Cingulate Activation Increases Dynamically with Response Speed under Stimulus Unpredictability

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Functional magnetic resonance imaging studies of cognition require repeated and consistent engagement of the cognitive process under investigation. Activation is generally averaged across trials that are assumed to tax a specific mental operation or state, whereas intraindividual variability in performance between trials is usually considered error variance. A more recent analysis approach postulates that these fluctuations can reflect variation in the very process taxed by the particular trial type. In the present study, participants responded to targets presented randomly in 1 of 4 peripheral locations. By employing a function of reaction time (RT) of individual trials as a linear regressor, brain regions were identified whose activation varied with RT on a trial-by-trial basis. Whole-brain analysis revealed that the anterior cingulate, posterior cingulate, and left angular/superior temporal gyri were more active in trials with faster RT but only when the target location was unpredictable. No such association was seen in trials where the target location was predicted by a central cue. These results suggest a role for the cingulate and angular gyri in the dynamic regulation of attention to unpredictable events. This is in accordance with the function of a default network that is active in the absence of top-down-focused attention and is thought to continuously provide resources for broad and spontaneous information gathering. Exploiting intertrial performance variability may be particularly suitable for capturing such spontaneous and elusive phenomena as stimulus-driven processes of attention.

Keywords: anterior cingulate, attention, bottom-up, intertrial variability, posterior cingulate, reaction time

Introduction

Functional magnetic resonance imaging (fMRI) studies of cognition (for a review of designs, see Aguirre 2003) require repeated engagement of the cognitive process under investigation. Activation is typically averaged across trials that are assumed to evoke a specific (set of) mental operation upon each presentation. The approach relies heavily on the consistent engagement of this operation across trials. Both inter- and intraindividual variability in performance between trials of the same type are usually considered error variance. If this variance is large, it results in a loss of sensitivity and reduces the likelihood that neural correlates of the process of interest can be detected.

However, performance variability has also been exploited to obtain deeper insight into associations between cognitive and brain functions. For this approach, it is assumed that variation in performance in part reflects variation in the cognitive process under investigation. Thus, variability in a task-relevant mental operation is used as a probe to identify brain structures engaged by this process. On an interindivdual level, an approach is to correlate subjects’ average performance with activation in predefined regions, or to perform a median split on individual performance values and test for group differences in brain activation or vice versa (e.g., Lawrence and others 2003; Hester and others 2004). In contrast, an intraindividual approach postulates that trial-by-trial fluctuations in performance covary with fluctuations in the very cognitive processes taxed by this trial type. Thus, a measure of individual trial performance is employed as a regressor, a common example being discrete performance events such as errors (e.g., Carter and others 1998; Hester and others 2004). Furthermore, recent studies successfully employed trial-by-trial reaction time (RT) as a regressor to verify regional engagement by external stimulus processing demands (Gilbert and others 2006) or by specific functions of language processing and generation (Binder and others 2005; Desai and others 2006). Another recent study related trial-by-trial performance accuracy to the blood oxygen level-dependent (BOLD) time course to demonstrate that cue-induced regional activity dynamically predicted target detection (Sapir and others 2005).

The differing approaches of averaging activation across trials or of exploiting intertrial variability may be optimal for capturing different phenomena. If some cognitive processes can be evoked more consistently than others then intertrial fluctuations in these processes may tend to be of different magnitudes. In the present study, it was hypothesized that a simple operation initiated by a clear instructive cue, such as attending to a specific spatial location in anticipation of a stimulus, would be evoked more reliably than a more spontaneous phenomenon such as shifting attention to an unpredicted stimulus. Thus, exploiting the intertrial variability could be a more sensitive approach for detecting those brain regions that regulate more elusive cognitive phenomena that unfold in the absence of clear top-down control signals and that are involved in dynamic and spontaneous behavioral adjustments.

