number of recent neuroimaging studies have provided direct empirical support for this prediction (Botvinick *et al.*, 1999; Barch *et al.*, 2000, 2001; Carter *et al.*, 2000; Casey *et al.*, 2000; MacDonald *et al.*, 2000).

A critical issue for further refining and testing the conflict hypothesis concerns the nature of the task conditions that elicit conflict. The possibility we focus on and test here is that conflict arises whenever infrequent responses are required, especially when these occur in the context of making stereotyped or habitual responses. Because the habitual or frequent response has a strong stimulus–response mapping it is likely to be at a higher baseline level of readiness or activity (e.g. primed) and so acts as a prepotent response. When the low frequency response is to be executed, it must compete with and eventually overcome the activation in the stronger pathway of the high-frequency response. The competition between the two response pathways is expected to result in processing conflict, which should be reflected in increased ACC activity. This kind of frequency-induced conflict may represent a minimal task condition that is sufficient to elicit ACC activity, even during the performance of otherwise simple cognitive tasks (e.g. choice-discrimination tasks).

To test this idea and the generality of the conflict hypothesis, we used functional magnetic resonance imaging (fMRI) to assess ACC activity during performance of simple choice-discrimination tasks involving differing event frequencies. We examined three task paradigms thought to tap different cognitive processes: 'Go/No-go' (response inhibition), 'oddball' (target detection), and two-alternative forced-choice (response selection). Our specific prediction was that the ACC would be engaged during performance of these tasks by responses to low-frequency events. Moreover, we hypothesized that ACC would be equivalently activated by these low-frequency responses across all three tasks, irrespective of their different cognitive demands. Such a result would provide support for the idea that the ACC serves as a 'generic' conflict detector, and would complement our recent work showing generic conflict-related ACC activation across different response modalities and processing domains (Barch *et al.*, 2001). Below, we describe in greater detail the design and predictions of the current study, relating them to the existing neuroimaging literature on the Go/No-go and other simple choice-discrimination tasks.

The Go/No-go task represents a classic paradigm in which the differing frequency of event types may result in response-related

processing conflict. The task involves visual discrimination and a simple choice: to respond (Go) or not respond (No-go) depending on the current stimulus. One interesting aspect of this task is that response conflict arises from competition between the execution and the inhibition of a single response (*response inhibition* conflict), rather than from competition between two alternative responses (*response selection* conflict). In a number of recent neuroimaging studies of the Go/No-go task, the ACC has been found to be reliably activated during Go/No-go performance, using a variety of methods including positron emission tomography (PET) (Kawashima *et al.*, 1996), block-design fMRI (Casey *et al.*, 1997; de Zubicaray *et al.*, 2000) and event-related fMRI (Garavan *et al.*, 1999; Kiehl *et al.*, 2000). The one exception was the event-related fMRI study of Konishi and colleagues, which did not observe ACC activity to No-go responses (Konishi *et al.*, 1998, 1999). However, this study also involved a small number of subjects (n = 6), and sampled a limited region of frontal cortex. Perhaps more interestingly, as discussed below, No-go trials occurred with 50% probability, and so did not constitute a low-frequency event.

Although the pattern of ACC activity during Go/No-go tasks is generally reliable, the nature of this activity is less clear. First, how does ACC activity associated with response inhibition conflict compare with that elicited during response selection conflict? In other words, is the act of suppressing or withholding a response qualitatively different from that of selecting an alternative response, in terms of the conflict it produces? Second, how does ACC activity associated with response inhibition conflict compare with that elicited during *target detection* conflict (i.e. the generation of a responses to an infrequent target). Target detection tasks, also commonly referred to as 'oddball' tasks, have typically been treated as qualitatively distinct from response inhibition tasks, and have garnered their own separate literature, commonly studied using event-related potential (ERP) methods (Sutton *et al.*, 1965; Duncan-Johnson and Donchin, 1977; Donchin and Coles, 1988), but more recently with fMRI (McCarthy *et al.*, 1997; Menon *et al.*, 1997; Linden *et al.*, 1999; Opitz *et al.*, 1999; Kiehl *et al.*, 2001). However, at some level the two tasks are mirror images of each other. The Go/No-go involves infrequent response inhibition in the context of frequent response generation, while target detection tasks involve infrequent response generation in the context of frequent response inhibition. Thus, a natural question is whether these two types of low-frequency events produce similar increases in response-related conflict, and thus result in similar patterns of ACC activity, as the conflict hypothesis would predict. A third question is whether the degree of ACC activity during response inhibition is influenced by the relative frequency of No-go versus Go events. The conflict hypothesis suggests that ACC activity will be dependent upon the relative frequency of responses, such that low-frequency responses elicit the highest levels of conflict. However, this pattern may be different for response inhibition tasks than for response selection tasks. In particular, response inhibition may be a 'special case' that produces high degrees of conflict irrespective of the frequency of No-go events.

The current study addressed these questions, by utilizing closely matched task conditions that enabled measurement of ACC activity during response inhibition, response selection, and target detection tasks. Furthermore, we manipulated stimulus frequency levels to determine whether ACC was always most responsive when the relevant task event occurred with low frequency. Event-related fMRI methods (Dale and Buckner, 1997; Buckner and Braver, 1999) were used to provide information regarding the ACC response to specific task events (e.g. Go versus No-go stimuli). Our hypothesis regarding the role of ACC in conflict detection allowed us to make specific predictions regarding the pattern of ACC activity that would be observed. First, we predicted that high levels of response conflict would occur during the processing of low-frequency events, regardless of whether these events were associated with response inhibition, response selection, or target detection. Thus, we predicted that there would be no differences in the location or degree of ACC activity across the three task conditions. Second, we predicted that when different task events were of equal frequency there would be no differences in their respective levels of response conflict, even if the task events were of different type (e.g. Go versus No-go trials). Interestingly, this second prediction also addresses the one anomalous finding from the previous neuroimaging literature on the Go/No-go task. Specifically, as mentioned above, Konishi *et al.* (1998) failed to find ACC activity to No-go events during Go/No-go performance. However, their task design involved an equal frequency of Go and No-go trials. Consequently, this factor may have accounted for the lack of differential ACC activity on No-go trials when compared with Go trials. Our study enabled us to interpret this finding by explicitly manipulating the frequency of Go versus No-go events.

Given our prediction of no differences in ACC activity across response inhibition, response selection and target detection tasks, a secondary goal of the study was to determine whether there are brain regions that do show selective responses to one of the tasks. In particular, previous findings suggest that response inhibition engages dorsolateral and ventrolateral prefrontal cortex (PFC), as well as striatal and parietal regions (Casey *et al.*, 1997; Garavan *et al.*, 1999; Kiehl *et al.*, 2000). Performance of target detection tasks is also thought to engage dorsolateral PFC and parietal cortex, but additionally elicits activity in superior temporal regions (Reinsel *et al.*, 1996; Menon *et al.*, 1997; Opitz *et al.*, 1999; Kiehl *et al.*, 2001). There has not been as much study of response selection tasks, but there is some indication that they may differentially engage motor cortex, such as premotor and supplementary motor areas (Kawashima *et al.*, 1996). Our use of whole-brain imaging enabled us to extend these findings by identifying brain regions which showed activation patterns that were task-specific.

