

# Executive Function and Error Detection: The Effect of Motivation on Cingulate and Ventral Striatum Activity

Cristina Simões-Franklin,<sup>1\*</sup> Robert Hester,<sup>2</sup> Marina Shpaner,<sup>3</sup>  
John J. Foxe,<sup>1,3,4</sup> and Hugh Garavan<sup>1,3</sup>

<sup>1</sup>*School of Psychology and Trinity College Institute of Neuroscience, Trinity College Dublin, Ireland*

<sup>2</sup>*Department of Psychology, School of Behavioral Science, University of Melbourne, Melbourne, Victoria, Australia*

<sup>3</sup>*Nathan S. Kline Institute for Psychiatric Research, Orangeburg, New York*

<sup>4</sup>*Program in Cognitive Neuroscience, The City College of the City University of New York, New York*

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**Abstract:** Reacting appropriately to errors during task performance is fundamental to successful negotiation of our environment. This is especially true when errors will result in a significant penalty for the person performing a given task, be they financial or otherwise. Error responses and monitoring states were manipulated in a GO/NOGO task by introducing a financial punishment for errors. This study employed a mixed block design alternating between punishment and no punishment (neutral) conditions, enabling an assessment of tonic changes associated with cognitive control as well as trial-specific effects. Behavioural results revealed slower responses and fewer commission errors in the punishment condition. The dorsal anterior cingulate cortex (ACC) had equal trial-specific activity for errors in the neutral and punishment conditions but had greater tonic activity throughout the punishment condition. A region of interest analysis revealed different activation patterns between the dorsal and the rostral parts of the ACC with the rostral ACC having only trial-specific activity for errors in the punishment condition, an activity profile similar to one observed in the nucleus accumbens. This study suggests that there is a motivational influence on cognitive processes in the ACC and nucleus accumbens and hints at a dissociation between tonic proactive activity and phasic reactive error-related activity. *Hum Brain Mapp* 31:458–469, 2010. © 2009 Wiley-Liss, Inc.

**Key words:** inhibitory control; error detection; fMRI; motivation; monetary loss; anterior cingulate; nucleus accumbens

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Contract grant sponsor: Irish Research Council for Science, Engineering, and Technology (IRCSET); Contract grant number: PD/2004/29; Contract grant sponsor: US National Institute of Drug Addiction (NIDA); Contract grant number: RO1 DA14100; Contract grant sponsor: US National Institute of Mental Health (NIMH); Contract grant number: RO1 MH65350; Contract grant sponsor: Center for Advanced Brain Imaging at the Nathan Kline Institute.

\*Correspondence to: Cristina Simões-Franklin, Institute of Neuroscience, Trinity College, Dublin 2, Ireland.

E-mail: Cristina.Simoes@tcd.ie

Received for publication 10 December 2008; Revised 26 May 2009; Accepted 20 July 2009

DOI: 10.1002/hbm.20879

Published online 28 August 2009 in Wiley InterScience (www.interscience.wiley.com).

## INTRODUCTION

Efficient executive control involves many processes, including task monitoring, response inhibition, error detection, and compensatory behavior. Response inhibition is crucial in human behavioral control since it allows us to suppress automatic, impulsive, or routine behavior, and therefore avoid errors. However, when an error is made, detecting that error helps us to adapt our behavior appropriately so as to avoid further errors. Impairment in these error-related processes has been reported in several clinical conditions including schizophrenia [Bates et al., 2002], attention-deficit hyperactivity disorder [Barkley, 1997], obsessive-compulsive disorder [Gehring et al., 2000; Herrmann et al., 2003], traumatic brain injury [Roche et al., 2004] and drug addiction [Bolla et al., 2000; Goldstein et al., 2001; Hester and Garavan, 2004; Kaufman et al., 2003].

Functional imaging and electroencephalographic studies that have attempted to map the brain areas involved in executive function and, in particular, error detection, have implicated the anterior cingulate cortex [ACC Carter et al., 1998; Gehring et al., 1993; Hester et al., 2004; O'Connell et al., 2007; Ridderinkhof et al., 2004; Van Veen and Carter, 2002]. Although its precise function(s) is not fully understood, a large body of evidence converges on a role for the ACC in performance evaluation. However, ACC activity has also been shown to be modulated by motivation, i.e., reward and/or punishment [Holroyd et al., 2003, 2004; Knutson et al., 2001b] and, consequently, one remaining challenge is to reconcile the region's cognitive functions with its sensitivity to these motivational manipulations. Functional subdivisions of the ACC have been proposed with the rostral ACC (rACC) thought to be more involved with "emotional" processing and the dorsal ACC (dACC) with cognitive and motor processing [Bush et al., 2000; Vogt et al., 1995]. However, contesting this model, a recent study by Taylor [2006] showed modulations in rACC to monetary losses and in dACC to both monetary gains and losses.