The intertrial variability of RT was used as the basis for analyzing data from a stimulus detection paradigm designed to differentiate neural substrates of top-down and bottom-up processes of visuospatial selective attention. Top-down or endogenous attentional control is intentional and directed by knowledge, expectation, and current goals. Bottom-up or exogenous attention, in contrast, is stimulus driven, that is, attention is spontaneously oriented toward an oncoming stimulus (Desimone and Duncan 1995; Egeth and Yantis 1997). In the current paradigm, by manipulating the predictability of the location of a target stimulus, attention could be either allocated endogenously to this location in advance of target onset or had to be oriented rapidly upon target onset. The purpose of the present study was to identify those brain regions
whose activation tended to coincide with fast RT, either under conditions of stimulus predictability that allowed top-down regulation of attention or under conditions of stimulus unpredictability where attention had to be shifted spontaneously.

Methods

Subjects

Subjects were 22 healthy, right-handed adults (13 females, 27.5 ± 7.55 years of age), who were recruited from the general population through advertising and referrals and gave informed consent for a protocol approved by the National Institute on Drug Abuse, Intramural Research Program Institutional Review Board. All participants were nonsmokers and had been asked to consume no more than half a cup of coffee in the 12 h preceding magnetic resonance (MR) scans and no alcohol in the preceding 24 h. Subjects were screened for major medical illnesses, claustrophobia, history of neurological or psychiatric disorders and drug abuse, pregnancy, and appropriateness for magnetic resonance imaging (MRI).

Procedure

The protocol required 3 separate visits. During the first visit, participants gave written informed consent and were trained on 2 cognitive tasks, initially on a bench computer and then in a mock scanner that mimicked all properties of the MRI scanner. Training in the mock scanner was equal in length to when the tasks were performed in the real scanner. Sessions 2 and 3 were identical and served as time controls for a pharmacological experiment reported elsewhere. Prior to both MR scans, participants were tested for recent drug use (TRIAGE®) and for alcohol intake or smoking via breath analysis; a pregnancy test was given to female participants. Subjects then received a 10-min reminder task training on a bench computer, during which their eye position was recorded. MR scans started with a brief central executive task (data not reported). Eight blocks of the spatial attentional resource allocation task (SARAT) were then performed, separated by 1-min rest periods, followed by anatomical scans. A previous report analyzed the same data set based on trial averages (Hahn and others 2006).

Paradigm

The SARAT required participants to detect a target signal (500 ms) that could occur at any of the 4 peripheral locations marked by empty circles (Fig. 1). Subjects were asked to keep their eyes fixated on a central circle containing a fixation cross during performance of the task. Target locations were positioned at 10°–12.5° of visual angle. Targets consisted of a circle filling with a checkerboard of gray and white squares of 3 × 3 pixels each. Two different target intensities (high: 80% gray, low: 20% gray) were tested. Upon presentation of a target, subjects were instructed to press a button with their right index finger as quickly as possible.

Cues appeared in the central circle ±3, 700, 1000, or 1300 ms (variable stimulus-onset-asynchrony [SOA]) prior to target onset and remained on display until 1000 ms after target onset, that is, until 500 ms after target termination. Cues consisted of quarters of the fixation circle turning black with their location indicating the probable location of the peripheral target. One, two, three, or four quarters could turn black simultaneously. Thus, predictability of the target location varied across trials with one cued location providing the most precise advance information and 4 cued locations leaving the target location completely unpredictable. The cue provided invalid information in 20% of trials with 1, 2, or 3 cued locations. In some trials, the cue was not followed by a target. Valid trials with high-intensity targets, valid trials with low-intensity targets, and no-target trials were presented with equal frequency. All trial types were randomized within runs. To create sufficient temporal jitter for event-related analysis, no-event trials, where no cues or targets were presented, were randomly interspersed. Trial duration was 2.7 s (Fig. 1). Each of the 8 runs consisted of 81 trials; 32 valid target trials, 16 no-target trials, 6 invalid target trials, and 27 no-event trials, resulting in a run duration of 3:39 min.