A final issue addressed by the current study is the effect of error commission on brain activity, especially with regards to activity in ACC. There is now quite a large literature, primarily stemming from ERP work, addressing the issue of error-related brain activity (Gehring *et al.*, 1990; Falkenstein *et al.*, 1991). A primary focus of this work has been on the ERN, or error-related negativity, an ERP component that is thought to be generated in the ACC (Dehaene *et al.*, 1994). Recent fMRI studies have confirmed this finding, and have also pointed to other brain regions that show sensitivity to errors (Carter *et al.*, 1998; Kiehl *et al.*, 2000). It has been hypothesized that ACC error-related activity is a response to the increased conflict occurring on such trials, rather than errors *per se* (Carter *et al.*, 1998). Our paradigm allowed us to extend this work, since subjects tend to make a high number of errors in rapid choice-discrimination tasks such as the Go/No-go. We conducted confirmatory analyses in the ACC region of interest (ROI) to determine whether this region shows sensitivity to error-induced conflict as well as frequency-induced conflict. We also conducted exploratory analyses that examined whether there were additional brain

regions showing sensitivity to errors, including more rostral/inferior ACC regions, as has recently been suggested (Kiehl *et al.*, 2000).

Materials and Methods

Participants

Fourteen neurologically normal right-handed subjects participated in this study. Subjects were five males and nine females, with a mean age of 22.9 (range 18–27 years). Subjects were paid $25 an hour for participation, and gave informed consent in accordance with guidelines set by the Human Studies Committee at Washington University.

Behavioral Procedures and Cognitive Tasks

A power Macintosh computer (Apple, Cupertino, CA, USA) and Psyscope software (Cohen *et al.*, 1993) displayed all visual stimuli. A LCD projector (Sharp, model XGE850) projected stimuli onto a screen placed at the head of the bore. Subjects viewed the screen via a mirror fastened to the head coil. Subjects responded by pushing a fiber optic light-sensitive key-press connected to a Psyscope Button Box (Carnegie Mellon University, Pittsburgh, PA, USA) that recorded both accuracy and reaction time.

Subjects viewed single uppercase letters, presented centrally in Helvetica 24 pt font, white on a black background. Each stimulus appeared for 250 ms, followed by a 1000 ms inter-trial interval. Three different tasks were performed.

Response Inhibition (Go/No-go). Subjects were instructed to withhold responding to infrequent No-go stimuli (the letter 'X' = 17% frequency) in the context of responding to frequent Go stimuli (the 25 'non-X' letters = 83% frequency).

Target Detection (Oddball). Subjects were instructed to generate a response to infrequent targets ('non-X' = 17% frequency) in the context of withholding responses to frequent non-targets ('X' = 83% frequency). In both Response Inhibition and Target Detection conditions, responses were made with the index finger of the right hand.

Response Selection (Two-alternative Forced-choice). Subjects were instructed to respond to all stimuli by selecting one of two alternative responses. If the stimulus was a 'non-X' a response was to be made with the index finger of the right hand. If the stimulus was an 'X', a response was to be made with the index finger of the left hand. Two different versions of this condition were run, to provide appropriate controls for both the response inhibition and target detection conditions. The *low 'X'* condition ('X' = 17% frequency, 'non-X' = 83% frequency) matched the frequencies of the response inhibition condition, while the *low 'non-X'* condition ('X' = 83% frequency, 'non-X' = 17% frequency) matched the frequencies of the target detection conditions.

Two additional conditions were also performed to examine the effect of manipulating frequency.

Equal-frequency Response Inhibition. Go and No-go stimuli each occurred with 50% frequency (note that this condition could alternatively be labeled equal-frequency target detection).

Equal-frequency Response Selection. This condition provided a control for the Equal-frequency Response Inhibition condition, and also had frequencies of 50% for both 'X' and 'non-X' stimuli.

Each participant performed two runs of each of the following six conditions (performed in a blocked fashion with block order counterbalanced across participants): (i) Response Inhibition; (ii) Target Detection; (iii) Response Selection – Low X; (iv) Response Selection – Low Non-X; (v) Equal-frequency Response Inhibition; and (vi) Equal-frequency Response Selection. During each run, the two stimulus types (X, non-X) were presented in a randomly intermixed fashion (subject to the block-wise frequency ratios) in a continuous series of 150 trials. To create a stable task baseline, each functional run began and ended with a 35 s rest epoch during which subjects passively viewed a fixation cross-hair.

The hemodynamic response to single events has been estimated to evolve over a period of 10–20 s, which is relatively slow in comparison to the fast stimulus presentation rates used in this study. Consequently, the hemodynamic response to high-frequency events is expected to be sustained and relatively constant. In contrast, the hemodynamic response to low-frequency events would be expected to occur as identifiable transient perturbations of this baseline activation pattern. It is not quite as clear whether the hemodynamic response to events in the equal-frequency conditions would be detectable using this rapid event-related design. Previous research suggests that, even with very rapid presentation rates, differences in activity levels between transient events are still detectable (Burock *et al.*, 1998; Miezin *et al.*, 2000). Nevertheless, we carried out a validation analysis to further examine this issue in the current dataset (see below).

Scanning Procedures

Images were acquired on a Siemens 1.5 T Vision System (Erlangen, Germany) with a standard circularly polarized head coil. A pillow and tape were used to minimize head movement. Headphones dampened scanner noise and enabled communication with participants. Structural images were acquired using a high resolution (1.25 × 1 × 1 mm) sagittal 3-D MP-RAGE (Mugler and Brookeman, 1990) T_1-weighted sequence (T_R = 9.7 ms, T_E = 4 ms, flip = 12°, T_I = 300 ms). Functional images were acquired using an asymmetric spin-echo echo-planar sequence (T_R = 2500 ms, T_E = 50 ms, flip = 90°). During each functional scanning run 103 sets of 16 contiguous, 8 mm thick axial images were acquired parallel to the anterior–posterior commissure plane (3.75 × 3.75 mm in-plane resolution), allowing complete brain coverage at a high signal-to-noise ratio (Conturo *et al.*, 1996). Each run lasted ~4.5 min, and a 2 min delay occurred between runs, during which time subjects rested.

Image Analysis Procedures

Functional imaging data were analyzed according to the following procedures. Following movement correction (Friston *et al.*, 1994; Snyder, 1996), all functional images were scaled to achieve a whole-brain mode value (used in place of mean because of its reduced sensitivity to variation in brain margin definition) of 1000 for each scanning run (to reduce the effect of scanner drift or instability). Functional images were then resampled into 3 mm isotropic voxels, transformed into standardized atlas space (Talairach and Tournoux, 1988), and smoothed with a Gaussian filter (6 mm FWHM). The data were then analyzed using rapid event-related methods to estimate an 8-scan (20 s) hemodynamic response time course for each stimulus (Buckner and Braver, 1999). Linear interpolation was used to estimate the BOLD signal for events occurring in the midpoint of a scan. For the low-frequency conditions, the high frequency stimulus was treated as the baseline. For the equal-frequency conditions, one of the stimuli (Go/non-X or No-go/X) was treated as the arbitrary baseline. Difference time courses were then computed by subtracting this baseline from the low-frequency event time courses, or from the response to the other stimulus in the equal-frequency conditions.

