The Role of the Dorsal Anterior Cingulate in Evaluating Behavior for Achieving Gains and Avoiding Losses

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Abstract

■ Effective goal-directed behavior relies on a network of regions including anterior cingulate cortex and ventral striatum to learn from negative outcomes in order to improve performance. We employed fMRI to determine if this frontal–striatal system is also involved in instances of behavior that do not presume negative circumstances. Participants performed a visual target/nontarget search game in which they could optionally abort a trial to avoid errors or receive extra reward for highly confident responses. Anterior cingulate and prefrontal cortex were equally activated for error avoidance and high reward trials but were not active on error trials, demonstrating their primary involvement in self-initiated behavioral adjustment and not error detection or prediction. In contrast, the insula and the ventral striatum were responsive to the high reward trials. Differential activation patterns across conditions for the nucleus accumbens, insula, and prefrontal cortex suggest distinct roles for these structures in the control of reward-related behavior. ■

INTRODUCTION

Prefrontal cortex, anterior cingulate cortex (ACC), and ventral striatum, including the nucleus accumbens (NAcc), constitute a complex brain network that has been implicated in various aspects of goal-directed behavior (Liu et al., 2007; Brown & Braver, 2005; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004; Bush et al., 2002; Holroyd & Coles, 2002; Knutson, Fong, Adams, Varner, & Hommer, 2001). The established role of ACC in reinforcement-learning theories of behavioral control (Brown & Braver, 2005; Botvinick, Cohen, & Carter, 2004; Ridderinkhof et al., 2004; Holroyd & Coles, 2002; Bush, Luu, & Posner, 2000; Gehring, Goss, Coles, Meyer, & Donchin, 1993), which associates negative events such as error detection (Holroyd & Coles, 2002; Falkenstein, Hoormann, Christ, & Hohnsbein, 2000; Gehring et al., 1993; Falkenstein, Hohnsbein, Hoormann, & Blanke, 1991), conflict monitoring (Yeung, Cohen, & Botvinick, 2004; Carter et al., 1998) or prediction of error likelihood (Brown & Braver, 2005), with ACC's aptitude to learn from them in order to improve performance, might have masked the possibility that the cognitive control function of this complex structure may not be limited to monitoring of performance guided by negative events. Consistent with a recent theory of ACC activity reflecting the prediction of error likelihood (Brown & Braver, 2005), our previous study (Magno, Foxe, Molholm, Robertson, & Garavan, 2006) showed ACC activity increases when errors were avoided and not when they were committed. We interpreted this in accord with an evaluation process wherein ACC, perhaps through the estimation of error likelihood, served to improve performance by identifying situations in which an error was likely enabling the error to be avoided. However, although Brown and Braver's theory emphasized the concept of error likelihood as the catalyst for ACC intervention in controlled behavior, our results did not rule out a more general ACC involvement in both loss- and gain-related behavioral intervention, consistent with other human and animal studies (e.g., Matsumoto, Matsumoto, Abe, & Tanaka, 2007; Amiez, Joseph, & Procyk, 2005, 2006; Walton, Devlin, & Rushworth, 2004; Ito, Stuphorn, Brown, & Schall, 2003; Knutson, Fong, Bennett, Adams, & Hommer, 2003; Gehring & Willoughby, 2002; Shidara & Richmond, 2002; Vidal, Hasbroucq, Grapperon, & Bonnet, 2000).

In agreement with other recent studies (Rushworth, 2008; Rushworth, Behrens, Rudebeck, & Walton, 2007; Walton, Croxson, Behrens, Kennerley, & Rushworth, 2007; Kennerley, Walton, Behrens, Buckley, & Rushworth, 2006; Rushworth, Walton, Kennerley, & Bannerman, 2004), we hypothesized that ACC assesses the value or utility of available response options, that operates whether those responses lead to a positive (reward) or negative (error likelihood) outcome. This evaluative function is of particular importance in circumstances in which a change in behavior from default or prepotent responding is required.

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For example, Walton et al. (2004) informed their subjects of three response rules and indicated when a rule was changed but without specifying which rule. Feedback on correct and incorrect responses was given to enable participants to monitor the consequences of their responses. These authors observed ACC activation for all feedback, indicating that it was the informative value of the outcome and not whether subjects were correct or incorrect that produced ACC activation. Similarly, in the animal literature, cells in medial frontal cortex respond when monkeys learn how to adjust their behavior from visual feedback (Matsumoto et al., 2007) or from the evaluation of previous actions (Seo & Lee, 2007). Furthermore, Quilodran, Rothe, and Procyk (2008) and Procyk, Tanaka, and Joseph (2000) have demonstrated ACC activity when learning and shifting between sequences of responses.

In human studies, ACC activity is typically observed on error trials (Hester, Fassbender, & Garavan, 2004), high-conflict trials (Carter et al., 1998), or expectancy violation trials (Somerville, Heatherton, & Kelley, 2006) as each type of trial prompts the evaluation of behavior in the service of subsequently changing one's behavior. That is, ACC evaluative function signals the need to adapt a different behavioral strategy. In circumstances in which no behavioral or strategic change results, then dorsal ACC activity is typically not observed.

To test the hypotheses that the dorsal ACC's primary cognitive control function is (a) action evaluation in the service of changing ongoing behavior, and (b) not limited to negative outcomes, we developed a visual search game (Figure 1) in which subjects won and lost points by correctly determining a target's presence or absence amidst distracters (low options). In addition to the standard target present/absent responses, subjects could abort a trial if they could not determine the correct response in time, and further, subjects could opt for a high reward response option, for which they won additional points, if they were confident of the target being present (high options). We predicted greater ACC involvement in rejections and high reward trials relative to correct and error trials. The rationale is that correct responses and errors on trials in which subjects make standard target present/absent responses reflect compliance with the default or standard task instructions. Errors on these trials do not affect how one performs the task in that the same target-seeking behavior occurs on a trial that follows either a correct or an error trial. In this regard, previous observations of greater error-related ACC activity leading to greater post-error behavioral changes can be interpreted as reflecting a strategic change in behavior (rather than, say, a heightened salience of the error). As a consequence, consistent with our previous results (Magno et al., 2006), error-related activity is predicted to be no different to activity levels on correct trials.

On the other hand, the trial reject and high reward response options both require a within-trial evaluation of performance and deviation from the standard responses.

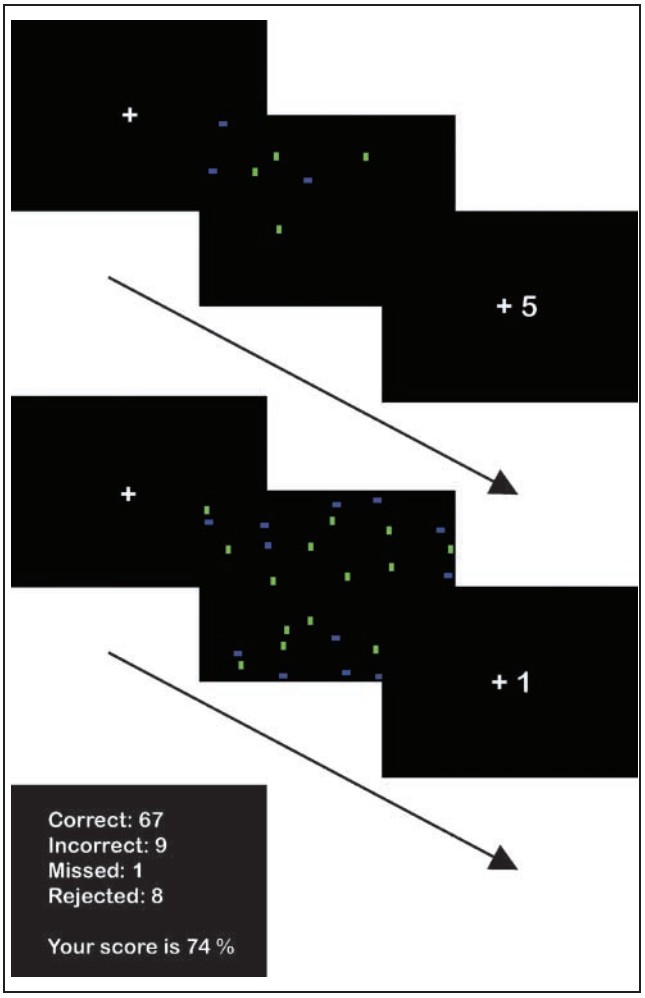


Figure 1. Examples of high options trials for two example stimuli. Eighty percent of stimuli contained 8 items and 20% of stimuli contained 32 items. Target (blue square) was present in half of each stimulus type. Stimuli types were randomized and presented until response or within 1100 msec. ISI was 700 msec. Each stimulus was preceded by a 200-msec fixation cross and followed by a 500-msec feedback indicating points earned (+) or lost (−) based on performance (e.g., high reward earned +5; simple correct earned +1). Following a 2-min task run, a final score was presented for 4 sec to keep subjects motivated for the next run.