For the current study, only valid target trials with one cued location (referred to as "CUED trials") or 4 cued locations (referred to as "UNCUED trials") were analyzed. Only those trials where a subject response occurred were analyzed. Thus, the study focused on 2 conditions: 1) a target is detected at a location to which attention was allocated endogenously prior to target onset and 2) the target location was unknown until target onset, at which point attention is drawn to this location by the physical appearance of the target stimulus.

Eye Tracking

Eye position on the screen was recorded during performance of the 10 min refresher training that preceded each MR scan, using a remote eye-tracking system consisting of a video camera and infrared light source (VIEW, Sensomotoric Instruments Inc., Needham, MA). The purpose was to verify that the task was not performed by refocusing the gaze to where the target was expected. This could have resulted in eye movement–related brain activation that differed systematically between CUED and UNCUED trials, thus potentially confounding results. Eye tracking was not performed in 8 subjects due to equipment unavailability. As described previously (Hahn and others 2006), participants for whom eye position was recorded spent 98.2 ± 2.8% of the time that eyes were directed at the screen fixating no further than 3° from its center. No participant displayed any indication that fixations outside this radius were systematically oriented toward target locations. Furthermore, the absolute distance of subjects’ gaze position from the center of the screen did not differ between CUED and UNCUED trials, neither for the vertical nor horizontal direction (t12 < 1 for each direction).

Magnetic Resonance Imaging

Scanning was performed on a 3-T Siemens Allegra scanner (Erlangen, Germany). Whole-brain functional echo planar images were acquired for measurement of T2*-weighted BOLD effects (4 mm sagittal slices, 64 × 64 matrix, field of view = 22 × 22 cm, time repetition [TR] = 2.7 s, time echo [TE] = 27 ms, flip angle [FA] = 85°). In each scanning session, a whole-brain sagittal T1-weighted structural image (magnetization-prepared rapid gradient echo) was acquired for anatomical reference (1 mm3 isotropic voxels, TR = 2.5 s, TE = 4.38 ms, FA = 8°).

Analysis of MRI Data

Data were processed using the AFNI software package version 2.55j (Cox 1996). Motion correction was performed by volume registering each 3-dimensional volume to a base volume. The time series was then analyzed by voxelwise multiple regression, where the main regressor of

Figure 1. Components of a CUED and an UNCUED target trial in the SARAT. Onset of a central cue preceded target onset by a variable SOA of 400, 700, 1000, or 1300 ms. The target was presented for 500 ms in the continuing presence of the cue, which remained on display until 500 ms after target offset. Only screen background was then presented for an intertrial interval that varied in length such that total trial duration was always 2700 ms.
interest was related to the RT of individual trials. To ensure that RT variability did not reflect shifts in response speed with time on task due to practice or fatigue, RT averaged across all valid target trials was compared between the 8 runs by paired t-tests, with Bonferroni adjustments made for 28 comparisons. RT was significantly faster in run 1 than in runs 2, 4, 5, and 7 (t31 > 3.9, P < 0.05 for each comparison), whereas RT in runs 2-8 did not differ significantly from each other. Thus, the regression analyses were based only on trials from runs 2-8, throughout which average RT appeared stable over time. Regressors were expressed as a simple delta function convolved with a model hemodynamic response function and its temporal derivative.

The RT regressor was a function of individual trial RT, that is, its amplitude was scaled according to these trial-by-trial values. For this regressor, the RT of individual trials i was expressed as \( \frac{1}{\sigma_{RT}^2} \), in order to optimize normal distribution as determined by Box-Cox transformation (Box and Cox 1964). These values were expressed as differences from the mean of each individual session in units of standard deviation. This was the standard deviation per session, averaged across subjects and sessions. Thus, although \( \frac{1}{\sigma_{RT}^2} \) was standardized relative to session means of each individual participant, the unit in which these values were expressed corresponded to the same net \( \frac{1}{\sigma_{RT}^2} \) change in all participants. The beta weight of this regressor represents the factor by which it had to be multiplied to best fit the data. Thus, this beta weight reflects the amplitude of activation change per standardized \( \frac{1}{\sigma_{RT}^2} \) unit and is equivalent to the slope of the association between \( \frac{1}{\sigma_{RT}^2} \) and voxelwise activation. This beta weight is henceforward referred to as betaslope. A separate betaslope was determined, in each session, for CUED and UNCUED trials with high and low target intensity.