The event-related time course data were submitted to a group analysis using voxelwise random-effects model ANOVAs (as described in more detail below). Event-related responses can be determined in this approach by using time (i.e. scan) as a factor of interest, and examining significant effects of this factor (both main effects and interactions). The primary advantage of this approach is that it makes no *a priori* assumptions about the particular shape of the hemodynamic response (Buckner and Braver, 1999). Given that this response may vary across brain regions, incorrect estimates regarding its shape may lead to a significant loss of power in detecting event-related effects. For whole-brain exploratory analyses, statistical parametric maps of the voxel-wise *F*-values were thresholded for significance using a cluster-size algorithm (Forman *et al.*, 1995). This algorithm takes account of the spatial extent of activation to correct for multiple comparisons. A voxel-wise significance threshold of $P = 1 \times 10^{-7}$ was chosen, along with minimum cluster-size of eight voxels. This is a conservative threshold that corrects for both multiple comparisons (Bonferroni correction) and the high degree of correlation occurring between successive time-points (Box correction) in rapid event-related designs, to produce an image-wise false positive rate of $P = 0.05$ (Miezin *et al.*, 2000). For purposes of graphic display, all effects are described in terms of percent signal change from baseline.

We carried out both confirmatory and exploratory analyses of the data. Based on our specific hypothesis regarding the role of the ACC in conflict monitoring, we first conducted a confirmatory analysis informed by previous neuroimaging studies of ACC activity. Specifically, we

generated a 10 mm spherical ROI based on the results of a recent meta-analysis localizing the anatomical coordinates of ACC activity in tasks thought to involve response conflict (Barch *et al.*, 2001). The region typically activated in these studies is situated posterior to the genu of the ACC, anterior to the anterior commissure line (vCA in the Tailarach atlas), and superior to the corpus callosum. The ROI was centered at the average coordinates of the ACC region identified in the meta-analysis (manual response paradigms; Talairach coordinates: 3, 19, 35). Picard and Strick, who conducted an extensive meta-analysis of cingulate functional neuroanatomy in both primate and humans, termed this region the posterior rostral cingulate zone (Picard and Strick, 1996). We analyzed the event-related activation in this ACC ROI across all of the task conditions in the current study, as well as in a comparison of error versus correct trials.

Results of the confirmatory analysis were extended through exploratory analyses of activity across the entire brain. A number of different exploratory analyses were conducted. The first was a conjunction test, which identified brain regions showing a consistent response to low-frequency events across all tasks (inhibition, detection, and selection). For a region to be identified in this analysis, it had to show a significant main effect of time in each of the four low-frequency conditions (positive responses only). The second analysis was a disjunction test, which identified brain regions showing a selective response to one of the task conditions. For a region to be identified in this analysis, it had to meet two simultaneous criteria: (i) a strong positive event-related response in one of the tasks (main effect of time); and (ii) a significant condition × time interaction when compared against each of the other conditions. The third analysis examined brain activity on errors versus correct trials. Error-related analyses (both confirmatory and exploratory) were conducted by selectively averaging correct and error trial responses after first collapsing across the four low-frequency task conditions, and the two equal-frequency conditions. Difference time-courses were then constructed for low-frequency errors (treating low-frequency correct as the baseline), equal-frequency errors (equal-frequency correct as baseline), and low-frequency correct (high-frequency correct as baseline). For a region to be identified as showing an error-related response in this analysis, it had to meet three simultaneous criteria: (i) an event-related response on low-frequency error trials; (ii) an event-related response on equal-frequency error trials; and (iii) a significant accuracy × time interaction when comparing low-frequency error versus low-frequency correct trial activity.

Results

Behavioral Data Analyses

Because of technical problems, behavioral data from four subjects were unusable. Consequently, analyses were conducted on the remaining 10 subjects. However, during pilot behavioral testing for the study, behavioral data were collected on an additional 30 subjects. The pattern of results (and primary statistical effects) discussed below were essentially the same in this larger sample of subjects. Thus, the results appear to be stable and reliable.

As can be seen in Table 1, across all task conditions subjects showed poorer performance in their responses to low-frequency events compared to high-frequency events. We formalized this assertion by submitting the accuracy data to a 4 × 2 ANOVA with task (inhibition, detection, selection – low X, and selection – low non-X) and frequency (low, high) as factors. A highly significant main effect of frequency was found [$F(1,9) = 12.3$, $P < 0.01$], such that greater errors were made to the low-frequency stimuli. In addition, both the main effect of task [$F(3,27) = 4.6$, $P = 0.01$] and the task × frequency interaction [$F(3,27) = 5.1$, $P < 0.01$] were significant. Both of these effects appeared to be due to the high rate of commission errors made on the Go/No-go inhibition task, which led both to an overall higher error rate and a greater difference in performance across low- and high- frequency stimuli.

Although the reaction time (RT) data on all four tasks could not be examined in an analogous fashion (because subjects did not respond to all stimuli in the response inhibition and target detection tasks), we did conduct an ANOVA for the two response selection tasks using condition (low X, low non-X) and frequency (low, high) as factors. Again a highly significant main effect of frequency was found [$F(1,9) = 160.4$, $P < 0.001$] such that responses were slower to the low-frequency stimulus. A condition × frequency interaction was also observed [$F(1,9) = 11.2$, $P < 0.01$], such that the difference in RT (correct trials only) between low- and high-frequency stimuli was greater in the low-X condition. Thus, across all task conditions, performance was poorer for low-frequency events than high-frequency events, which is consistent with the hypothesis that low-frequency events elicit a greater degree of conflict.

We next examined the effect of the frequency manipulation on performance. For each task condition, we compared performance on the low versus equal frequency conditions (see Table 1). For response inhibition, subjects made significantly fewer errors of commission on No-go trials in the equal-frequency condition [$F(1,9) = 3.22$, $P < 0.01$]. In comparing Go trial responses in this condition against the target detection condition (which had low-frequency Go trials), it was found that accuracy was unchanged [$F(1,9) = 0.1$, NS] and RTs were faster [$F(1,9) = 10.9$, $P < 0.01$]. In the equal-frequency response selection task, performance improved for both the X (errors: $F(1,9) = 14.1$, $P < 0.01$; RT: $F(1,9) = 3.2$, $P > 0.1$] and non-X stimuli [errors: $F(1,9) = 4.73$, $P = 0.06$; mean RT: $F(1,9) = 7.8$, $P < 0.05$]. Thus, across all three task conditions, increasing the frequency of the relevant events led to improved performance on those events.

Of the 10 subjects with usable behavioral data, eight made over five errors on low-frequency trials (when collapsing across the four low-frequency task conditions). Consequently, these

Table 1
Behavioral performance data

Task condition	Low frequency			High frequency		
	Stimulus	% errors	RT (ms)	Stimulus	% errors	RT (ms)
Response inhibition	No-go	23.0 (6.9)	N/A	Go	0.2 (0.1)	361 (18)
Target detection	Target	5.2 (5.2)	454 (18)	Non-target	0.6 (0.3)	N/A
Response selection — low X	X	14.7 (3.3)	478 (20)	Non-X	1.1 (0.4)	367 (18)
Response selection — low non-X	Non-X	9.9 (4.1)	451 (28)	X	0.9 (0.5)	378 (19)
	Equal frequency					
Response inhibition/target detection	No-go/non-target	5.6 (1.9)	N/A	Go/target	5.1 (5.3)	410 (19)
Response selection	X	7.2 (2.7)	457 (20)	Non-X	3.2 (1.0)	430 (19)

Values are means with standard errors of the mean (SEM) in parentheses. N/A = not applicable.

eight subjects' data were used for analyses of error-related brain activity.