The limbic and mesencephalic dopaminergic systems have been identified as a crucial network in affective neuroscience and, in particular, in reward processing. Parts of this network include the ACC, the orbitofrontal cortex, prefrontal cortex, and nucleus accumbens (NAcc). In 1997 Schultz et al. observed that dopaminergic neurons in the midbrain fired not only to rewards, but to cues that have been associated with later rewards [Schultz et al., 1997]. They suggested that this dopaminergic activity carries a reward prediction error signal which is essential in reinforcement learning. BOLD activity in the NAcc reflects dopaminergic input in this area and can be used to monitor this reward error signal [for a review see Knutson and Gibbs, 2007]. NAcc has also been suggested to signal the valence of a reward [Breiter et al., 2001] and the salience of events [Berridge and Robinson, 1998; Zink et al., 2003]. More recently Cooper and Knutson [2008] reported that its activity can follow both of these patterns.

By introducing a monetary manipulation in executive function tasks, for instance a monetary loss when making an error, it is possible to study cognitive-motivational interactions in ACC and NAcc. One would expect that dACC would be involved in on-going cognitive control over the task to avoid errors [Magno et al., 2006], whereas rACC and NAcc would process the motivational component of the task, such as signaling the salience of an error when it results in a monetary loss.

To assess the cognitive and motivational influences on these control systems, subjects performed a Go-NoGo task during two different conditions: a punishment condition where an error of commission resulted in a monetary loss and a neutral condition with no monetary consequence for errors. The mixed design of the present task enable us to follow the temporal dynamics of the BOLD fMRI signal with respect to sustained tonic activity associated with the punishment condition, and the transient phasic activity elicited by the commission errors. With this kind of design we aimed to dissociate tonic and phasic activity during this particular task. We expected tonic preparatory activity in cognitive control regions such as the dACC that have been previously implicated in proactive control [Brown and Braver, 2005; Magno et al., 2006]. Furthermore, we expected these proactive control effects to be distinct from phasic reactive processes in affective regions like the rACC and the Nacc that may be responsive to the motivational manipulation.

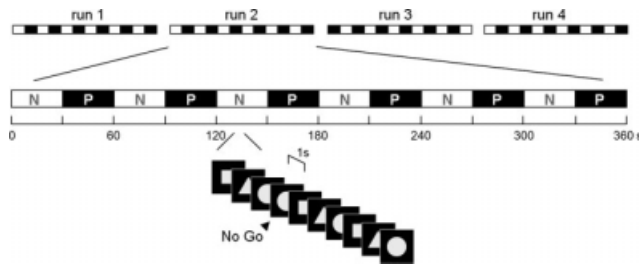
## MATERIALS AND METHODS

### Subjects

Sixteen subjects (11 females; 1 left-handed mean age 24.8 years; range 21–34) participated in this study. All subjects had normal or corrected to normal vision, no history of neurological or psychiatric disorders. Subjects provided written informed consent after all details of the study and procedures were fully explained to them. The Institutional Review Board of the Nathan Kline Institute for Psychiatric Research approved the experimental procedures.

### Task

The subjects performed a Go-NoGo task in which a square, a circle, and a triangle were presented serially at 1 Hz in a repeating cyclic pattern (see Fig. 1). Subjects were required to make a right index finger button press for each symbol and to inhibit their response to unpredictable, random NoGo stimuli: a NoGo occurred when the cycling pattern of the symbols was interrupted (i.e. when one of the symbols repeated). A NoGo trial was always followed by a Go trial, that is, there were never two NoGo trials in a row. The task alternated between neutral and punishment conditions. In the neutral condition the symbols were presented in white against a black background and the subjects were instructed to perform the task as well as they could. In the