We propose that this within-trial evaluation of performance is the common key element of both these nonstandard or interventionist response options and both are predicted to produce ACC activation greater than the correct and error trials. Note that both nonstandard response options differ in many other important respects. For example, the trial reject response enables subjects to avoid errors in situations of uncertainty, whereas the high reward response enables subjects to score extra points for target detection in situations of certainty (or, at least, high confidence). Subjects win extra points on high reward trials but obtain no points on the rejection trials. The high options task places a high demand on within-trial cognitive control and enables the performer to exercise active, self-initiated control; in contrast to many tasks in which executive control functions are assessed by

the participant's reaction to response conflict or performance errors, the high options task allows one to identify instances in which the participant actively selects to intervene in their own behavior by availing of the nonstandard response options.

If dorsal ACC does not have a primary function in processing errors then, given the importance of detecting mistakes so that they can be corrected, it would seem plausible that other brain structures might have more specific error-related functions. Previous research with the earlier variant of the present task showed error-specific activity in the anterior insula (Magno et al., 2006), consistent with robust activity noted here in a review of error processes (Hester et al., 2004), and plausibly linked to an insula-mediated arousal or emotional response to errors. Another structure of a priori interest, the ventral striatum, has been implicated in reward and reinforcement processes and shows an activity profile that can reflect either the salience or valence of events (Cooper & Knutson, 2008). In addition to elaborating the contribution of ACC to cognitive control, the present study seeks to exploit the systems-level capability of functional neuroimaging by examining the contribution of these subcortical regions to the implementation of control.

In summary, this study sought to demonstrate that ACC is involved in evaluating behavior so as to implement change, and that this ACC-mediated function is not limited to loss or error events but includes positive, rewarding events. Finally, this study sought to reveal the coordinated involvement of other subcortical regions that have also been implicated in similar error- and reward-related processes.

METHODS

Participants

Twenty-six right-handed volunteers, ranging from 19 to 34 years old, with normal or corrected-to-normal vision, and no known neurological disorders, took part in the fMRI study. Written informed consent was obtained from all participants prior to the study. Payment was provided in the form of research credits or at a rate of €10 per hour. Seven participants were excluded from analyses due to brain anomaly (1), insufficient rejection trials (e.g., below 1%, 3), insufficient error trials (e.g., 1%, 1), or insufficient correct responses (e.g., 4–28%, 2). Of the remaining 19 participants, 8 were women, and their mean age was 24.6 years (±4).

Experimental Design

Similar to the previous version of the task (Magno et al., 2006), the high options (Figure 1) consisted of displays of rectangular shapes of different colors and orientations (vertical green and horizontal blue) in which subjects were required to find a blue square target. Stimuli were presented using Presentation software (www.neurobs.com). A central fixation cross shown for 200 msec was followed by a task display containing a target square in 50% of the trials. Subjects were instructed to respond during the display presentation, which was terminated by button press or after 1100 msec if no response occurred. There were four possible responses: target present (e.g., right index finger), target absent (e.g., right middle finger), trial rejection (e.g., left index finger), and high confidence target detection (e.g., left middle finger). Hand use was counterbalanced across participants. A 500-msec feedback was then shown containing the outcome value of the response in points earned or lost: "+1" when correct with target present/absent responses ("correct" trials); "−1" when incorrect with target present/absent responses ("error" trials); "+5" when correct with high confidence target detection responses ("high reward" trials); "−5" when incorrect with high confidence target detection responses ("punishment" trials); "−1 missed" to notify a point loss due to late or missing response ("missed" trials); and "rejected" for trials that were intentionally rejected and for which no points were lost or earned ("rejected" trials). Eighty percent of the trials contained a small number of items (7 distracters and 1 target, or 8 distracters), and 20% of the trials contained a larger number of items (31 distracters and 1 target, or 32 distracters). These proportions of high- and low-frequency trials were used to generate a prepotent pattern of response (target/nontarget search) and to obtain sufficient numbers of rejection trials (more common on large set trials). Intertrial interval was 700 msec (500 msec feedback plus 200 msec fixation).

Subjects were instructed to maximize their task score, which was shown at the end of each 2-min run, and reflected the difference between number of correct responses (including "correct" and "high reward" trials) and the sum of incorrect ("error" and "punishment" trials) and missed trials. Two 2-min practice runs were performed prior to scanning. The first practice run was a 2-min visual search game with only the target present/absent response options (low options), followed by a 2-min visual search game with the additional reject and high reward options (high options). For the fMRI session, subjects completed the high options during twelve 2-min runs (in total, 940 ± 36 trials across subjects), and ended with two 2-min runs of the low options (in total, 158 ± 8 trials across subjects). The inclusion of the low options provided a measure of error-related activity when it was not possible to intervene with either the rejection or high reward options. In addition, it also gave a measure of overall performance improvements brought by the addition of the rejection and high reward options.

fMRI Acquisition and Analysis

All scanning was conducted on a Philips Intera Achieva 3.0 Tesla MR system (Best, The Netherlands) equipped

with a mirror that reflected a 640 × 480 pixel display, projected on a panel placed behind the subject's head outside the magnet. The mirror was mounted on the head coil in the subject's line of vision. Imaging started with 31.5 sec of standard scout images to adjust the head positioning, followed by a reference scan to resolve sensitivity variations. Imaging used a parallel SENSitivity Encoding (SENSE) approach (Pruessmann, Weiger, Scheidegger, & Boesiger, 1999) with reduction factor 2. One hundred eighty high-resolution T1-weighted anatomic MP-RAGE axial images (FOV = 230 mm, thickness = 0.9 mm, voxel size = 0.9 × 0.9 × 0.9) were then acquired (total duration = 5.44 min) to allow subsequent activation localization and spatial normalization. Thirty-two noncontiguous (10% gap) 3.5-mm axial slices covering the entire brain were collected using a T2*-weighted echo-planar imaging sequence (TE = 35 msec, TR = 2000 msec, FOV = 224 mm, 64 × 64 mm matrix size in Fourier space). The functional scans had a total duration of 4.50 min with each containing two task runs.

All analyses were conducted using AFNI software (Cox, 1996). Activation outside the brain was removed using edge-detection algorithms. For high options, three separate hemodynamic response functions at 2 sec temporal resolution were modeled for rejections, high rewards (+5 trials), and errors (−1 trials) using the onsets of each of these events of interest as regressors in a multiple regression deconvolution analysis. The correct responses (+1 trials) were used as the baseline. Therefore, all activations and deactivations described here are defined relative to this baseline. Events were excluded from the regressors in situations in which more than one type of event of interest occurred within the same 2-sec TR window. These excluded events were ignored and contributed to the baseline. Separate regressors were included to accommodate errors on high reward trials (punishment) (3%) and missed trials (8%), but they were not analyzed further due to their low numbers. This is because only 8 out of 19 subjects had sufficient numbers of punishment trials, and because missed trials were ambiguous trials, consisting of a mixture of late correct responses (38%), late high rewards (14%), late rejections (14%), late errors (13%), late punishment trials (4%), and errors of omission (17%). For low options, all procedures were identical except that errors constituted the only events of interest versus a baseline of correct responses.

The hemodynamic response functions were fitted to a gamma-variate function using nonlinear regression as previously described (Murphy & Garavan, 2005). Brain activation was operationalized as the area under these event-related response functions expressed as a percentage of the area under the baseline. Activation maps were resampled to 1 mm^3, then warped into standard Talairach space (Talairach & Tournoux, 1988) and spatially blurred (3 mm isotropic rms Gaussian kernel filter).

Group activation maps for each condition were determined with one-sample t tests against the null hypothesis of zero event-related activation changes. Significant voxels passed a voxelwise statistical threshold ($t = 3.20$, $p \leq .005$) and were required to be part of a larger 273 mm^3 cluster of contiguous significant voxels. The cluster size was determined through Monte Carlo simulations and resulted in a 5% probability of a cluster surviving due to chance. Mean activation was calculated by averaging over the voxels of a cluster and between-condition t-test contrasts were performed on these activation means.