Method Validation

We began the analysis of the fMRI data by validating that our imaging methods were sufficient to identify event-related brain responses even with a rapid-presentation design. To perform this analysis we examined data from the equal-frequency response selection condition. In this condition, subjects made responses to X and non-X stimuli with equal-frequency by making button-presses with either the right (non-X) or left (X) hand. Consequently, these responses would be expected to result in event-related brain activity occurring in contralateral somatomotor cortex. The analysis procedure used the response to the 'X' (left hand) as the baseline condition. As a consequence, we predicted that left somatomotor cortex would show a positive response (indicating greater activation to non-X stimuli/right-hand responses) and right somatomotor cortex would show a negative response (indicating greater activation to X stimuli/right-hand responses). To test this prediction, we examined the main effect of time in the random-effects ANOVA from this condition. Large focal activation was observed in somatomotor cortex in both the left and right hemispheres, along with activation of a few small cerebellar regions. The time courses of the event-related responses in these somatomotor regions show the expected effects (see Fig. 1*A*): a robust positive response in the left hemisphere region and a robust negative response in the right hemisphere region (0.15–0.2% signal change). The same pattern also held in the cerebellar regions (with an ipsilateral rather contralateral organization, as expected; see Fig. 1*B*), even though these regions had a response amplitude of about half the magnitude of the somatomotor regions (i.e. 0.04–0.08% signal change). This analysis thus supports our assumption that event-related activity can be detected in this paradigm even with very rapid presentation rates and equal-frequency presentation of stimuli.

Confirmatory Analysis

As described above, we first focused on an ACC ROI defined based on coordinates derived from a meta-analysis of ACC activation in manual response tasks eliciting high degrees of conflict. The location of this region is shown in Figure 2*A*. We examined the response of this ROI across the different conditions of the task. As can be seen in Figure 2*B*, this region showed a significant event-related response in all four low-frequency task conditions (indicated by significant main effects of time, all *P*s < 0.005). More importantly, there appeared to be no difference in response magnitude across the different conditions. We quantified estimates of the ACC response in each condition, by computing the peak amplitude, 'area-under-the-curve' (AUC; for the activated period only), and time-to-peak for each subject (see Table 2). We then performed ANOVAs on these estimates to determine whether there were any significant differences in the measures across conditions. There were no condition differences present in any of these three measures (*P*s > 0.1).

We then examined the activity of this ACC ROI in the two equal-frequency conditions. As can be seen in Figure 2*C*, we found no evidence of an event-related response in either of these conditions (main effects of time, $P > 0.1$). Moreover, direct comparison (i.e. paired *t*-test) of the response measures in the equal frequency conditions against the low-frequency conditions revealed that both the peak response amplitude [$t(13) = 2.55$, $P < 0.05$] and AUC [$t(13) = 3.1$, $P < 0.01$] were significantly lower in the equal-frequency conditions. Thus, the results suggest that the ACC shows differences in event-related activation as a function of the frequency of the event. However, it is important to note that our data do not indicate that ACC activity was not present in the equal-frequency conditions, only that the ACC response did not differentiate between event types (e.g. Go versus No-go).

Finally, we examined the activity of this region in response to errors. As predicted, the ACC region showed a robust event-related response to errors (relative to correct responses), whether these occurred in the low-frequency or equal-frequency conditions (both *P*s < 0.01; see Fig. 2*D*). Moreover, the low-frequency error response was greater than the response for low-frequency correct trials, although the pattern did not reach statistical significance. It is also important to note that when considering the low-frequency correct trials alone, there still remained a significant ACC response (main effect of time, $P < 0.001$). This indicates that the ACC response to low-frequency events is not solely due to the errors that more frequently occur to these events.

Exploratory Analyses

Conjunction Test

We first performed a conjunction test to identify brain regions showing a consistent response to low-frequency events. This test corroborated the findings of the confirmatory analysis by

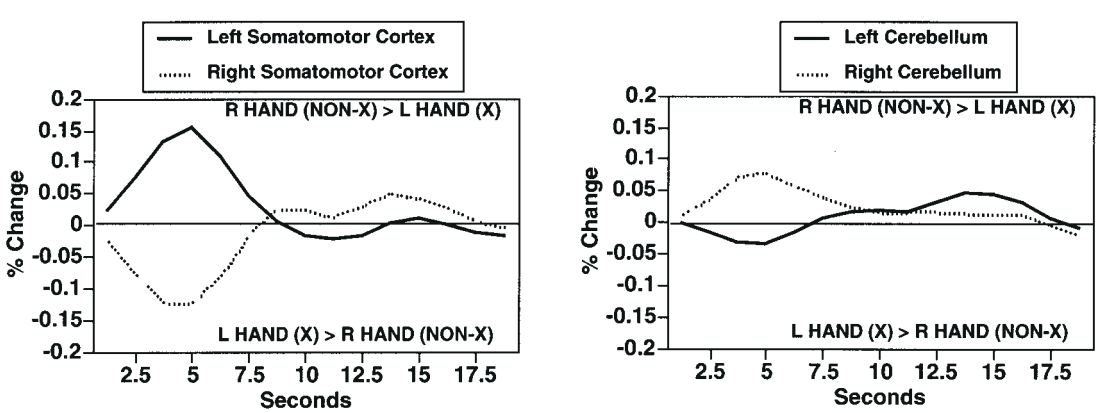

Figure 1. Validation of rapid presentation event-related fMRI methods. Time course indicates event-related activity in left and right hemisphere somatomotor cortex (*A*) and cerebellum (*B*).