**Figure 1.**

Schematic representation of the experimental design. The experiment consisted of four runs (five runs for four subjects) with 360 trials each. During the task subjects were asked to make a button response to each stimulus (presented at 1 Hz) and to withhold their response whenever the repeating cyclic pattern of the stimuli was broken (lure trial). This task employed a mixed block design alternating between two different conditions: the neutral condition and the punishment condition. The stimuli were presented in white or red against a black background for the neutral and punishment conditions, respectively. Stimuli were on screen for 500 ms and were followed by 500 ms of blank screen. Participants were instructed to respond while the stimulus was on screen but responses were recorded if made at any point in the 1-s trial duration.

punishment condition the symbols were presented in red and the subjects were informed that they would lose 25¢, from an initial amount of \$20, each time they made an error of commission (see Fig. 1). In both conditions subjects were instructed to perform the task as accurately and as fast as they could. Before recording, subjects had a 2-min period to familiarize themselves with the task outside the scanner. Four runs of 360 trials, divided into 12 alternating blocks of neutral and punishment conditions (each block containing 30 trials), were administered to the subjects. There were 144 NoGos (72 in each condition) distributed throughout the 1,296 Go trials. Because of insufficient number of errors in the punishment condition (two subjects) or successful inhibitions in the control condition (two subjects), four subjects performed a fifth run of the task.

### Recording

Image data were recorded with a 1.5 T Siemens Vision (Erlangen, Germany) scanner. For each run, 195 volumes were acquired with each comprising 22 slices (slice thickness 5 mm; gap = 0) using a single shot echo planar (EPI) pulse sequence (TR = 2,000 ms; TE = 50 ms; sagittal in-plane resolution 4 mm × 4 mm; interleaved).

The stimuli were presented via a 640 × 480 LCD display mounted on the head coil. One hundred seventy two high-resolution T1-weighted structural images (FOV = 307 mm; thickness = 1.2 mm, no gap) were acquired after the functional imaging to allow subsequent spatial normalization and activation localization.

### Data Analysis

All analyses were conducted using AFNI software (<http://afni.nimh.nih.gov/afni>, [Cox, 1996]). After image reconstruction, time differences in the slice acquisition were removed using a Fourier interpolation. The time-series data were then motion corrected using 3D volume registrations (least-squares alignment of three translational and three rotational parameters). An edge detection algorithm was then used to remove activation outside the brain.

A mixed regression analysis was employed comprising five task-related regressors. A square-wave regressor coded for the neutral-punishment pattern in a block design manner, using the neutral condition as a baseline and the punishment condition as the ON period (block regressor). Four separate regressors were employed to calculate impulse response functions (IRFs) for successful inhibitions and errors of commission in both neutral and punishment conditions (event-related regressors). All events of interest occurred at, and were time-locked to, the beginning of the 2-s whole-brain volume acquisitions. The motion-corrected time-series files were also included as regressors to accommodate nuisance variance.

The IRFs were fitted to a  $\gamma$ -variate function using nonlinear regression as previously described in Murphy et al. [2005]. The area under the curve of the  $\gamma$ -variate function was expressed as a percentage of the area under the baseline (from which variance associated with tonic activity differences between the neutral and punishment conditions had been removed with the block regressor). The percentage area (for the event-related activation) and the percentage change (for the block activation) maps were resampled at 1-mm<sup>3</sup> resolution, then warped onto the Talairach space [Talairach and Tournoux, 1988], and spatially blurred with a 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 no activation change. Significant voxels passed a voxel-wise statistical threshold ( $t = 4.3$ ,  $P \leq 0.001$ ) and were required to be part of a larger 126- $\mu$ l cluster of contiguous significant voxels. This cluster size was determined through a Monte Carlo simulation and resulted in less than a 5% probability of a cluster surviving due to chance.

To conduct between-conditions comparisons, combined maps of events from either neutral and punishment conditions were produced. These maps, normally referred to as Boolean OR-maps, include the voxels of activation identified as significant from any of the constituent maps and separate OR maps were created for successful inhibitions and errors of commission. The mean activation for clusters of significant voxels in the combined maps was calculated for the purpose of a functionally defined ROI analysis, and these data were subjected to a series of  $t$  test comparisons between conditions.

To assess the importance of accommodating baseline shifts between the neutral and punishment conditions, we

**TABLE I. Behavioral results**

	Neutral condition		Punishment condition		$t_{(15)}$	$P$
	$M$	SEM	$M$	SEM		
NoGo accuracy (%)						
Errors	53.7	4.7	33.9	4.4	5.574	***
Inhibitions	46.3	4.7	66.1	4.4	5.574	***
Reaction times (ms)						
Go RT	344.5	20.2	366.5	19.9	6.871	***
Error RT	322.4	18.1	340.7	17.2	3.059	**
Pre-post error RT difference	6.1	13.4	6.2	13.3	0.017	
Pre-post inhibition RT difference	74.5	11.4	82.0	10.2	1.322	

Note:  $P$  indicates significant differences between the Neutral and Punishment conditions (\*\* $P < 0.01$ ; \*\*\* $P < 0.001$ ).

repeated all analyses with only the four event-related regressors and without the block regressor.