In order to demarcate functional activity into distinct anatomical regions, we created an intersection map between all significant activation clusters calculated as described above, for all of the three conditions of interest (error, high reward, and rejection), with a number of ROIs from the Talairach and Tournoux (1988) atlas available in the AFNI toolbox (Cox, 1996). The activation clusters included voxels that were significant for any of the three conditions and the intersection between these clusters and the anatomically defined ROIs allowed us to separate the activations into anatomically constrained regions of a priori interest. These ROIs were: rostral–ventral ACC (rACC) and dorsal–caudal ACC (dACC), created by subdivision (based on a vertical line drawn at the most anterior part of the corpus callosum, as in Bush et al., 2000) of the combined Brodmann's area (BA) 32, BA 24, and cingulate gyrus; dorsolateral prefrontal cortex (DLPFC), created by combining the superior frontal gyrus (SFG), middle frontal gyrus (MFG), and BA 9; insula/inferior frontal gyrus (BA 13/BA 47); and nucleus accumbens (NAcc). Separate ROIs were created for the left and right hemispheres. The resulting ROIs were the functionally defined clusters of activity (combined across all response types) that fell within the distinct anatomically defined areas. This combination generated a map with 10 ROI subclusters. Consequently, the intersection results in ROIs that are a subset (i.e., the functionally active portion) of the initial anatomically defined region. The mean activation for each ROI was subjected to repeated measures ANOVAs with factors of response (error, high reward, and rejection) and hemisphere (except for right superior DLPFC and left mid-DLPFC, which did not show a cluster in the contralateral hemisphere). All effects are reported with Greenhouse–Geisser correction when appropriate. Main effects were examined with Bonferroni-corrected pairwise comparisons when appropriate ($p < .05$).

RESULTS

Behavioral Results

Tables 1 and 2 show proportions and response times (RTs) of correct responses (hits and correct rejections), errors (false alarms and misses), high rewards and rejections by set size (8 vs. 32), and type (target vs. nontarget). Table 1 shows a higher proportion of target trials, as well

Table 1. Behavioral Data

(a) High Options Tasks					
Target	*Correct (Hit)*	*Error (Miss)*	*Target*	*High Reward*	*Rejection*
Size 8	0.10 (0.15)	0.18 (0.08)	Size 8	0.64 (0.19)	0.03 (0.02)
Size 32	0.03 (0.04)	0.28 (0.20)	Size 32	0.14 (0.12)	0.48 (0.25)
Nontarget	*Correct (CR)*	*Error (FA)*	*Nontarget*		*Rejection*
Size 8	0.78 (0.13)	0.03 (0.06)	Size 8		0.04 (0.05)
Size 32	0.36 (0.23)	0.02 (0.02)	Size 32		0.50 (0.26)
Total (Including Rejections)	*Correct*	*Error*		*High Reward*	*Rejection*
	0.39 (0.07)	0.11 (0.04)		0.27 (0.08)	0.13 (0.06)
Total (Excluding Rejections)	*Correct + High Reward*	*Error + Punish*			
	0.75 (0.07)	0.16 (0.05)			
(b) Low Options Tasks					
Target	*Correct (Hit)*	*Error (Miss)*			
Size 8	0.80 (0.07)	0.17 (0.06)			
Size 32	0.26 (0.14)	0.64 (0.15)			
Nontarget	*Correct (CR)*	*Error (FA)*			
Size 8	0.85 (0.11)	0.09 (0.07)			
Size 32	0.78 (0.17)	0.14 (0.17)			
Total	*Correct*	*Error*			
	0.76 (0.06)	0.18 (0.04)			

Proportions of correct responses separated by hits and correct rejections (CR); errors separated by misses and false alarms (FA); high rewards and rejections. Standard deviations are in parentheses. Totals calculated excluding rejections are used for comparison with the control task.

as greater d' indices (Table 3), for high rewards relative to hits, indicating that subjects appropriately availed of (i.e., were more likely to be accurate when using) the high confidence response option. Rejections were equally likely on target and nontarget trials. This suggests that rejections constituted an alternative to the target/nontarget responses rather than being a substitute or proxy for one of these response options.

Repeated measures ANOVAs of RT data showed a significant main effect of response type [$F(1, 25) = 7.74$, $p < .01$] with high rewards being faster than correct responses and errors. This pattern of results is indicative of subjects using the high reward option when confident of success. Rejections did not differ in RT from the other response types, suggesting that no extra effort or conflict was intrinsic to this response type.

Errors were more likely in the low options (18 ± 4%) relative to the errors in the high options (16 ± 5%, including errors on trials in which subjects used the high reward response option) [$t(18) = 2.23$, $p < .05$]. As the proportion of correct responses in the low options (76 ± 6%) did not differ from the proportion of correct plus high reward trials in the high options (75 ± 7%), it follows that the reduced error rates in the high options are a consequence of being able to avail of the trial rejection option. The performance benefit of having the rejection and high reward options was confirmed by the higher final percentage scores obtained across runs during

the high options (66% ± 14) relative to the low options [53 ± 13%; $t(18) = 5.78, p < .0001$].

fMRI Results

Activation was observed in rACC and dACC, SFG/BA 9 (or superior DLPFC), MFG/BA 9 (or mid DLPFC), insula/inferior frontal gyrus, and NAcc (Table 4), across the high reward, rejection, and error response types. Repeated measures ANOVAs on each ROI were used to contrast the three response types across the two hemispheres. Where the ROI averages were calculated over multiple clusters falling within the ROI, additional statistical analyses on the individual clusters (unreported) were consistent with the ROI analyses. Errors deactivated right rACC, whereas rejections and high rewards both activated bilateral rACC (Figure 2). The ANOVA on rACC showed a significant main effect of response [$F(2, 36) = 13.28, p < .0001$]. Post hoc analyses indicated that rejections and high rewards did not differ from one another and each was significantly more activated than errors. Similarly, dACC activity also did not differ between rejections and high rewards, but unlike rACC, errors produced no activation changes in dACC relative to baseline (Figure 2). The ANOVA on dACC showed a significant main effect of response [$F(2, 36) = 8.28, p < .005$] with post hoc tests indicating that only rejections showed greater dACC activation relative to errors. There were no hemisphere

Table 2. Mean Response Times (RTs, msec) with Standard Deviations in Parentheses

(a) High Options Tasks					
Target	*Correct (Hit)*	*Error (Miss)*	*Target*	*High Reward*	*Rejection*
Size 8	813 (19)	829 (14)	Size 8	760 (11)	861 (16)
Size 32	823 (40)	783 (31)	Size 32	812 (24)	773 (21)
Nontarget	*Correct (CR)*	*Error (FA)*	*Nontarget*		*Rejection*
Size 8	824 (13)	898 (27)	Size 8		882 (16)
Size 32	788 (26)	839 (36)	Size 32		774 (21)
Total (Including Rejections)	*Correct*	*Error*		*High Reward*	*Rejection*
	818 (57)	823 (64)		764 (48)	791 (82)
Total (Excluding Rejections)	*Correct + High Reward*	*Error + Punish*			
	792 (4)	813 (16)			
(b) Low Options Tasks					
Target	*Correct (Hit)*	*Error (Miss)*			
Size 8	743 (57)	804 (91)			
Size 32	850 (108)	816 (117)			
Nontarget	*Correct (CR)*	*Error (FA)*			
Size 8	808 (76)	807 (74)			
Size 32	803 (110)	810 (143)			
Total	*Correct*	*Error*			
	801 (69)	810 (78)			

RTs are reported for correct responses separated by hits and correct rejections (CR); errors separated by misses and false alarms (FA); high rewards and rejections. Standard deviations are in parentheses. Totals calculated excluding rejections are used for comparison with the control task.

Table 3. d' and C Derived from the Corrected Probability Scores (Snodgrass & Corwin, 1988) of Hits − FA (Error), and of High Rewards − FA (Punish)

(a) High Options Tasks		
(Hit + High Reward) − FA (Error + Punish)	*d′*	*C*
Size 8	2.05 (0.48)	0.39 (0.21)
Size 32	0.63 (0.43)	1.38 (0.48)
Hit − FA (Error)	*d′*	*C*
Size 8	0.44 (0.11)	1.90 (0.66)
Size 32	0.04 (0.43)	2.10 (0.48)
High Reward − Punish	*d′*	*C*
Size 8	1.96 (0.51)	0.62 (0.35)
Size 32	0.63 (0.42)	1.53 (0.50)
(b) Low Options Tasks		
Hit − FA (Error)	*d′*	*C*
Size 8	2.24 (0.52)	0.27 (0.22)
Size 32	0.67 (0.66)	1.03 (0.58)

Total d' and C for hits and high rewards are also shown for comparison with the control task.

main effects or interactions for either rACC or dACC. The right and left hemisphere rACC and dACC activations for rejections were positively correlated with each other (min $r = .491$, $p < .05$; and max $r = .692$, $p < .01$). A similar pattern of associations was found for the high reward trials' rACC and dACC activations (min $r = .471$, $p < .05$; and max $r = .699$, $p < .01$).