Additional regressors corresponded to 18 different trial types (CUED/UNCUED × high/low target intensity), voxelwise betaslope, and betamean values were normalized to baseline for each subject and each test session. The resulting maps were resampled to a higher (1 μl) resolution, converted to standard stereotaxic space (Talairach and Tournoux 1988), and spatially blurred using a Gaussian 4.2-mm full width half maximum isotropic kernel.

Functional regions of interest (ROIs) were derived by performing voxelwise 1-sample, random effects t-tests against zero on betaslope, separately for CUED and UNCUED trials averaged over target intensity. One-tailed t-tests were performed, testing only for voxels with a significantly positive betaslope, that is, an increase in activation with faster RT. Increases in activation with slower RT could simply reflect a longer period of neuronal activation. A range of previous studies employing simple sensory stimulation paradigms reported that the BOLD signal increased in amplitude with prolonged or repeated stimulation (e.g., Boynton and others 1996; Dale and Buckner 1997), even on a millisecond scale (Robson and others 1998). Thus, in trials where more time is spent on signal processing or response preparation, voxels of underlying brain regions may display higher signal amplitude as a direct result of their longer engagement. Such effects were not of interest in the present investigation. Areas that increased in activation with slower responding were extensive and are listed in Supplementary Table S1.


dMRI

One-sample t-tests performed on voxelwise average betaslope of CUED trials did not identify any region that activated with faster responding. In contrast, 1-sample t-tests performed on voxelwise betaslope of UNCUED trials identified 3 regions whose activation was positively related to response speed: rostral anterior cingulate gyrus, posterior cingulate gyrus, and left inferior parietal lobule in the area of the angular gyrus, possibly reaching into superior temporal gyrus (STG) (Table 1 and Figure 2). RT (mean ± standard error of mean) differed with SOA, and this effect depended on trial type (***P < 0.05, **P < 0.01, ***P < 0.001, paired t-tests).

### Results

**Performance of the SARAT**

Detailed behavioral analyses across all trial types can be found in Hahn and others (2006). Briefly, RT decreased parametrically with increasing cue precision and was faster with high than low target intensity. Three-factor repeated measures ANOVA of the 4 trial types included in the present study (CUED and UNCUED, each with high or low target intensity) revealed main effects of cue condition (\( F_{2,21} = 67.4, P < 0.001 \)) and target intensity (\( F_{2,21} = 164.4, P < 0.001 \)) but no cue × target interaction, confirming that average RT was overall faster in CUED than UNCUED trials (340 ± 81 vs. 457 ± 83 ms) and faster with high- than low-intensity targets (421 ± 80 vs. 466 ± 85 ms). The main effect of SOA (\( F_{2,63} = 12.7, P < 0.001 \)) was due to shorter RT at the 2 intermediate SOA (Fig. 2). Also the SOA × cue interaction was significant (\( F_{2,63} = 4.0, P < 0.05 \)); the RT difference between CUED and UNCUED trials was particularly large with SOA 700 ms, where CUED RT was substantially lower than in all other conditions. Accordingly, the effect of SOA in 1-way ANOVA was more pronounced in CUED (\( F_{2,63} = 13.1, P < 0.001 \)) than in UNCUED trials (\( F_{2,63} = 4.77, P < 0.01 \)). The fact that RT differed with SOA necessitated controls for the possibility that associations between RT and BOLD signal were secondary to regional responsivity to SOA.