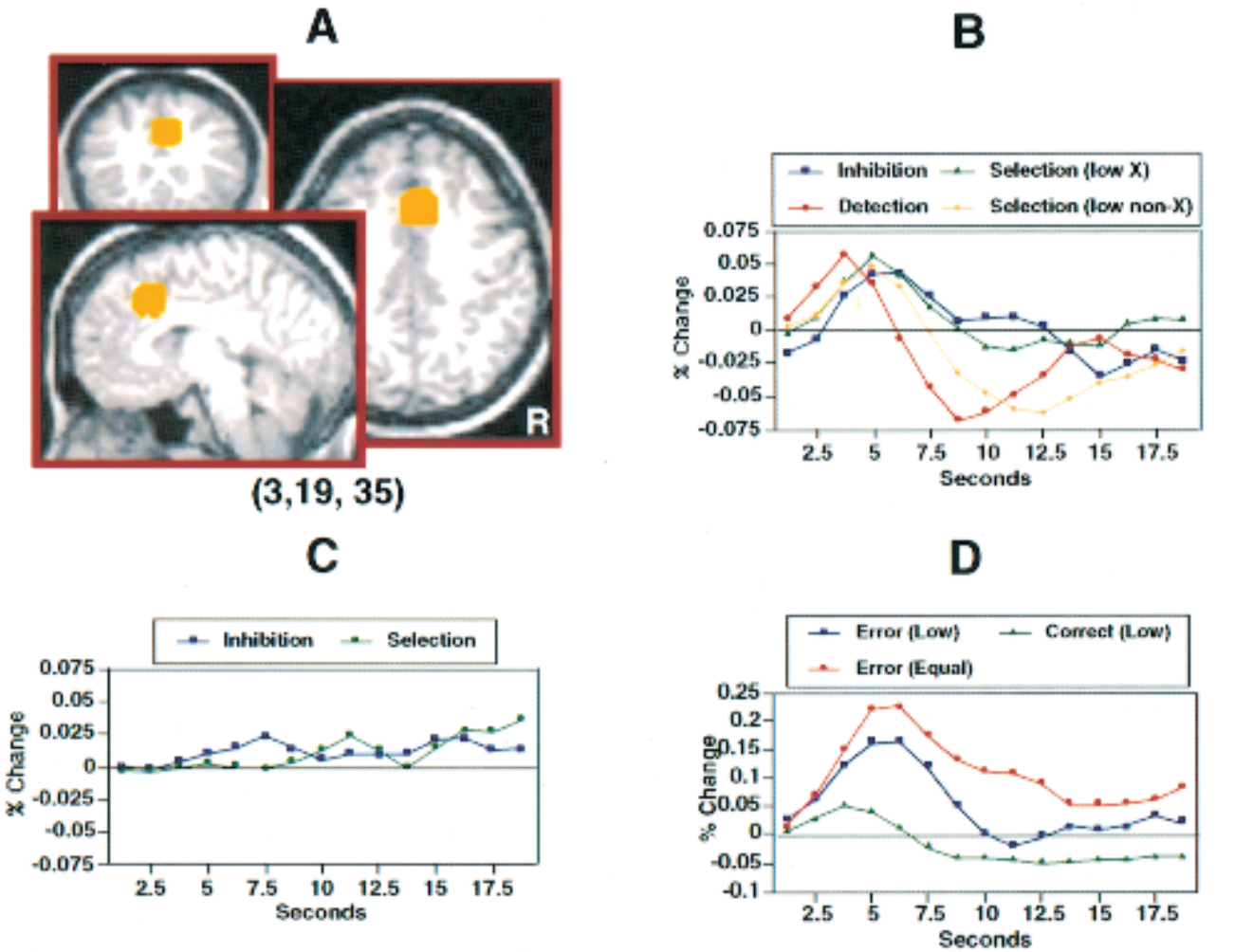

Figure 2. Confirmatory ACC region. (*A*) Anatomical location of ROI. (*B*) Time course of activation in four low-frequency conditions. (*C*) Time course of activation in two equal-frequency conditions. (*D*) Time course of activation in error analysis.

Table 2
Event-related response data for a confirmatory ACC region

Task condition	Time-to-peak (s)	Peak amplitude (% change)	AUC
Low frequency			
Response inhibition	4.38 (0.5)	0.062 (0.03)	0.253 (0.12)
Target detection	3.93 (0.5)	0.075 (0.03)	0.340 (0.18)
Response selection — low X	5.00 (0.5)	0.074 (0.03)	0.260 (0.09)
Response selection — low non-X	4.64 (0.4)	0.073 (0.04)	0.414 (0.16)
Equal frequency			
Response inhibition/target detection	3.39 (0.5)	0.028 (0.02)	0.102 (0.07)
Response selection	3.84 (0.5)	0.002 (0.02)	–0.008 (0.07)

Values are means (and SEMs). AUC = area under the curve.

identifying an ACC region that significantly overlapped with the anatomical location of the confirmatory region (see Fig. 3*A*). However, some of the volume of the exploratory region was located more superiorly, and blended into the supplementary motor area (SMA; BA 6). There were a number of other brain regions identified in the conjunction analysis (see Table 3), including bilateral frontal operculum, right dorsolateral PFC (BA 46), and medial superior parietal cortex (BA 7).

Error Test

Another exploratory analysis examined event-related responses to error versus correct trials. There was only a single brain region that showed increased activity to errors for both the low-frequency and equal-frequency conditions, as well as significantly greater activity for low-frequency errors compared to low-frequency correct trials. This region was in the ACC (see Fig. 3*B*). The activated region was found to extend slightly more inferiorly (Talairach coordinates: –1, 21, 27) than the either the ACC region identified in the frequency conjunction analysis or the confirmatory ACC ROI.

Disjunction Test

Finally, we performed a disjunction test to detect brain regions that were preferentially activated in one of the low-frequency task conditions. Table 4 displays the location of all such regions showing task selectivity. The test for regions selective to response inhibition (i.e. No-go responses) identified an almost wholly right-lateralized network, including prominent regions in dorsolateral (BA 46/9) and ventrolateral (BA 44) PFC, and inferior (BA 40) and superior (BA 7) parietal cortex. Interestingly, this analysis also identified a small region of inhibition-selective activation within the ACC, very close to the