In the NAcc (Figure 2), high rewards produced positive activity, whereas both errors and rejections produced deactivations. However, only the left NAcc deactivation for rejections significantly differed from baseline. Post hoc tests on the significant effect of response [$F(2, 36) = 29.93$, $p < .0001$] indicated that high rewards activated NAcc more than both errors and rejections. Consistent with our previous findings (Magno et al., 2006), a t test contrasting NAcc activity between errors and rejections determined that errors showed the most negative activation in the right NAcc [$t(18) = 2.36$, $p < .05$].

Errors produced activation in just three brain regions: the left and right insula/inferior frontal gyrus and the left MFG/BA 9 (Figure 3). The latter positively correlated with the right insula ($r = .48$, $p < .05$). Although the right insula differed from baseline for rejections, neither the left insula nor the left MFG did so for either rejections or high rewards. A main effect of response was significant in the ANOVA on the left and right insula clusters [$F(2, 36) = 3.72$, $p < .05$] with post hoc tests showing more activation for errors than rejections and high rewards. In addition, an effect of hemisphere was also significant [$F(1, 18) = 4.74$, $p < .05$], which identified the right cluster as more activated than the left. An ANOVA comparing response types for the left MFG (there was no right MFG activity) showed a main effect of response [$F(2, 36) = 6.07$, $p < .01$], which post hoc tests revealed to be due to greater activation for errors than high rewards.

Only the rejections activated the right superior DLPFC (Figure 3), and significantly so more than errors [$F(2, 36) = 10.50$, $p < .0001$], as shown by post hoc analyses. Rejection-related activation in the right superior DLPFC correlated with rejection-related activity in the left and the right dACC ($r = .62$ and $r = .65$, $p < .01$), indicative of functional associations between these areas.

The errors from the low options deactivated the NAcc relative to baseline, but an ACC response (a deactivation of rACC) was only observed at a lower voxelwise statistical threshold of $p < .01$ (uncorrected). No other activation was observed in any ROIs for the low options. Of course, one cannot entirely rule out the possibility of some subthreshold activation in the dACC given the small number of error trials on this task. Nonetheless, although an involvement of the dACC in error processing cannot be ruled out, the results of the low options are valuable in showing a more robust NAcc response for errors in this task.

Functional Dissociations

In order to test for dissociations across brain areas that are likely driven by the same dopamine system, a Response × Region × Hemisphere ANOVA was used to contrast error, high reward, and rejection activation in rACC, dACC, and NAcc clusters, over the left and right hemispheres. A main effect of region was significant [$F(2, 36) = 14.59$, $p < .0001$] with post hoc tests indicating that both dACC and rACC clusters were more activated than the NAcc. The interaction between response and region [$F(2, 44) = 9.17$, $p < .0001$] was also significant. A Newman–Keuls post hoc test ($p < .05$) on this interaction indicated that the high rewards equally activated all regions, whereas rejections activated rACC and dACC more than the NAcc. The errors deactivated all regions except for dACC, which showed no error response. This result is consistent with our previous findings in that we find larger ACC activations for rejections and larger NAcc deactivations for errors.

Previously, we have shown an error-specific response in the insula and not dACC (Magno et al., 2006). We confirm this here with a final ANOVA with factors of response, region (dACC, insula), and hemisphere, which showed a significant interaction of Response × Region

$[F(2, 36) = 27.31, p < .0001]$. A Newman–Keuls post hoc test indicated that the errors had the greatest insular activations and the least dACC activations relative to both rejections and high rewards.

fMRI and Behavioral Measures Correlations

Correlations between activation clusters and behavioral measures showed that three of the ACC regions correlated with the percentage of rejections. These were right rACC ($r = -.59, p < .01$), left dACC ($r = -.55, p < .05$), and right dACC ($r = -.68, p < .01$). The left NAcc also correlated positively with the same behavioral measure ($r = .54, p < .05$). In other words, ACC activations and NAcc deactivation for rejections were stronger in those participants with smaller numbers of rejections. This is consistent with ACC being involved in evaluating and implementing behavioral change relative to the default target present/absent responses in that the more often one invokes this change than the less of a deviation it is from the default task. The biphasic response of the NAcc suggests activity that codes for the valence of an event, and the correlation with the percentage of rejections, trials on which no points are won, suggests that the salience of this loss of a possible reward diminishes with increased frequency.

Figure 4 shows plots of significant correlations between the activations and the behavioral data. High reward trial

Table 4. Combined Activation Maps

Structure	*Hem*	*BA*	*Volume*	*x*	*y*	*z*
Anterior cingulate (rACC)	L	32	50	−8	41	4
Anterior cingulate (rACC)	L	32	38	−10	37	24
Anterior cingulate (rACC)	L	32	31	−6	18	−8
Anterior cingulate (rACC)	L	32	11	−8	36	10
Anterior cingulate (rACC)	R	32	1670	2	40	10
Anterior cingulate (rACC)	R	32	14	8	18	−8
Anterior cingulate (rACC)	R	32	10	20	32	21
Cingulate gyrus (dACC)	L	24	309	−3	−13	34
Medial frontal gyrus (dACC)	L	32	168	−16	9	45
Cingulate gyrus, medial frontal gyrus (dACC)	L	32	2	−11	19	43
Cingulate gyrus (dACC)	R	32	216	4	23	32
Cingulate gyrus, medial frontal gyrus (dACC)	R	24, 6	78	6	3	48
Cingulate gyrus (dACC)	R	24	70	2	−12	35
Middle frontal gyrus	L	9	182	−48	15	28
Superior frontal gyrus	L	10	13	−10	61	25
Superior frontal gyrus	L	9	5	−17	37	33
Superior frontal gyrus	L	9	4	−10	47	31
Inferior frontal gyrus	L	9	1	−42	10	28
Superior frontal gyrus	R	9	392	19	54	31
Insula, IFG	L	13, 47	209	−35	18	0
Insula	L	13	9	−48	−23	18
Insula	L	13	3	−29	−24	14
Insula	L	13	1	−49	−27	21
Insula, IFG	R	13, 47	440	36	19	4
NAcc	L		80	−12	10	−6
NAcc	R		190	13	9	−9

Activation maps in conjunction with 10 ROIs for rejections, errors, and high rewards. rACC = rostral anterior cingulate ROI; dACC = dorsal anterior cingulate ROI; Hem = hemisphere; L = left; R = right; BA = Brodmann's areas. Volume (μl) equals the number of voxels in each cluster. Coordinates (x, y, z) are in Talairach space.

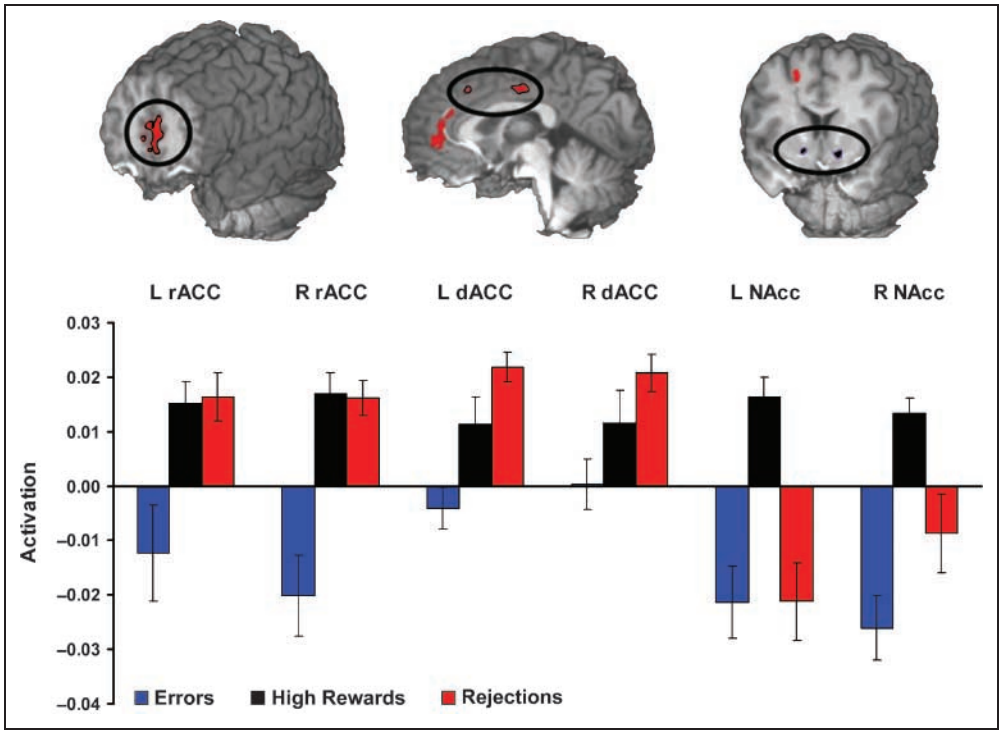


Figure 2. Combined maps for the cingulate–striatal regions. (Top, from left to right) Activation maps for the rostral and dorsal cingulate region are shown in sagittal view. NAcc clusters are shown in coronal view. (Bottom) Bar charts for the mean activations of left (L) and right (R) rACC, dACC, and NAcc. Error bars represent standard errors of the mean.