### Table 1

<table>
<thead>
<tr>
<th>Brain region</th>
<th>Side</th>
<th>Center of mass (mm)</th>
<th>Brodmann areas</th>
<th>Volume (μl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior cingulate gyrus</td>
<td>B</td>
<td>1.8, 41.2, 13.2</td>
<td>24, 32</td>
<td>5427</td>
</tr>
<tr>
<td>Posterior cingulate gyrus</td>
<td>B</td>
<td>-0.2, -43.6, 28.3</td>
<td>23, 31, 30</td>
<td>2131</td>
</tr>
<tr>
<td>Angular gyrus/STG</td>
<td>L</td>
<td>-47.4, -64.5, 31.1</td>
<td>39</td>
<td>541</td>
</tr>
</tbody>
</table>

Note: Regions in Talairach space where the BOLD signal intensity increased linearly with SOA is that, with faster responding, on a trial-by-trial basis. B, bilateral; L, left.
Fig. 3. Anterior cingulate cortex (ACC) activation was located mostly in areas 24a, b, c, and 32, as defined by Vogt and others (1995), with little spread into areas 24a' and b' and no overlap with areas 24c' and 32'. Activation within the posterior cingulate cortex (PCC) comprised regions 23a and b, but not c, with spread also into areas 31 and 30.

In all 3 regions, 3-factor ANOVA for repeated measures revealed a significant main effect of cue condition ($F_{3,21} > 8.27, P < 0.01$ in each region). One-sample $t$-tests against zero confirmed significantly positive beta slope in UNCUED trials ($t_{21} > 4.56, P < 0.001$ in each region), but not in CUED trials ($t_{21} < 1.47, P > 0.05$). Figure 4 displays the association between $\frac{1}{RT}$ and activation in each of the 3 regions, separately for CUED and UNCUED trials. Beta slope neither differed between sessions or target intensities nor did the effect of cue condition interact with these factors in any region. To test whether the

![Figure 3](image-url)

**Figure 3.** Brain regions whose activation in UNCUED trials increased with $\frac{1}{RT}$ on a trial-by-trial basis. Group activation maps are overlaid onto one anatomical scan in Talairach space. All 3 regions significantly increased in activation with faster responding in UNCUED but not in CUED trials. Activation is expressed as the percentage of change in the amplitude of activation per standard deviation (stdev) unit of change in $\frac{1}{RT}$.

![Figure 4](image-url)

**Figure 4.** Activation in the anterior and posterior cingulate and in the left angular gyrus plotted against $\frac{1}{RT}$ for CUED and UNCUED trials. Graphs are based upon measured beta weights. A significant positive association is observed in UNCUED but not in CUED trials.
difference in beta_{d-loop} between CUED and UNCUED trials may have been related to larger intertrial RT variability in UNCUED trials, intraindividual variability was compared between CUED and UNCUED trials. The average standard deviation of RT in CUED trials (120.0 ms) and in UNCUED trials (117.5 ms) did not differ ($t_{21} < 1$, paired $t$-test).

The differential BOLD-RT association in UNCUED trials could not have reflected regional responsivity to SOA. First, SOA effects on RT were more pronounced in CUED trials, where the 3 ROIs did not display any such brain-behavior relationship. Second, these regions were not responsive to SOA; the same data set had previously been analyzed for separate SOAs (for methods, see Hahn and others 2006), and these activation values were averaged across voxels of each of the present ROIs. Two-factor ANOVA for repeated measures identified no effect of SOA ($F_{3,63} < 1.5$, NS, for each of the 3 regions) and no interaction of SOA with cue condition ($F_{3,63} < 2.62$, NS).

Next, the average activation beta_{mean} was determined within each region for each cue condition, session, and target intensity and analyzed by 3-factor repeated measures ANOVA. A significant main effect of cue condition was identified in the ACC and PCC ($F_{1,21} > 5.0$, $P < 0.05$) but not in the left angular gyrus ($F_{1,21} = 1.79$, NS). Figure 5 shows that in both structures, this was due to negative mean activation values in CUED trials and positive values in UNCUED trials. However, in 1-sample $t$-tests, average activation did not differ from zero in either CUED or UNCUED trials ($t_{21} < 1$ for both trial types and regions). The effects of cue did not interact with session or with target intensity in any region.