Finally, for specific anatomically-defined region-of-interest analyses, right and left NAcc and rostral and dorsal ACC (BA24 and BA32) regions were defined by the Talairach and Tournoux atlas [1998] of the AFNI toolbox [Cox, 1996]. ACC was further divided into dorsal and rostral regions (dACC and rACC, respectively) by drawing a line, perpendicular to the intercommisural plane, at the anterior boundary of the genu of the corpus callosum [Vogt et al., 1995].

## RESULTS

### Behavioral Results

Behavioral results, summarized in Table I, show that the subjects were slower performing the task in the punishment condition than in the neutral condition ( $366.5 \pm 19.9$  ms vs.  $344.5 \pm 20.2$  ms,  $t_{(15)} = -6.871$ ,  $P < 0.0001$ ) and made significantly fewer commission errors in the punishment condition ( $33.9\% \pm 4.4\%$  vs.  $53.7\% \pm 4.7\%$ ,  $t_{(15)} = 5.547$ ,  $P < 0.001$ ). During the punishment condition the number of commission errors was negatively correlated with the GO response time ( $r = -0.73$ ,  $P < 0.01$ ). These results validate the experimental manipulation in so far as the financial punishment produced more careful and accurate performance. A measure of posterror behavior was calculated by subtracting the response time to the trial that immediately preceded the error from the response time to the trial that followed the error. Subjects showed no behavioral adaptation after errors in either condition (neutral:  $6.1 \pm 13.4$  ms,  $t_{(15)} = 0.452$ , NS; punishment:  $6.2 \pm 13.3$  ms,  $t_{(15)} = 0.470$ , NS) and no significant differences were observed across conditions. A similar measure for post-STOP behavior was calculated for each condition. In both neutral and punishment conditions subjects responded significantly faster in the trial following a correct inhibition (neutral:  $-74.5 \pm 11.4$  ms,  $t_{(15)} = 6.525$ ,  $P < 0.001$ ; punishment:  $-82.0 \pm 10.2$  ms,  $t_{(15)} = 8.075$ ,  $P < 0.001$ ) although no difference was observed across conditions.

### Tonic Block-Related Activation

The block analysis revealed 13 regions that were tonically more active during the punishment condition relative to the neutral condition (see Table II). Of particular interest are the right ACC (areas 32 and 24), bilateral insula, and bilateral presupplementary motor area (pre-SMA) since these areas are frequently implicated in phasic (i.e., trial-specific) error detection/correction.

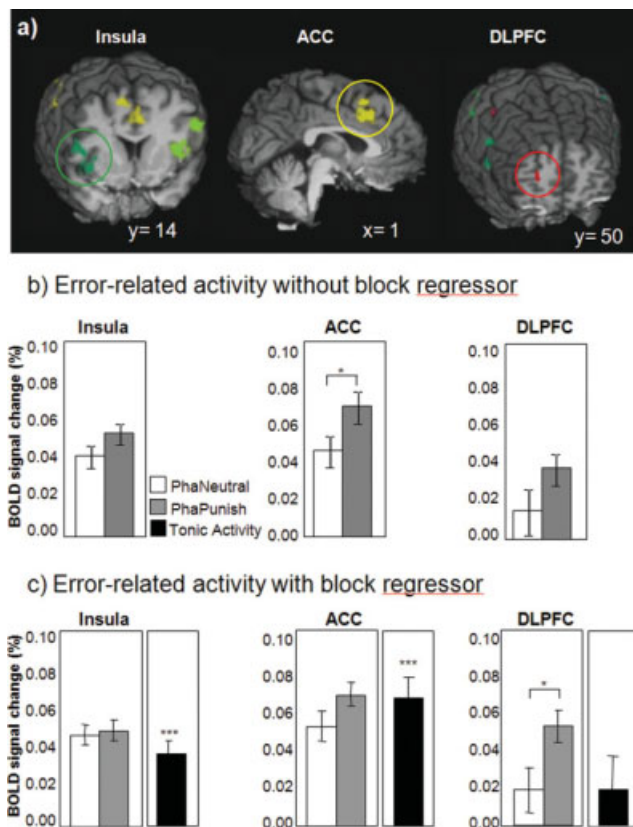
### Error-Related Activation

Figure 2a shows some of the brain regions showing phasic activity for errors of commission in the neutral and