RTs were positively correlated with the right NAcc ($r = .57$, $p < .05$) and left rACC ($r = .47$, $p < .05$). Therefore, subjects with longer RTs for high rewards showed greater activity of the rostral cingulate and ventral striatum. The left and right NAcc also negatively correlated with the percentage of high rewards (left: $r = -.66$; right: $r = -.64$, $p < .01$), indicating that subjects who chose and received more high rewards engaged less the ventral striatum. This is consistent with the relative value or salience of a reward decreasing when they are more frequent, similar to what

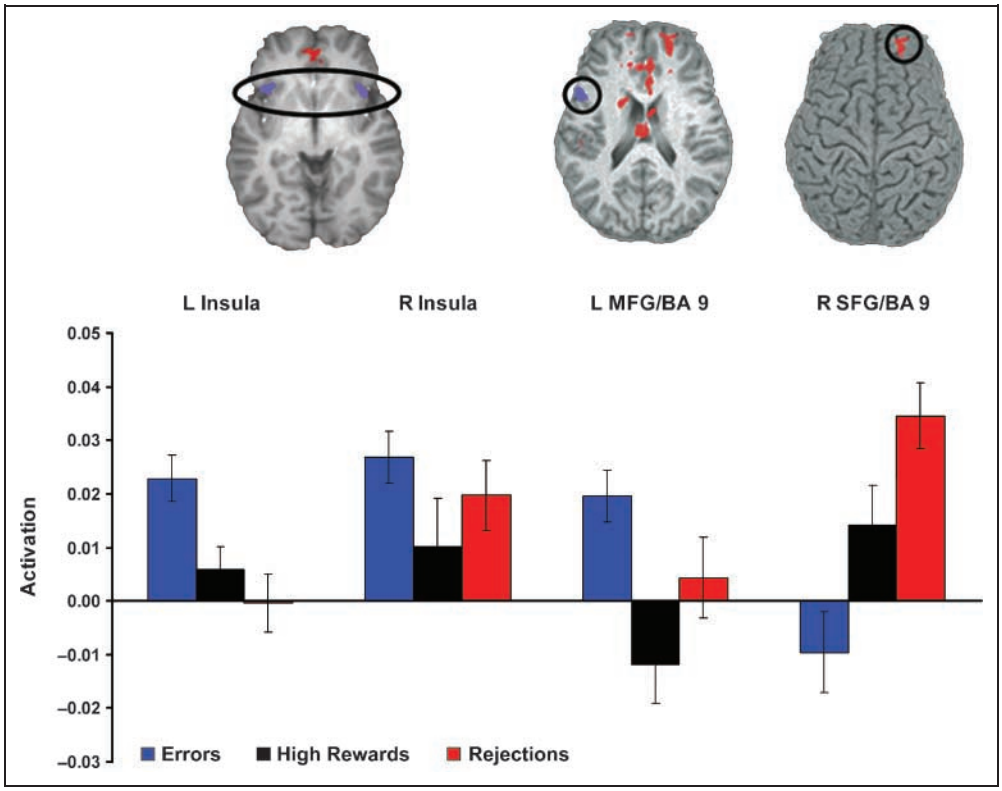
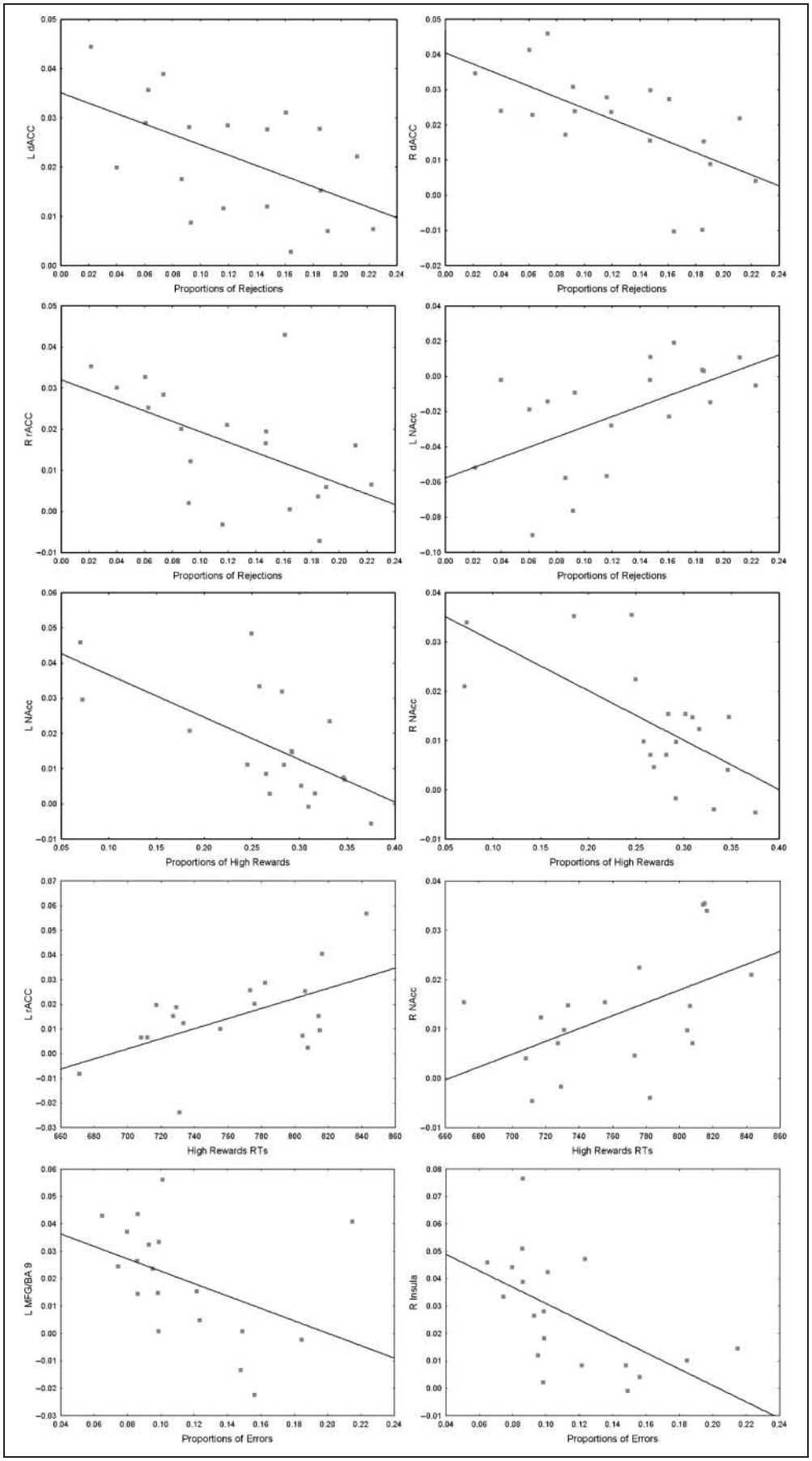


Figure 3. Combined maps for the prefrontal–limbic regions. (Top) Axial slices with activations, from left to right, in the left (L) and right (R) insula, left middle frontal gyrus (MFG) at BA 9, and right superior frontal gyrus (SFG) at BA 9. (Bottom) Bar charts for the mean activations of the above clusters. Error bars represent standard errors of the mean.

Figure 4. Scatterplots for the significant correlations between behavioral data and activations for rejections, high rewards, and errors.



was suggested above regarding the frequency and salience of the loss of possible rewards. An alternative interpretation, consistent with prediction error encoding (for a review, see O'Doherty et al., 2004), is that the accumbens is more sensitive to high rewards when there are fewer.