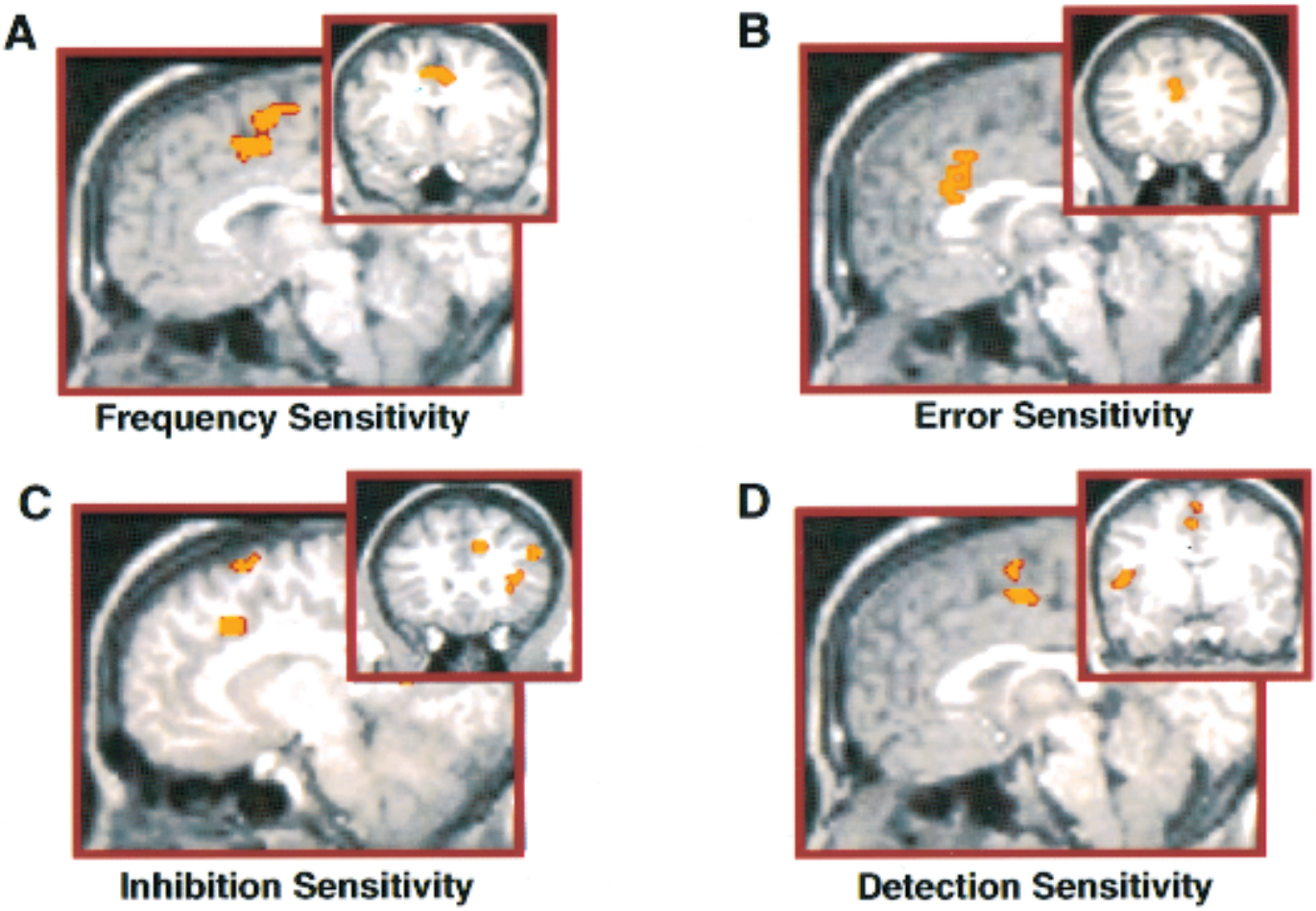

Figure 3. Cingulate regions identified in exploratory analyses. (*A*) ACC region identified as frequency sensitive (conjunction analysis). (*B*) ACC region identified to be error sensitive (error analysis). (*C*) ACC region identified to be inhibition sensitive (disjunction analysis). (*D*) Mid-cingulate region identified to be detection sensitive (disjunction analysis).

Table 3
Regions showing consistent response to low-frequency events in conjunction analyses

Regions of interest	Brodmann area(s)	X[a]	Y[a]	Z[a]	No. of voxels
Right dorsolateral prefrontal cortex	46	35	42	18	25
Right frontal operculum	45/insula	35	15	0	122
Left frontal operculum	45/insula	–32	15	3	59
Anterior cingulate/SMA	32/6	2	3	48	119
Right tempoparietal cortex	22/40	56	–48	24	24
Right parietal cortex	40/7	38	–42	48	14
Medial superior parietal cortex	7	11	–69	45	52
Medial superior parietal cortex	7	–8	–69	51	25
Left cerebellum	–	–26	–60	–30	15

[a]*X*, *Y* and *Z* are coordinates in a standard stereotactic space (Talairach and Tournoux 1988) in which positive values refer to regions right of (*X*), anterior to (*Y*) and superior to (*Z*) the anterior commissure (AC).

centroid of the confirmatory ROI, but further right-lateralized (see Figs 3*C* and 4*A*). Such a finding was not predicted by the conflict hypothesis. The test for regions selective to target detection identified a very different network, one which engaged both left-lateralized temporoparietal and mid-cingulate motor regions (i.e. posterior rather than anterior to the anterior commissure line; see Figs 3*D* and 4*B*). The test for regions selective to response selection identified a single region in SMA (BA 6).

We were interested in determining whether the regions showing selective responses in the response inhibition and target detection conditions showed similar patterns in the equal-frequency conditions. In particular, one might predict that regions which are truly selective to inhibitory processing *per se* would show a response on inhibitory trials (i.e. No-go trials) even in situations where these occur with equal frequency as response trials (i.e. Go trials). Conversely, regions truly sensitive to target detection might be expected to show a response on target trials (i.e. Go trials) even when these occur with equal frequency as non-target trials (i.e. No-go trials). Moreover, these patterns would be expected to be distinct from those observed on the equal-frequency response selection condition, which does not differentiate between Go versus No-go or target versus non-target trials.

When we examined the response of the inhibition-selective regions in the equal-frequency conditions we found that none of the regions showed a significant response to No-go trials (all *P*s for the main effect of time > 0.1), nor were there any regions showing a significant condition × time interaction when comparing responses in the two equal-frequency conditions. In contrast, when we examined the response of the detection-selective regions in the equal frequency conditions we found that all of the regions showed a significant response to target (Go) trials (all *P*s for the main effect of time < 0.005). Furthermore, in the mid-

cingulate (BA 24) and left temporoparietal cortex (BA 42/40), the response to target trials was significantly greater than that observed in the comparison condition of the equal-frequency response selection task. This finding was confirmed by a significant condition × time interaction when the responses across the two conditions were compared (Ps < 0.05).

Discussion

The current study was motivated by a recently proposed hypothesis suggesting a specific role for the ACC in monitoring the presence of conflict during information processing (Carter *et al.*, 1998; Botvinick *et al.*, 2001). Our goals for the study were two-fold: (i) to better operationalize minimal task situations which would be expected to elicit processing conflict; and (ii) to characterize the role of the ACC in these situations. We suggested that even in simple choice discrimination tasks, response-related conflict should reliably occur under conditions where a low-frequency response is required in the context of making other, high-frequency responses. Consequently, we predicted that these task situations would be associated with increased ACC activity, regardless of the specific nature of the task. In contrast, we predicted that in task situations where different responses are given with equal frequency, we would not see differential ACC activity across response types. To test this prediction, we used event-related fMRI to measure brain activity during the performance of three choice discrimination tasks: response inhibition (Go/No-go), target detection ('odd-ball'), and response selection (two-alternative forced-choice). Consistent with our prediction, we observed a reliable and equivalent ACC response to low-frequency events in all three tasks. Furthermore, in conditions of these tasks where responses occurred with equal frequency, we did not detect any differential ACC response.

These findings regarding the nature of ACC activity are consistent with previous work. In a similar event-related fMRI study, Kiehl *et al.* (2000) identified a ACC region that was engaged by both Go/No-go and target detection tasks. Using PET methods, Kawashima *et al.* observed ACC activity in both Go/No-go and response selection tasks (Kawashima *et al.*, 1996). In a blocked fMRI Go/No-go study, de Zubicaray *et al.* found that an ACC region was sensitive to No-go frequency, with the greatest activity found when No-go trials were the lowest frequency (de Zubicaray *et al.*, 2000). The current study ties together and extends these previous findings, by showing that the same ACC region is engaged in all three conditions – response inhibition, target detection, and response selection – and that in all conditions, event-related activity is modulated by the frequency of the relevant event. This latter characteristic of the ACC response also provides an account of the one study (Konishi *et al.*, 1998) failing to observe ACC activity associated with response inhibition in the Go/No-go task. Our findings suggest that the ACC does not show a 'No-go-dominant' response when No-go trials occur with equal frequency as Go trials. In other words, ACC activity in the Go/No-go, and other simple choice discrimination tasks, reflects the conflict that occurs to low-frequency versus high-frequency responses. When the two responses are of equal frequency, there is no differential conflict between them, and thus no difference in ACC activity.