**TABLE II. Regions showing greater tonic activity in the punishment block relative to the neutral block**

Anatomical structure	BA	Center of mass			Volume $\mu$ l
		$x$	$y$	$z$	
Frontal					
Med frontal G	6	22	-2	57	482
Mid frontal G	6	-20	-11	55	240
Precentral G	6	34	3	29	277
Inf frontal G	9	-36	5	28	133
Cingulate G	24	3	-1	46	300
Cingulate G	32	2	12	37	1,170
Parietal					
Precuneus	7	25	-62	42	1,213
Sup parietal lob	7	-28	-49	44	1,687
Basal Ganglia					
Caudate		-15	-4	16	469
Lentiform nucleus		14	0	6	4,226
Lentiform nucleus		-22	3	1	1,346
Insula and subcortical					
Insula	13	31	22	0	489
Insula	13	-28	21	1	305

Note: The coordinates are given within the framework of the standardized stereotaxic brain atlas of Talairach and Tournoux [1988]. Positive values for  $x$ ,  $y$ , and  $z$  denote, respectively, locations to the right, anterior and superior of the anterior commissure.



**Figure 2.**

Brain activation elicited by errors of commission during the neutral and punishment conditions. (a) Clusters of activity include the right insula (green), the ACC (yellow), and the right DLPFC (red). (b) The bar charts show the mean ( $\pm$  SEM) event-related error activity (white and grey bars for the neutral and the punishment conditions, respectively) resulting from the analysis ignoring the block regressor. (c) Mean ( $\pm$  SEM) event-related error activity resulting from the analysis including the block regressor. White and grey bars represent the BOLD signal change for the phasic event-related activity for error in the neutral and the punishment conditions -PhaNeutral and PhaPunish, respectively. Tonic activity (the difference between tonic levels of activity in the punishment and neutral conditions) for these error-specific clusters was calculated and is represented by the black bars (\* $P < 0.05$ ; \*\*\* $P < 0.001$ ).

punishment conditions. These regions resulted from the analysis that included both the event-related and the block regressors. Figure 2b,c show the error-related phasic activity for the ACC, right insula, and right DLPFC for the two different analysis, that is, when the block regressor was omitted (Fig. 2b) and when it was included in the analysis (Fig. 2c). For each one of the graphs, the white and grey bars represent the phasic activity elicited by errors of commission during the neutral and the punishment conditions, respectively. The tonic activity levels for the block regressor (i.e., punishment—neutral condition) within these spe-

cific error-related regions were also calculated and are depicted by the black bars in Figure 2c.

The two different analyses, that is with and without the block regressor, revealed different patterns of activation in these regions. Specifically, in the ACC region, the omission of the block regressor results in a significant greater phasic activity for errors occurring during the punishment condition than for errors in the neutral condition ( $t_{(15)} = 2.328$ ;  $P < 0.05$ ). This difference of activity between the two conditions is no longer present when the block regressor is included in the analysis ( $t_{(15)} = 1.812$ ; n.s.). This analysis demonstrates the importance of accounting for tonic activity changes between conditions when looking at differences in event-related, phasic activity. All further results are from the five-regressor analysis that included the block tonic-related regressor.

Figure 2c shows that, although there were no differences in error-related activity in the ACC and insula between the neutral and the punishment conditions, both areas, as noted above, were tonically more activated during the punishment condition (ACC:  $t_{(15)} = 5.884$ ,  $P < 0.0001$ ; insula:  $t_{(15)} = 5.636$ ,  $P < 0.001$ ). Conversely, BA10 ( $t_{(15)} = 2.372$ ;  $P < 0.01$ ), right and left thalamus ( $t_{(15)} = 6.183$ ,  $P < 0.001$  and  $t_{(15)} = 3.499$ ,  $P < 0.01$ , respectively) and the right fusiform gyrus ( $t_{(15)} = 3.933$ ,  $P < 0.001$ ) all showed greater activation for errors in the punishment condition (areas with superscript “a”) in Table III).