Finally, the MFG ($r = -.54$, $p < .05$) and the right insula ($r = -.65$, $p < .01$) were negatively correlated with the percentage of errors, indicating that participants who made fewer errors had increased activity in these regions.

DISCUSSION

The results reveal a distributed network of cortical and subcortical regions, previously implicated in cognitive, affective, and reward-related processes, functioning together but with distinct profiles across the different task conditions. For example, rostral and dorsal cingulate regions were equally activated by high rewards and rejections, despite these response types representing quite opposite decisions: Rejections are based on uncertainty of target presence or absence, whereas high rewards are the product of certainty of target presence. They also differ in their outcome magnitude, with rejections generating no points and high rewards generating five. The observed ACC activation cannot therefore be a consequence of decision uncertainty (Huettel, Song, & McCarthy, 2005; Critchley, Mathias, & Dolan, 2001), nor can it reflect processing of the outcome magnitude (Rogers et al., 2004; Bush et al., 2002). An alternative view may be that ACC signal reflects outcome certainty or confidence as the outcome of a rejection is certain: No points will be won or lost. Similarly, the high rewards entail high confidence of success. That said, the literature appears to suggest higher ACC when there is more uncertainty, not when there is less (Huettel et al., 2005; Critchley et al., 2001). Instead, as predicted, ACC activation may be due to both high rewards and rejections requiring deviations from the standard target present/absent search operations and responses.

We expand our previous interpretation of ACC's evaluative function beyond error avoidance (Magno et al., 2006) to a role in evaluating the need to implement behavioral change to attain one's goals which could include both the avoidance of an error as well as the attainment of a higher reward. This finding and interpretation is also consistent with a number of recent animal and human studies (Quilodran et al., 2008; Walton et al., 2004; Procyk et al., 2000; Shima & Tanji, 1998).

Functional Dissociations within ACC

The profile of activation across the different conditions varied within ACC. Errors deactivated rACC but had no effect on dACC. This rostral area is within the region of mesial PFC that Knutson, Fong, et al. (2001) reported to deactivate in response to omission of expected monetary rewards. These authors also found that mesial PFC activated when an expected reward was obtained (Knutson et al., 2003), and they further suggested that this area may be sensitive to reward outcomes rather than reward anticipation. This view is consistent with the present results insofar as the errors and high rewards are concerned, but fails to explain the rejection-related activation, in light of these authors' findings that avoidance of aversive monetary outcomes did not recruit this region. The rACC response is similar to the bivalent response of the NAcc (discussed below), which perhaps reflects the anatomical connections between the regions and the role that rACC has in affective processing (Simmons, Stein, Matthews, Feinstein, & Paulus, 2006; Taylor et al., 2006; Bush et al., 2000; Kiehl, Liddle, & Hopfinger, 2000).

Although the positive correlations between rACC and dACC for both rejections and high rewards suggest that these cingulate regions work in concert in the control of behavior, the response to errors differs across regions with rACC, but not dACC, deactivating on error trials. dACC did not deviate from the baseline of correct trial activity on error trials. Instead, the rejections produced significantly more dACC activation relative to the errors. We propose that the lack of error trial activity was due to dACC's evaluative functions loading on the high reward and rejection trials; in a task in which subjects can avoid errors by rejecting a trial, errors might be considered to be occasions in which monitoring or evaluative functions lapsed. Consequently, error-related dACC activity observed in many previous studies (e.g., Taylor, Stern, & Gehring, 2007; Holroyd et al., 2004; Ridderinkhof et al., 2004; Garavan, Ross, Kaufman, & Stein, 2003; Gehring & Knight, 2000) may reflect the evaluative function that, in the present task, is separated from error trials by virtue of there being a trial-abort response option. The dACC clusters were in proximity to the dorsal cingulate region where we previously found error avoidance effects (Magno et al., 2006), and thus, these results confirm our previous findings while extending dACC's role to more general behavioral interventions that go beyond the detection or prediction of negative outcomes to include the attainment of positive outcomes.

Reinforcement-learning theories of ACC function (Frank, Woroch, & Curran, 2005; Nieuwenhuis, Holroyd, Mol, & Coles, 2004; Ridderinkhof et al., 2004; Hadland, Rushworth, Gaffan, & Passingham, 2003; Holroyd & Coles, 2002) are based on the fundamental idea that ACC responds to errors in a reactive manner. For example, greater ACC activity during error trials is associated with greater post-error slowing (Kerns et al., 2004). In the absence of dACC activation, we found post-error slowing of 41 ± 20 msec relative to the average RT of all trials in the high options [$t(18) = 9.16$, $p \leq .0001$]. In this task, post-error slowing would appear to have been reasonable and adaptive insofar as the subjects do not

slow down so much as to risk a post-error omission. However, note that the response deadline rewards faster responding as demonstrated by significant negative correlations (min $r = -.48$, $p < .05$; max $r = -.78$, $p < .0001$) between the numbers of high rewards and correct responses and RTs on those trial types. It is notable that the evidence suggests a distinction between the neural systems that underlie post-error slowing from those that underlie changes in behavioral responding. Whereas the results implicate dACC in the latter (insofar as there was greater activity here for rejection and high reward trials), there was no activation here relative to correct trials despite there having been significant post-error slowing. Consistent with this interpretation, a previous investigation (Ullsperger & von Cramon, 2006) that compared post-error signaling to post-error correction (the former requires a behavioral change to ongoing task performance) observed a larger ERN for post-error signaling, indicating that dACC, the probable source of the ERN, was more active when a more substantial departure from ongoing task behavior was required. In addition, Li et al. (2008) have localized post-error slowing to right ventrolateral PFC and not dACC. Alternatively, it is possible that post-error slowing in this task simply reflected a carryover effect from the recognition/processing of an error after feedback presentation. However, in both the high options and low options, task performance does not substantively or strategically change following an error, as the error does not lead to a change in how one performs the task (i.e., subjects would perform the same visual search operations on trials following either errors or correct responses). In contrast, choosing the rejection or high reward options engages dACC as these options constitute a behavioral adjustment to the standard target present/absent task responses. The two interpretations of the dACC function presented here are not mutually exclusive. An evaluation function that is involved in implementing behavioral control on a trial may also provide a learning signal to change how one performs a task: In both cases, dACC signals the need to alter ongoing behavior, and whether this is interpreted as within-trial behavioral control or across-trials learning may reflect the time scale on which one focuses.

It is unlikely that the greater ACC activation on rejections reflects increased mental effort (Walton, Bannerman, Alterescu, & Rushworth, 2003; Paus, Koski, Caramanos, & Westbury, 1998), although this might be considered a plausible explanation given that rejection responses were most frequent on the more demanding trials, that is, those trials that contained larger set sizes. Mental effort was previously discounted in the precursor to the current study, in which an fMRI analysis of rejections and error trials, matched for numbers of large and small set sizes (and whenever possible on target presence/absence), replicated the findings of greater dACC and DLPFC activations on rejections relative to error trials (Magno et al., 2006). Moreover, as in the previous task, RTs for rejections of trials with set size 32 were faster than rejections of trials with set size 8 [$t(18) = 4.75$, $p < .0001$]. An analysis using only events of small set size for high rewards, rejections, errors, and the baseline of correct responses (all other events were modeled separately in order to be excluded from baseline and events of interest) replicated the previous and current results showing greater rACC [$F(2, 20) = 11.13$, $p < .0001$] activations for rejections and high rewards relative to errors; greater dACC [$F(2, 20) = 10.17$, $p < .0001$] and DLPFC activations [$F(2, 20) = 10.09$, $p < .0001$] for rejections relative to errors; and greater NAcc activations [$F(2, 20) = 4.09$, $p < .05$] for high rewards relative to errors. This analysis demonstrates that the present results are not confounded by trial types loading differentially on the large and small set trials.

Systems-level Overview of Cognitive Control

The results confirmed our previous finding of greater superior DLPFC activation for rejections relative to errors (Magno et al., 2006). There was a significant positive correlation between superior DLPFC and dACC on rejection trials, consistent with the anatomical connections between the regions (Pandya, Yeterian, Fleminger, & Dunnett, 1996; Robbins, Weinberger, Taylor, & Morris, 1996) and perhaps with the view that dACC triggers superior DLPFC intervention to implement additional control (Dreher & Grafman, 2003; MacDonald, Cohen, Stenger, & Carter, 2000). Because the decision to reject may damage task score (if implemented too frequently), additional control may be needed for this choice, compared to other response types. For example, the additional control provided by superior DLPFC may contribute to rejections by resolving the uncertainty under which the decision to reject is made. For high rewards, this additional control may not be needed, as these responses are based on high confidence judgments, as indicated by their relatively fast RTs. Further, the lack of dACC and superior DLPFC activity on errors would indicate that errors occur when cognitive control is reduced.