To test whether each region’s average activation was associated with average RT on an interindividual basis, Pearson correlations were determined between beta_{mean} and average RT, separately in CUED and UNCUED trials. There were no significant correlations ($P > 0.2$ in each case).

**Discussion**

The present study identified 3 brain structures whose signal amplitude was related to performance of a visuospatial stimulus detection task on a trial-by-trial basis. Activation in the ACC, PCC, and left angular gyrus/STG was positively associated with response speed, and this association occurred only in the condition where stimuli were detected at unpredictable locations. When the target location was predicted by a central cue, no region was found to be more active in trials with faster RT. Thus, whereas RT variability in UNCUED trials in part reflected fluctuation rooted in the function of specific brain areas, variability of RT in CUED trials, despite being of equal magnitude, may have constituted variance not based on task-specific brain processing.

Although we hypothesized that covariation between regional activation and trial-by-trial performance reflects fluctuation in an underlying cognitive function, the ACC is also known as an effector region that controls output to skeletomotor systems (Vogt and others 1992). As such, activation that accompanies faster responding could also be a reflection of more efficient response initiation. In monkeys, one area of ACC and one of PCC were activated by voluntary hand movements (Shima and others 1991). They were located in area 24c (mostly c) of the anterior and 23c of the posterior cingulate sulcus, consistent with cingulate motor areas localized by retrograde labeling and intracortical microstimulation (Dum and Strick 1991; Lupino and others 1991; Morecraft and Van Hoesen 1992; Nimchinsky and others 1996; Wang and others 2001). Notably, these cingulate subregions did not overlap with those identified in the present study. Similarly, in a human positron emission tomograph study, the area of ACC that displayed a rise in blood flow when subjects made manual responses (but not when responding verbally or by saccades) was located in posterior parts of the anterior cingulate sulcus (Paus and others 1993), remote from the current regions. Thus, the current association between cingulate activation and RT most likely is not based on variation in a motor output but in a stimulus-processing function.

Covariation between RT and regional activation does not however answer the question of causality, that is, if activation facilitated fast responding or if it constituted a response to fast RT, for example reflecting rapid performance evaluation. In ACC, rapid (250-300 ms) neuronal responding to performance feedback is a well-studied phenomenon (Ridderinkhof and others 2004), but such responses are larger in amplitude for negative than positive feedback (Holroyd and Coles 2002; Ullsperger and von Cramon 2004). Thus, assuming that the brain is indeed able to differentially process responses with different RTs, one would expect increasing ACC activation with “unsuccessful” slow responding (the instruction was to respond as fast as possible) instead of the increase with faster responding according to which the current regions were identified. Another possibility is that faster responding created more postresponse conflict or uncertainty, that is, it may have unfolded without complete certainty of having detected a target. If this was the case, the association between RT and the BOLD signal would have been stronger in trials with low-intensity targets where such uncertainty must have been more pronounced. However, there was no difference in beta_{d-loop} between trials with high and low target intensity despite large behavioral differences. Overall, regional activation affecting performance appears to be the more likely alternative.

The regions may have fulfilled a preparatory function, mobilizing resources in response to the cue signaling unpredictability of the target location, or they may have constituted the actual resource that supported the spontaneous, rapid orienting toward the target stimulus. Adopting the latter interpretation, the selectivity of covariation between regional activation and RT for the condition of stimulus unpredictability may suggest that exploiting intertrial variability of performance

![Figure 5](image-url)
is a particularly suitable approach to capture phenomena that unfold spontaneously in the absence of voluntary cognitive control, like stimulus-driven orienting of attention. Such processes can be expected to be more difficult to detect with analyses based on trial averages because they are less likely to be engaged in a consistent manner across trials. Indeed, within the regions identified with the intertrial approach, the average activation across trials did not significantly differ from zero in either CUED or UNCUED trials and did not correlate with average RT on an interindividual basis. Thus, by analyzing trial averages, an association of BOLD signal in these regions with UNCUED trial performance would not likely have been detected.