### Inhibition-Related Activation

Figure 3 depicts the activity for successful inhibitions in the neutral and punishment conditions (white and grey bars, respectively). As above, tonic activity levels in these specific, functionally-defined brain regions were calculated during the punishment condition relative to the neutral condition (black bar). The majority of the brain areas active during correct inhibitions (Table IV) showed significantly more event-related activity during the neutral condition compared to the punishment condition, a pattern of results that stands in contrast to that observed for the event-related error activity. Exceptions included the right insula and the DLPFC where no significant differences in event-related activation between conditions were observed. As expected, given the previous results, ACC and right insula showed increased tonic activation throughout the punishment block relative to the neutral block (ACC:  $t_{(15)} = 4.536$ ,  $P < 0.0001$ ; insula:  $t_{(15)} = 5.244$ ,  $P < 0.0001$ ).

### Anatomically Defined Analysis

#### ACC activation

To test the same ACC regions across the different contrasts, an anatomically defined analysis of the ACC was performed. The subregions, defined by the Talairach and Tournoux atlas [1988] of the AFNI Toolbox, were dorsal ACC, depicted in red in Figure 4a (11,791  $\mu$ l; centre-of-

**TABLE III. Regions of phasic-related activity during errors**

Anatomical structure	BA	Center of mass			Volume μl	$t_{(15)}$	$P$
		$x$	$y$	$z$			
Frontal							
Precentral G	4	-47	-16	40.1	780	2.023	
Med frontal G	6	31	12	43	739	1.381	
Precentral G	6	42	-6	49	145	1.686	
Mid frontal G	9	-29	24	33	148	3.093	**
Sup frontal G	9	34	36	28	216	0.157	
Mid frontal G	10	40	40	11	185	0.778	
Mid frontal G	10	-30	45	19	522	1.512	
Sup frontal G <sup>a)</sup>	10	21	52	12	161	2.372	*
Ant cingulated	32	-7	27	21	467	1.200	
Cingulate G	32	2	14	40	2,656	1.820	
Parietal							
Precuneus	7	9	-69	34	895	0.062	
Inf parietal lob	40	49	-37	45	1,685	1.371	
Inf parietal lob	40	-35	-45	43	448	0.064	
Supramarginal G	40	-54	-49	35	341	2.770	*
Postcentral G	43	-51	-19	21	148	0.575	
Temporal							
Fusiform G <sup>a)</sup>	37	46	-40	-8	238	3.933	***
Mid temporal G	37	-44	-58	17	286	1.317	
Mid temporal G	39	54	-55	7	345	2.399	*
Sup temporal G	41	49	-35	10	714	2.058	
Occipital							
Cuneus	18	-11	-75	20	266	1.317	
Cuneus	18	13	-68	11	247	2.826	*
Basal ganglia							
Caudate		-17	11	8	354	2.109	
Lentiform nucleus		15	11	2	845	2.437	*
Insula and subcortical							
Insula	13	39	14	9	6,023	0.381	
Insula	13	-40	10	10	4,848	0.638	
Nucleus accumbens		-16	7	-3	331	0.170	
Thalamus <sup>a)</sup>		5	-31	5	933	6.183	***
Thalamus <sup>a)</sup>		-5	-16	11	397	3.499	**

Note: The coordinates are given within the framework of the standardized stereotaxic brain atlas of Talairach and Tournoux [1988]. Positive values for  $x$ ,  $y$ , and  $z$  denote, respectively, locations to the right, anterior and superior of the anterior commissure. Clusters with superscript <sup>a)</sup> showed stronger phasic responses to errors in the punishment than in the neutral condition. The  $t_{(15)}$  and  $P$  columns show the statistics for the pairwise comparison of the activation levels between the neutral and punishment conditions (\* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ ).