Error-related activation was observed in bilateral insulae/inferior frontal gyri and the mid-DLPFC. Both the right insula and mid-DLPFC were negatively correlated with the percentage of errors subjects committed and were positively correlated with one another. Mid-DLPFC activity can be produced by word pairs evoking negative feelings (Teasdale et al., 1999), whereas the anterior insula has also been frequently implicated in negative emotional processing (Liu et al., 2007; Wager, Phan, Liberzon, & Taylor, 2003; Phan, Wager, Taylor, & Liberzon, 2002), suggesting a negative affective response particular to the error trial.

The implementation of cognitive control often occurs in the service of securing reward, and the present results provide insights into the interrelationships and processes of both control and reward-related brain structures. The

pattern of the subcortical NAcc region, being positively activated for high rewards and deactivated for errors, matches previous investigations focusing on monetary reward in which the NAcc increases when reward is anticipated and obtained (Breiter, Aharon, Kahneman, Dale, & Shizgal, 2001; Knutson, Adams, Fong, & Hommer, 2001), and decreases when reward is expected but not obtained (Breiter et al., 2001; Delgado, Nystrom, Fissell, Noll, & Fiez, 2000).

The NAcc was also deactivated on rejection trials (although the deactivation was significantly greater for errors than rejections in the right NAcc), which may result from rejections having been perceived as moderately negative events (e.g., some subjects reported that they detected the target after the rejection response had already been implemented). The bivalent response of the NAcc (positive activation for high rewards but deactivation for errors and intermediate levels of deactivation for rejections) suggests that on this task this structure codes the reward-related value of an outcome (Spicer et al., 2007; Breiter et al., 2001) and not the salience of an outcome which would be expected to produce positive activation on both the high reward and rejection trials. However, it is important to note that although the NAcc and rACC were clearly less activated for errors than for rejections and high rewards, the negativity of such activations is only relative to the baseline of correct responses.

The NAcc and dACC show different activation profiles with the former appearing to code the valence of a trial's outcome and the latter involved in implementing change. The fine-grained time course of activity within these regions cannot be discerned due to the sluggish hemodynamic response. A body of evidence has identified the ventral striatum with both reward anticipation and outcome (Spicer et al., 2007; O'Doherty et al., 2004; Breiter et al., 2001; Knutson, Fong, et al., 2001). As subjects may be unaware of having committed an error until receiving feedback, it is likely that the error-related deactivation of this structure follows this outcome. The reward-related activation and rejection-related deactivation may either follow feedback or may be anticipatory, commencing at the initiation of the response selection. Indeed, one cannot rule out the possibility that the valenced response of the NAcc to the available response options precedes their selection and may even contribute to their selection by providing valence information for their further evaluation.

Although we cannot clearly disentangle decision and feedback related activity, our results of greater dACC activations for high rewards and rejections (generating opposite outcomes), and of opposite positive or negative NAcc activations for high rewards and errors (based on opposite outcomes, but possibly similar expectations), we believe that our interpretations above are the most parsimonious for the current results. We acknowledge, however, that our interpretations of activation being choice or feedback-related are to be read as viable post hoc interpretations.

Summary

The current data suggest alternative performance monitoring networks for rejections and errors: Superior DLPFC, in coordination with dACC, contributes to the decision to reject, in pursuit of the task goals, whereas mid-DLPFC, in coordination with the insula/inferior frontal gyrus, detects errors. High reward trials, on the other hand, do not appear to engage DLPFC due, we suggest, to the lack of response uncertainty characteristic of the relatively fast and largely accurate high reward responses. The evaluative function of dACC, however, is engaged for both the high reward and rejection trials, that is, on both occasions when there is a deviation from the standard target present/absent responses. In our view, these results suggest a role for dACC in within-trial evaluation of available actions; they do not support a role for dACC in reactively monitoring the outcomes of one's behavior such as errors, or task demands such as response conflict.

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REFERENCES

Amiez, C., Joseph, J. P., & Procyk, E. (2005). Anterior cingulate error-related activity is modulated by predicted reward. *European Journal of Neuroscience, 21,* 3447–3452.

Amiez, C., Joseph, J. P., & Procyk, E. (2006). Reward encoding in the monkey anterior cingulate cortex. *Cerebral Cortex, 16,* 1040–1055.

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: An update. *Trends in Cognitive Sciences, 8,* 539–546.

Breiter, H. C., Aharon, I., Kahneman, D., Dale, A., & Shizgal, P. (2001). Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron, 30,* 619–639.

Brown, J. W., & Braver, T. S. (2005). Learned predictions of error likelihood in the anterior cingulate cortex. *Science, 307,* 1118–1121.

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences, 4,* 215–222.

Bush, G., Vogt, B. A., Holmes, J., Dale, A. M., Greve, D., Jenike, M. A., et al. (2002). Dorsal anterior cingulate cortex: A role in reward-based decision making. *Proceedings of the National Academy of Sciences, U.S.A., 99,* 523–528.

Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science, 280,* 747–749.

Cooper, J. C., & Knutson, B. (2008). Valence and salience contribute to nucleus accumbens activation. *Neuroimage, 39,* 538–547.

Cox, R. W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computer and Biomedical Research, 29,* 162–173.

Critchley, H. D., Mathias, C. J., & Dolan, R. J. (2001). Neural activity in the human brain relating to uncertainty and arousal during anticipation. *Neuron, 29,* 537–545.

Delgado, M. R., Nystrom, L. E., Fissell, C., Noll, D. C., & Fiez, J. A. (2000). Tracking the hemodynamic responses to reward and punishment in the striatum. *Journal of Neurophysiology, 84,* 3072–3077.

Dreher, J. C., & Grafman, J. (2003). Dissociating the roles of the rostral anterior cingulate and the lateral prefrontal cortices in performing two tasks simultaneously or successively. *Cerebral Cortex, 13,* 329–339.

Falkenstein, M., Hohnsbein, J., Hoormann, J., & Blanke, L. (1991). Effects of crossmodal divided attention on late ERP components. II. Error processing in choice reaction tasks. *Electroencephalography and Clinical Neurophysiology, 78,* 447–455.

Falkenstein, M., Hoormann, J., Christ, S., & Hohnsbein, J. (2000). ERP components on reaction errors and their functional significance: A tutorial. *Biological Psychology, 51,* 87–107.

Frank, M. J., Woroch, B. S., & Curran, T. (2005). Error-related negativity predicts reinforcement learning and conflict biases. *Neuron, 47,* 495–501.

Garavan, H., Ross, T. J., Kaufman, J., & Stein, E. A. (2003). A midline dissociation between error-processing and response-conflict monitoring. *Neuroimage, 20,* 1132–1139.

Gehring, W. J., Goss, B., Coles, M. G. H., Meyer, D. E., & Donchin, E. (1993). A neural system for error detection and compensation. *Psychological Science, 4,* 385–390.

Gehring, W. J., & Knight, R. T. (2000). Prefrontal–cingulate interactions in action monitoring. *Nature Neuroscience, 3,* 516–520.

Gehring, W. J., & Willoughby, A. R. (2002). The medial frontal cortex and the rapid processing of monetary gains and losses. *Science, 295,* 2279–2282.

Hadland, K. A., Rushworth, M. F., Gaffan, D., & Passingham, R. E. (2003). The anterior cingulate and reward-guided selection of actions. *Journal of Neurophysiology, 89,* 1161–1164.

Hester, R., Fassbender, C., & Garavan, H. (2004). Individual differences in error processing: A review and reanalysis of three event-related fMRI studies using the GO/NOGO task. *Cerebral Cortex, 14,* 986–994.

Holroyd, C. B., & Coles, M. G. (2002). The neural basis of human error processing: Reinforcement learning, dopamine, and the error-related negativity. *Psychological Review, 109,* 679–709.

Holroyd, C. B., Nieuwenhuis, S., Yeung, N., Nystrom, L., Mars, R. B., Coles, M. G., et al. (2004). Dorsal anterior cingulate cortex shows fMRI response to internal and external error signals. *Nature Neuroscience, 7,* 497–498.

Huettel, S. A., Song, A. W., & McCarthy, G. (2005). Decisions under uncertainty: Probabilistic context influences activation of prefrontal and parietal cortices. *Journal of Neuroscience, 25,* 3304–3311.

Ito, S., Stuphorn, V., Brown, J. W., & Schall, J. D. (2003). Performance monitoring by the anterior cingulate cortex during saccade countermanding. *Science, 302,* 120–122.