Furthermore, the current results are of particular interest because they suggest that the ACC response in these tasks is primarily linked more to the requirement to make low-frequency responses than it is to the particular distinguishing features of any of the tasks – response inhibition, target detection, or

Table 4
Regions showing preferential response to one task condition in disjunction analyses

Regions of interest	Brodmann area(s)	X[a]	Y[a]	Z[a]	No. of voxels
Response inhibition					
Right dorsolateral prefrontal cortex	46/9	32	39	30	54
Right posterior prefrontal cortex	44/45	44	9	27	86
Right ventrolateral prefrontal cortex	44/6	50	6	9	15
Right anterior cingulate cortex	32	11	18	33	10
Right SMA	6	14	6	57	10
Right temporal cortex	21/37	53	–54	3	22
Right parieto-occipital cortex	40/19	26	–69	30	51
Right inferior parietal cortex	40	50	–42	33	63
Left inferior parietal cortex	40	–56	–48	30	43
Right superior parietal cortex	7	14	–72	48	16
Right superior parietal cortex	7	32	–57	60	8
Target detection					
SMA	6	2	–3	57	12
Mid-cingulate cortex	24	–2	–6	45	15
Left motor cortex	1/2/3/4	–35	–30	51	302
Left superior temporal cortex	22	–47	–6	6	26
Left tempo-parietal cortex	42/40	–53	–27	24	16
Left occipital cortex	19/37	–35	–72	–15	9
Right cerebellum	–	32	–52	–42	8
Response selection					
Right SMA	6	20	–12	57	19

[a]*X*, *Y* and *Z* are coordinates in a standard stereotactic space (Talairach and Tournoux, 1988) in which positive values refer to regions right of (*X*), anterior to (*Y*) and superior to (*Z*) the anterior commissure (AC).

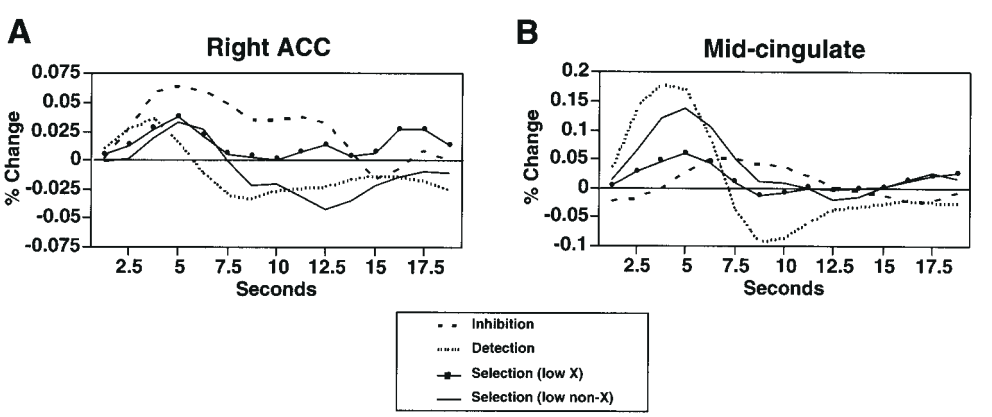

Figure 4. Time course of event-related response in cingulate regions identified in exploratory analyses. (*A*) Inhibition-sensitive region in right ACC. (*B*) Detection-sensitive region in mid-cingulate.

response selection. Moreover, it is particularly noteworthy that in both the inhibition and detection tasks, the conflict appears to be generated from competition between the generation of a single response and the suppression of that response rather than competition between multiple different responses. Thus, the results raise an important issue regarding the nature of conflict. A key avenue of support for the conflict hypothesis has been computational simulations of conflict dynamics during performance of tasks eliciting ACC activity (Botvinick *et al.*, 2001). However, in previous simulation studies, conflict was simulated in terms of direct competition between multiple different response representations. In the current model of ACC activity, it is not clear how conflict would arise with only a single response representation, as in inhibition and detection tasks. One interpretation of the finding that ACC activity is present in these tasks is that there is an internal representation of 'don't respond' that becomes activated, and which competes with other representations of overt responses. This interpretation is consistent with recent primate studies examining response inhibition in the countermanding saccade paradigm (Stuphorn *et al.*, 2000). In these studies, in the activation level of medial frontal cortex neurons (in supplementary eye field) was found to be directly related to the degree of co-activation of gaze-shifting (i.e. 'respond') and gaze-holding (i.e. 'don't respond') neurons. Alternatively, it is still possible that the current pattern of results could occur without postulating such an internal mechanism that actively represents response withholding. Thus, it remains a challenge to determine whether the current pattern of results can in fact be captured in computer simulations of ACC activity using a conflict detection mechanism that is based on competition between different response representations.

We also replicated previous findings implicating the ACC in the processing of errors (Carter *et al.*, 1998; Kiehl *et al.*, 2000). In our previous work (Carter *et al.*, 1998), error-related and conflict-related activity were co-localized within the same region of ACC, which would suggest that this region does not respond to errors *per se*, but rather the increased conflict that typically results in error commission. The results of our confirmatory analyses of ACC activity corroborate the Carter *et al.* (1998) findings (which also used an confirmatory approach). Specifically, the confirmatory ACC ROI showed both generalized conflict-related activity as well as a response to errors. Moreover, although the ACC response was greater to errors than to correct trials, there was still a significant response to low-frequency events, even when only correct response trials were considered. Although the greater ACC response to error versus high-conflict correct trials may seem to pose a problem for the conflict hypothesis, in fact, the model predicts exactly this pattern of results (Botvinick *et al.*, 2001). This is because error trials are associated with even higher levels of activity in the incorrect response pathway (which is what leads to the error) compared to equally high-conflict trials in which the correct response is eventually made.

At first blush, the current findings and those of Carter *et al.* (1998) appear to be incompatible with the error and conflict-related effects observed in ACC by Kiehl and colleagues (Kiehl *et al.* 2000). Kiehl *et al.* (2000) used an exploratory analysis approach, and observed an apparent dissociation between ACC regions responding to conflict versus error commission in the Go/No-go and target detection tasks. In their study, a more rostral, inferior ACC region was associated with error commission, whereas a more caudal, superior ACC region was identified both during low-frequency No-go and target detection trials. Interestingly, the results of our exploratory analyses align fairly closely to the results of Kiehl *et al.* (2000). Specifically, the low-frequency conjunction analysis identified a more superior caudal region of ACC extending into SMA (z = +36 to +60) whereas the error analysis a more rostral inferior region of ACC (z = +18 to +36). It is worth noting that these two different ACC regions have been subdivided by other authors based on both functional and anatomical criteria (Paus *et al.*, 1993; Devinsky *et al.*, 1995; Picard and Strick, 1996). In particular, Picard and Strick (1996) have suggested a subdivision of anterior cingulate into three different functional zones, caudal cingulate zone (cCZ), posterior rostral cingulate zone (rCZp), and anterior rostral cingulate zone (rCZa). Based on their criteria, the frequency-sensitive ACC region is located on the border between the cCZ and rCZp, while the error-sensitive ACC region is located clearly within the rCZa. The fact that the two different regions identified in the current study map onto two different putative anatomic zones within ACC lends further credence to the hypothesis that these regions are functionally dissociated.

How is it that confirmatory and exploratory analyses of ACC activation [performed both in the current study, and in the studies by Carter *et al.* and Kiehl *et al.* (Carter *et al.*, 1998; Kiehl *et al.*, 2000)] yield such differing results? In the current study, the pattern can be explained by the fact that the centroid of the ACC ROI defined for the confirmatory analysis (based on the results of a meta-analysis of conflict tasks) is located in the overlap between the two subregions identified in the exploratory analyses of error and frequency effects (at z = +35). This accounts for why that region shows both strong error and conflict effects. Thus, it is possible that there exists some continuous functional differentiation within the ACC itself along a caudal–rostral superior–inferior dimension, from regions more specifically sensitive to conflict (including the conflict occurring during errors) to regions more sensitive to other aspects of information processing more specifically tied to errors. For example, it is possible that the inferior ACC region is more sensitive to affect-related components associated with error commission (Devinsky *et al.*, 1995; Whalen *et al.*, 1998). However, it must be noted that the apparent dissociation was also one of specialization rather than complete selectivity. Specifically, the caudal ACC region *did* show responsivity to errors, and the rostral ACC *did* show responsivity to conflict. It was only the case that the relative magnitude of the two types of response differed among the regions (i.e. conflict > errors in caudal ACC and errors > conflict in rostral ACC). This could also explain why confirmatory analyses (i.e. performed on ACC ROIs defined through some other criteria) might reveal both error and conflict effects in the ACC. In particular, the greater statistical power afforded by a confirmatory analysis increases the chances of detecting effects that may not be robust enough to survive an exploratory analysis using conservative statistical criteria for false positive protection.