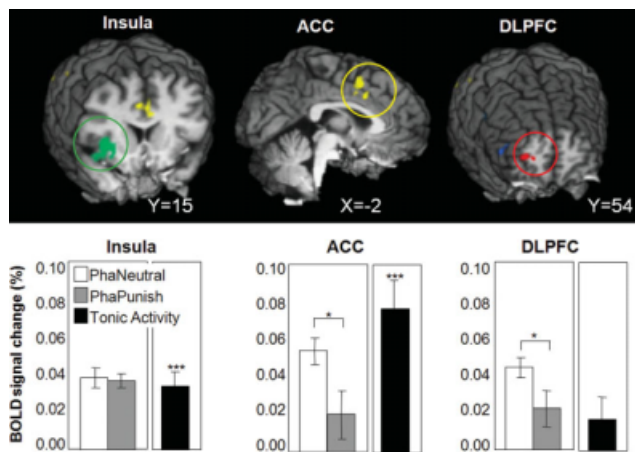
mass:  $x = -1$ ,  $y = 7$ ,  $z = 36$ ) and rostral ACC depicted in blue (7,370 μl; centre-of-mass:  $x = -1$ ,  $y = 37$ ,  $z = 7$ ). A region (dorsal vs. rostral) by condition (neutral vs. punishment) ANOVA for phasic error-related activity revealed a significant main effect for region ( $F_{(1,15)} = 7.68$ ;  $P < 0.05$ ) with the dACC showing stronger activity than the rACC. There was neither a significant main effect for condition ( $F < 1$ ) nor a significant interaction between region and condition ( $F_{(1,15)} = 3.01$ ;  $P = 0.10$ ).

Despite the lack of a significant interaction, an a priori interest in the responsivity of these ACC subregions to the task manipulation warranted further exploratory contrasts. One-sample  $t$  tests against baseline revealed significant error-related dACC activity in both neutral and punishment conditions (neutral:  $t_{(15)} = 5.718$ ;  $P < 0.001$ ; punish-

ment:  $t_{(15)} = 5.118$ ;  $P < 0.001$ ) but significant rACC activity in only the punishment condition (neutral:  $t_{(15)} = 1.609$ ;  $P = 0.1$ ; punishment:  $t_{(15)} = 2.735$ ;  $P < 0.05$ ). Concerning tonic activity, dACC showed a trend to be more active during the punishment condition than during the neutral condition, although this difference did not reach significance ( $t_{(15)} = 2.014$ ;  $P = 0.06$ ). Furthermore, a significant correlation was observed between the tonic activity in dACC during the punishment block and the reduced number of errors during this condition ( $r = 0.72$ ,  $P < 0.01$ ).

#### **NACC activation**

Figure 4b shows the right and left NAcc clusters defined by the Talairach and Tournoux atlas [1988] of the AFNI



**Figure 3.**

Functional activation associated with successful inhibitions in the neutral and punishment conditions. Regions of activity include the right insula (green), the ACC (yellow), and the right DLPFC (red). White and grey bars represent the BOLD signal change for the phasic event-related activity for inhibitions in the neutral and the punishment conditions -PhaNNeutral and PhaN Punish, respectively. Tonic activity (the difference between tonic levels of activity in the punishment and neutral conditions) for these inhibition-specific clusters was calculated and is represented by the black bars (\* $P < 0.05$ ; \*\*\* $P < 0.001$ ).

Toolbox (right: 130  $\mu$ l; centre-of-mass:  $x = 11, y = 9, z = -8$ ; left: 157  $\mu$ l; centre-of-mass:  $x = -13, y = 9, z = -8$ ) and the corresponding activations for the errors in each condition. A hemisphere (right vs. left) by condition (neutral vs. punishment) ANOVA revealed a significant main effect for condition ( $F_{(1,15)} = 9.38; P < 0.01$ ) with NAcc event-related activity stronger during errors in the punishment condition than in the neutral condition. One-sample  $t$  tests against baseline revealed that both right and left NAcc were only active for errors that occurred during the punishment condition (right:  $t_{(15)} = 3.383; P < 0.01$ ; left:  $t_{(15)} = 3.738; P < 0.01$ ) but the activation difference between the neutral and the punishment conditions only reached significance for the right NAcc ( $t_{(15)} = 2.675; P < 0.05$ ). For the successful inhibitions, a hemisphere by condition  $2 \times 2$  ANOVA did not show significant main effects or an interaction, although there was a trend for a main effect for condition ( $F_{(1,15)} = 3.61; P < 0.07$ ). One-sample  $t$  tests against the baseline showed that both right and left NAcc were only active for successful inhibition events in the punishment conditions (right:  $t_{(15)} = 3.502; P < 0.01$ ; left:  $t_{(15)} = 2.461; P < 0.05$ ). No tonic activity difference was observed in the NAcc.

## DISCUSSION

The results reveal brain activity differences associated with tonic and phasic control functions. This was enabled

by the mixed block and event-related design, the importance of which was underscored by the contrasting results obtained from the additional analysis that excluded the block regressor. The exclusion of the block regressor revealed a pattern of results similar to Taylor et al. [2006] in which the dACC region showed greater event-related activity for financially consequential errors compared with inconsequential errors. The present results demonstrate that this apparent event-related effect may in fact be driven by changing baselines more properly characterized as increased tonic activity. Such a result may reflect dynamics between tonic proactive error avoidance and phasic reactive error-related processes.