Kennerley, S. W., Walton, M. E., Behrens, T. E., Buckley, M. J., & Rushworth, M. F. (2006). Optimal decision making and the anterior cingulate cortex. *Nature Neuroscience, 9,* 940–947.

Kerns, J. G., Cohen, J. D., MacDonald, A. W., III, Cho, R. Y., Stenger, V. A., & Carter, C. S. (2004). Anterior cingulate conflict monitoring and adjustments in control. *Science, 303,* 1023–1026.

Kiehl, K. A., Liddle, P. F., & Hopfinger, J. B. (2000). Error processing and the rostral anterior cingulate: An event-related fMRI study. *Psychophysiology, 37,* 216–223.

Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *Journal of Neuroscience, 21,* RC159.

Knutson, B., Fong, G. W., Adams, C. M., Varner, J. L., & Hommer, D. (2001). Dissociation of reward anticipation and outcome with event-related fMRI. *NeuroReport, 12,* 3683–3687.

Knutson, B., Fong, G. W., Bennett, S. M., Adams, C. M., & Hommer, D. (2003). A region of mesial prefrontal cortex tracks monetarily rewarding outcomes: Characterization with rapid event-related fMRI. *Neuroimage, 18,* 263–272.

Li, C. S., Huang, C., Yan, P., Paliwal, P., Constable, R. T., & Sinha, R. (2008). Neural correlates of post-error slowing during a stop signal task: A functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience, 20,* 1021–1029.

Liu, X., Powell, D. K., Wang, H., Gold, B. T., Corbly, C. R., & Joseph, J. E. (2007). Functional dissociation in frontal and striatal areas for processing of positive and negative reward information. *Journal of Neuroscience, 27,* 4587–4597.

MacDonald, A. W., III, Cohen, J. D., Stenger, V. A., & Carter, C. S. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science, 288,* 1835–1838.

Magno, E., Foxe, J. J., Molholm, S., Robertson, I. H., & Garavan, H. (2006). The anterior cingulate and error avoidance. *Journal of Neuroscience, 26,* 4769–4773.

Matsumoto, M., Matsumoto, K., Abe, H., & Tanaka, K. (2007). Medial prefrontal cell activity signaling prediction errors of action values. *Nature Neuroscience, 10,* 647–656.

Murphy, K., & Garavan, H. (2005). Deriving the optimal number of events for an event-related fMRI study based on the spatial extent of activation. *Neuroimage, 27,* 771–777.

Nieuwenhuis, S., Holroyd, C. B., Mol, N., & Coles, M. G. (2004). Reinforcement-related brain potentials from medial frontal cortex: Origins and functional significance. *Neuroscience and Biobehavioral Review, 28,* 441–448.

O'Doherty, J., Dayan, P., Schultz, J., Deichmann, R., Friston, K., & Dolan, R. J. (2004). Dissociable roles of ventral and dorsal striatum in instrumental conditioning. *Science, 304,* 452–454.

Pandya, D. N., Yeterian, E. H., Fleminger, S., & Dunnett, S. B. (1996). Comparison of prefrontal architecture and connections [and discussion]. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences, 351,* 1423–1432.

Paus, T., Koski, L., Caramanos, Z., & Westbury, C. (1998). Regional differences in the effects of task difficulty and motor output on blood flow response in the human anterior cingulate cortex: A review of 107 PET activation studies. *NeuroReport, 9,* R37–R47.

Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: A meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage, 16,* 331–348.
Procyk, E., Tanaka, Y. L., & Joseph, J. P. (2000). Anterior cingulate activity during routine and non-routine sequential behaviors in macaques. *Nature Neuroscience, 3,* 502–508.
Pruessmann, K. P., Weiger, M., Scheidegger, M. B., & Boesiger, P. (1999). SENSE: Sensitivity encoding for fast MRI. *Magnetic Resonance in Medicine, 42,* 952–962.
Quilodran, R., Rothe, M., & Procyk, E. (2008). Behavioral shifts and action valuation in the anterior cingulate cortex. *Neuron, 57,* 314–325.
Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *Science, 306,* 443–447.
Robbins, T. W., Weinberger, D., Taylor, J. G., & Morris, R. G. (1996). Dissociating executive functions of the prefrontal cortex [and discussion]. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences, 351,* 1463–1471.
Rogers, R. D., Ramnani, N., Mackay, C., Wilson, J. L., Jezzard, P., Carter, C. S., et al. (2004). Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. *Biological Psychiatry, 55,* 594–602.
Rushworth, M. F. (2008). Intention, choice, and the medial frontal cortex. *Annals of the New York Academy of Sciences, 1124,* 181–207.
Rushworth, M. F., Behrens, T. E., Rudebeck, P. H., & Walton, M. E. (2007). Contrasting roles for cingulate and orbitofrontal cortex in decisions and social behaviour. *Trends in Cognitive Sciences, 11,* 168–176.
Rushworth, M. F., Walton, M. E., Kennerley, S. W., & Bannerman, D. M. (2004). Action sets and decisions in the medial frontal cortex. *Trends in Cognitive Sciences, 8,* 410–417.
Seo, H., & Lee, D. (2007). Temporal filtering of reward signals in the dorsal anterior cingulate cortex during a mixed-strategy game. *Journal of Neuroscience, 27,* 8366–8377.
Shidara, M., & Richmond, B. J. (2002). Anterior cingulate: Single neuronal signals related to degree of reward expectancy. *Science, 296,* 1709–1711.
Shima, K., & Tanji, J. (1998). Role for cingulate motor area cells in voluntary movement selection based on reward. *Science, 282,* 1335–1338.
Simmons, A., Stein, M. B., Matthews, S. C., Feinstein, J. S., & Paulus, M. P. (2006). Affective ambiguity for a group recruits ventromedial prefrontal cortex. *Neuroimage, 29,* 655–661.
Snodgrass, J. G., & Corwin, J. (1988). Pragmatics of measuring recognition memory: Applications to dementia and amnesia. *Journal of Experimental Psychology: General, 117,* 34–50.
Somerville, L. H., Heatherton, T. F., & Kelley, W. M. (2006). Anterior cingulate cortex responds differentially to expectancy violation and social rejection. *Nature Neuroscience, 9,* 1007–1008.
Spicer, J., Galvan, A., Hare, T. A., Voss, H., Glover, G., & Casey, B. J. (2007). Sensitivity of the nucleus accumbens to violations in expectation of reward. *Neuroimage, 34,* 455–461.
Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme.
Taylor, S. F., Martis, B., Fitzgerald, K. D., Welsh, R. C., Abelson, J. L., Liberzon, I., et al. (2006). Medial frontal cortex activity and loss-related responses to errors. *Journal of Neuroscience, 26,* 4063–4070.
Taylor, S. F., Stern, E. R., & Gehring, W. J. (2007). Neural systems for error monitoring: Recent findings and theoretical perspectives. *The Neuroscientist, 13,* 160.
Teasdale, J. D., Howard, R. J., Cox, S. G., Ha, Y., Brammer, M. J., Williams, S. C. R., et al. (1999). Functional MRI study of the cognitive generation of affect. *American Journal of Psychiatry, 156,* 209–215.
Ullsperger, M., & von Cramon, D. Y. (2006). How does error correction differ from error signaling? An event-related potential study. *Brain Research, 1105,* 102–109.
Vidal, F., Hasbroucq, T., Grapperon, J., & Bonnet, M. (2000). Is the ''error negativity'' specific to errors? *Biological Psychology, 51,* 109–128.
Wager, T. D., Phan, K. L., Liberzon, I., & Taylor, S. F. (2003). Valence, gender, and lateralization of functional brain anatomy in emotion: A meta-analysis of findings from neuroimaging. *Neuroimage, 19,* 513–531.
Walton, M. E., Bannerman, D. M., Alterescu, K., & Rushworth, M. F. S. (2003). Functional specialization within medial frontal cortex of the anterior cingulate for evaluating effort-related decisions. *Journal of Neuroscience, 23,* 6475.
Walton, M. E., Croxson, P. L., Behrens, T. E., Kennerley, S. W., & Rushworth, M. F. (2007). Adaptive decision making and value in the anterior cingulate cortex. *Neuroimage, 36(Suppl. 2),* T142–T154.
Walton, M. E., Devlin, J. T., & Rushworth, M. F. (2004). Interactions between decision making and performance monitoring within prefrontal cortex. *Nature Neuroscience, 7,* 1259–1265.
Yeung, N., Cohen, J. D., & Botvinick, M. M. (2004). The neural basis of error detection: Conflict monitoring and the error-related negativity. *Psychological Review, 111,* 931–959.