Results from the current analytical approach that evade clear interpretation are increases in regional activity with slower responding (Supplementary Table S1). As mentioned, such a pattern may simply reflect longer neuronal engagement in response-relevant cognitive processes in trials with longer RT. Sensory stimulation experiments showed that prolonging the stimulation duration or adding further stimuli within the time frame of the hemodynamic response to a prior stimulus resulted in fMRI responses that were not only longer but also reached a higher peak (e.g., Boynton and others 1996; Dale and Buckner 1997; Robson and others 1998). Larger response amplitudes were seen even with adding only one 100-ms auditory stimulus after a 100-ms off-period (Robson and others 1998). Although trial-by-trial fluctuations in the present study are based on an even shorter timescale, it is likely that in trials with slower RT, more time is spent on signal processing or response preparation, and it is possible that corresponding brain regions displayed higher signal amplitude as a direct result of their longer engagement. Areas that displayed this pattern indeed included regions involved in functions such as these. It is also possible that lower activation with faster responding reflected an increasing automaticity of responding. A shortfall of the trial-by-trial analysis approach is that increases in activation with longer RT are currently not interpretable.

The present results suggest a role of the cingulate and angular gyri in the dynamic regulation of processing unpredictable, behaviorally relevant signals. For the ACC, this is in agreement with studies reporting activation when performance was not under clear top–down control and there was conflict regarding which stimulus aspect should control performance (Carter and others 1998, 2000; Botvinick and others 1999; MacDonald and others 2000; Kerns and others 2004). These studies supported the notion that the ACC responds to conflict, specifically to response competition, that is, conflict between evoked motor action plans (Carter and others 2000; Milham and others 2001, 2003; Matsumoto and Tanaka 2004). This was consistent with cingulate projections to motor areas discussed above and with the proximity of regions identified by these studies to cingulate motor areas. Few studies reported ACC responsiveness to perceptual or semantic conflict, that is, conflict in the input domain (Weissman and others 2003; van Veen and Carter 2005).

The current behavioral paradigm differed from those typically used to probe the ACC in that it did not evoke any conflict in the response domain. Responses were always made to the same type of stimulus by pressing the same response button with the right index finger, and stimuli were always of the same temporal predictability. Thus, CUED and UNCUED trials enabled the same degree of response preparation. However, only UNCUED trials evoked conflict in the input domain in the form of uncertainty regarding the stimulus location. ACC activation was associated with task performance in these but not in CUED trials that reduced this uncertainty by evoking a visuospatial processing bias in preparation for target detection. Thus, the current findings may extend theories of a late evaluative function of ACC in the absence of advance top–down selection for action, specifically in the input domain of information processing.

Further, there is evidence that some areas of ACC are responsive to the perceived likelihood of committing an error on a given trial (Brown and Braver 2005). In the current paradigm, the percentage of omission errors was slightly higher in UNCUED than CUED trials (11% vs. 14%, Hahn and others 2006), but it is unlikely that participants were aware of this small difference in success rate or even of having missed a target (almost 30% of trials were cue-only trials). A global description of ACC function may be a more general responsiveness to conditions where behavior is not under tight stimulus control and there is uncertainty, be it regarding stimulus processing, response selection, or outcome.

The ACC’s well-known functional heterogeneity (Devinsky and others 1995) beckons the suggestion that different sub-regions respond to different types of conflict or uncertainty. Typically, the ACC has been probed with cognitively demanding tasks that involve high levels of control. These studies report activation in dorsal areas of ACC, such as 24a, b’, c’, and 32’ (Carter and others 1998, 2000; Botvinick and others 1999; MacDonald and others 2000; Milham and others 2001; Weissman and others 2003; van Veen and Carter 2005), termed its cognitive subdivision (Bush and others 2000). ACC responses in these, but not rostral areas, are frequently accompanied by activation in dorsolateral prefrontal cortex (Paus 2001), where they appear to recruit control processes (Kerns and others 2004; Riddelrnikhof and others 2004). It is striking that the current area of ACC associated with simple stimulus detection performance in the absence of top-down selection fell so clearly outside this area and into a rostral region that has been reported to even deactivate during cognitively demanding tasks (Bush and others 2000). We suggest that functions of dorsal and rostral ACC are complementary in that dorsal ACC responds to conflict that demands increased top-down control by other regions, whereas rostral ACC exerts influence over performance when such control would not reduce uncertainty.