Our exploratory analyses also identified other brain regions besides ACC that showed a generalized response to low-frequency events. We observed similar patterns of activity in a network of regions, including frontal operculum, superior parietal cortex, SMA and dorsolateral prefrontal cortex. The particular functions of these different regions during task performance may be somewhat different from that played by the ACC. In particular, it has been frequently suggested that low-frequency events engage an orienting response, which serves to focus attention on potentially salient changes in the environment (Luria, 1973). This orienting response might

account for the activation of parietal and dorsolateral prefrontal cortex, as these regions have long been thought to play a role in orienting attention to rare or novel events (Knight, 1984; Posner and Petersen, 1990; Halgren *et al.*, 1998; Corbetta *et al.*, 2000). Additionally, executing or suppressing low-frequency responses is likely to be require more extensive motor planning and response selection procedures. This is consistent with our finding of activity in SMA and frontal operculum. Activity in the frontal operculum has frequently been noted in tasks involving difficult response selection decisions (Nathaniel-James *et al.*, 1997; Thompson-Schill *et al.*, 1997).

In addition to identifying brain regions showing generalized responses to low-frequency events through conjunction analyses, we also observed brain regions showing a heightened response to one of the task conditions. Our findings are very consistent with previous neuroimaging studies of response inhibition, target detection and response selection. In the current study, we observed preferential activity associated with inhibition in dorsolateral and ventrolateral PFC, posterior parietal cortex and SMA. Furthermore, the pattern of activity was almost wholly right-lateralized. Nearly identical observations have been noted in other event-related studies of the Go/No-go, such as that of Kiehl *et al.* (Kiehl *et al.*, 2000) and Garavan *et al.* (Garavan *et al.*, 1999) as well as other blocked fMRI and PET studies (Kawashima *et al.*, 1996; Casey *et al.*, 1997; de Zubicaray *et al.*, 2000). However, our study is the first to show this event-related pattern of selectivity in a direct comparison against two other similar tasks – target detection and response selection. Interestingly, we also noted a small region of activity within the right ACC showing preferential activation during response inhibition. This result is hard to interpret, given that it was not predicted by the conflict hypothesis. However, the finding of an inhibition-selective ACC region, along with the slight differences in the centroids of ACC activation for frequency effects versus error commission, suggests the possibility of functional specializations within subregions of the ACC. Given that these subregions are very near those showing generalized conflict effects, one interpretation is that these regions are specialized to respond to different sources of conflict, such as those specifically related to inhibition, error commission, or possibly the affective responses associated with those situations. Future work is needed to further test these hypotheses.

We also observed heightened responses in specific brain regions associated with response selection and target detection tasks. In the response selection, only a single region within SMA showed such a pattern. However, the location of this region is consistent with the idea that higher-order motor planning areas would be involved in the selection of a low-frequency response over a more frequently executed one. Moreover, in a very similar response selection task, Kawashima *et al.* also found preferential activity in a superior frontal region near SMA (Kawashima *et al.*, 1996). The brain areas showing a heightened response during target detection showed a very different distribution from those sensitive to response inhibition. Prominent activation was observed in left hemisphere superior temporal cortex and tempoparietal junction, as well as in a mid-cingulate (rather than anterior cingulate) region corresponding to the well-known cingulate motor area (Picard and Strick, 1996). The pattern of activation in these regions replicates numerous previous studies of the target detection or oddball task (Reinsel *et al.*, 1996; Menon *et al.*, 1997; Linden *et al.*, 1999; Opitz *et al.*, 1999), including event-related fMRI studies that have demonstrated these regions become activated when responding to low-frequency target stimuli (Kiehl *et al.*, 2001).

The selective response of these regions to detection of targets was demonstrated most strongly in the equal-frequency condition, where a significant event-related response was observed even when targets occurred with the same frequency as non-targets. This finding demonstrated that the response of these regions occurs irrespective of the frequency of target events. Moreover, the response in mid-cingulate and tempoparietal cortex was significantly greater than that found during the equal-frequency response selection condition, which further suggests that the target-related response cannot be explained by differential sensitivity to one stimulus or response hand.

It is noteworthy that we did not observe an analogous pattern of preferential responding in any of the inhibition-related brain regions to No-go trials in the equal-frequency condition. None of the brain regions showing heightened activity during low-frequency response inhibition showed any hint of an event-related response during the equal-frequency condition. This finding is at odds with other studies, such as Konishi *et al.*, which have observed 'No-go-dominant' patterns of activity in dorsolateral prefrontal regions even under conditions of equal frequency Go and No-go trials (Konishi *et al.*, 1998, 1999). One possible explanation of the discrepancy between our findings and those of Konishi *et al.* is that our study used a very rapid pace of stimulus presentation (1.25 s per trial), whereas Konishi and others have used a more slow-paced designs (10–15 s per trial). This difference in task pacing may have significantly affected strategies engaged by subjects during task performance. For example, it is possible that the rapid pace of the task induced subjects to treat it more as a target detection than a Go/No-go task. Future research will be needed to investigate this possibility more directly.

In summary, the current study indicates that ACC is reliably activated by the requirement to make low-frequency responses across multiple different types of simple choice discrimination tasks. The ACC response was consistently greater for low-frequency than high-frequency responses, but did not differentiate between response types when these responses occurred with equal frequency. This finding is consistent with the idea that ACC serves as a generic detector for the presence of processing conflict, particularly when this conflict occurs at the response stage of processing. The results also complement well our recent work showing a generalized ACC response to response conflict situations across multiple response modalities and processing domains (Barch *et al.*, 2001). However, it is important to note that the finding of generalized frequency-sensitive responding within the ACC does not in and of itself allow for the rejection of alternative interpretations of ACC function. Indeed, the pattern of frequency-sensitive responding observed in the ACC is also consistent with other possible functional interpretations, such as attentional orienting, motor planning, and response selection. As discussed above, we have suggested that these other functions might best characterize the engagement of other identified brain regions showing a consistent response to low-frequency events (e.g. prefrontal and parietal cortex in attentional orienting). Nevertheless, the pattern of ACC activation in the current study converges well with the growing number of studies supporting the conflict hypothesis of ACC function (Botvinick *et al.*, 1999; Barch *et al.*, 2000, 2001; Carter *et al.*, 2000; Casey *et al.*, 2000; MacDonald *et al.*, 2000), and thus make the conflict detector hypothesis our favored interpretation. Furthermore, our additional finding that

ACC subregions are preferentially activated by response inhibition and error commission leave open the possibility that there is further functional specialization within ACC for different types of response-related conflict. The question of what is the specific nature of these differences in types of conflict awaits further study.

Notes

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