An association of rostral ACC activation with RT performance in simple stimulus detection tasks has been observed previously (Gilbert and others 2006). Notably, ACC along with PCC activation occurred when task demands were restricted to remaining alert to external events and was reduced in the presence of higher order cognitive engagement. Generally, rostral ACC displayed preference for simple task conditions involving minimal stimulus processing. The conclusion that rostral ACC plays a role in maintaining attention toward the external environment and all incoming visual information, specifically during low-demand tasks in the absence of internal processing requirements, appears compatible with its current association with unbiased visuospatial stimulus detection.

The association of PCC activation with RT performance likely reflects involvement in fast visuospatial orienting. The current activation largely overlapped with the PCC’s “visuospatial area,” which is involved in spatial orienting and monitoring of visual events, especially in the periphery (reviewed by Vogt and others 1992; Gusnard and Raichle 2001). Importantly, Vogt and others (1992) report PCC responses to previously unattended but
salient peripheral stimuli, but not to attended foveal stimuli, indicating a role in stimulus-driven orienting of attention in space. Gusnard and Raichle (2001) suggested that the PCC provides resources for the rapid and automatic allocation of attention to previously unattended input, enabling the detection of unforeseen events that may be relevant for survival. With regard to the present results, this would be in agreement with PCC activation supporting fast responding to targets when their location was unpredictable, although, as mentioned, the question of causality remains open.

The left angular gyrus/STG activation may be located in the vicinity of an area termed temporoparietal junction (TPJ) shown to be activated by target detection, especially at unexpected locations (Corbetta and others 2000), and suggested to form part of a ventral frontoparietal exogenous orienting system (Corbetta and Shulman 2002). Thus, activation with faster responding selectively under conditions of target unpredictability may be explained by a role in stimulus-driven orienting of attention, for this region, as well. In the above-cited studies, TPJ activation occurred predominantly in the right hemisphere, whereas the current activation was left lateralized, consistent with Hahn and others (2006). This report, based on the same data set as the current study, also demonstrated that activation in or near TPJ was dependent on the presence of a target, suggesting it reflected target-induced activity in accordance with stimulus-driven attentional processes.

One commonality between all 3 anatomical regions is their overlap with areas that consistently displayed higher activation during rest than during various goal-directed behavioral activities (Shulman and others 1997; Mazoyer and others 2001). These areas form part of a network that displayed elevated blood flow and oxygen metabolism under resting conditions and that has been suggested to maintain an organized baseline default mode of brain function (Raichle and others 2001). Thus, these regions display sustained and intercorrelated (Greicius and others 2003) activity at rest that is attenuated by focused attention and that may reflect, among other functions, the continuous provision of resources for spontaneous, broad, and exogenously driven information gathering (Gusnard and Raichle 2001). The present association with performance variability exclusively in the absence of top-down-focused attention supports involvement in regulating attentional resource allocation when the individual is not engaged in a specific endogenous task. UNCUED trials with many possible target locations appear to have created a condition that taps into the broad information-gathering function that may be a default mode of these regions.

In summary, employing trial-by-trial performance variability as a regressor is a sensitive approach to identifying brain regions involved in spontaneous orienting in space. A brain structure with known responsiveness to uncertainty and to the absence of clear top-down control (ACC) was identified, as well as 2 regions with likely involvement in processes of stimulus-driven orienting (PCC, angular gyrus/STG). The present findings expand the view of the ACC’s conflict-monitoring function to include responsiveness to uncertainty in the input domain of information processing and to demands on maintaining broad unbiased attention to the external environment.

Supplementary Material
Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

References

Notes
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