## Tonic Activity

Several brain regions, previously implicated in cognitive control, were more activated for the duration of the punishment block relative to the neutral block. These regions included dACC, bilateral insula, and the pre-SMA. This increased tonic activity in dACC and frontal cortex suggests that these areas may be responsible for more cautious performance during the punishment condition, reflected in slower RTs and fewer commission errors. dACC is known to play a role in monitoring goal-oriented behaviors [Bush et al., 2000; Kerns et al., 2004]. Accumulating evidence also suggests that the monitoring role of dACC is temporally flexible; heightened activity can guard against errors either prior to a trial [Ridderinkhof et al., 2003], within a trial [Magno et al., 2006], or can be sustained for a period of time following an error if another critical trial is anticipated soon [Hester et al., 2007]. The tonic activity observed in the dACC during the punishment block might reflect a proactive performance monitoring function [Brown and Braver, 2005; Magno et al., 2006] which is accentuated during the punishment condition when an error might result in a financial loss.

The tonic activity observed in the dACC and the insula during the punishment condition is also in line with recent work by Dosenbach et al. [2007]. Based on activation profiles in functionally connected areas during resting state fMRI, these authors proposed two distinct task-control networks, an adaptative frontoparietal and a stable cingulo-opercular network. The frontoparietal network, comprising dorsolateral prefrontal cortex and the intraparietal sulcus, is involved in error processing and shows adaptative control on a trial-by-trial basis. In contrast, the cingulo-opercular network, consisting of the dACC, the anterior insulae and the anterior prefrontal cortex, showed sustained activity across a longer task period suggesting a role in maintaining stable goal-directed behavioral control. Furthermore, increased sustained activity in frontal and parietal regions have also been recently observed by Locke and Braver [2008] when subjects performed a cognitive task under reward and penalty conditions, as opposed to

**TABLE IV. Regions of phasic-related activity during successful inhibitions**

Anatomical structure	BA	Center of mass			Volume μl	$t_{(15)}$	<i>P</i>
		<i>x</i>	<i>y</i>	<i>z</i>			
Frontal							
Med frontal G	6	3	-9	57	334	4.884	***
Inf frontal G	9	43	7	24	318	2.145	*
Mid frontal G	9	30	33	23	222	2.049	
Mid frontal G	10	39	44	11	266	1.808	
Sup frontal G	10	24	55	9	377	2.671	*
Cingulate G	24	-3	16	30	516	2.149	*
Ant cingulate	32	7	24	29	141	2.236	*
Cingulate G	32	3	7	45	457	2.105	
Parietal							
Postcentral G	43	-46	-11	25	164	4.497	***
Temporal							
Mid temporal G	37	-46	-63	9	192	2.780	*
Basal ganglia							
Lentiform nucleus		22	2	-5	309	2.990	**
Lentiform nucleus		-19	6	6	529	2.996	**
Supramarginal G		52	-40	31	2,556	3.292	**
Insula and subcortical							
Insula	13	33	15	1	2,857	0.278	
Insula	13	-29	24	1	192	2.301	*
Nucleus accumbens		13	10	3	163	3.505	**
Thalamus		7	-6	13	162	4.702	***

Note: The coordinates are given within the framework of the standardized stereotaxic brain atlas of Talairach and Tournoux [1988]. Positive values for *x*, *y*, and *z* denote, respectively, locations to the right, anterior and superior of the anterior commissure. The  $t_{(15)}$  and *P* columns show the statistics for the pairwise comparison of the activation levels between the neutral and punishment conditions (\**P* < 0.05; \*\**P* < 0.01; \*\*\**P* < 0.001). In all clusters with significant *t*-value activation levels were larger for inhibitions during neutral condition than during punishment condition.

a nonincentive condition. Tonic activity during the punishment condition was also observed in motor areas such as the precuneus, precentral gyrus, and basal ganglia. The greater involvement of these motor control areas may underlie the slower response times observed during this condition. The basal ganglia in particular, have been implicated in higher-order aspects of motor control but activity here has also been shown to be modulated by reward [Graybiel et al., 1994]. In this particular task, the greater subcortical activity in the punishment condition may reflect the slower, more cautious responding in this condition.

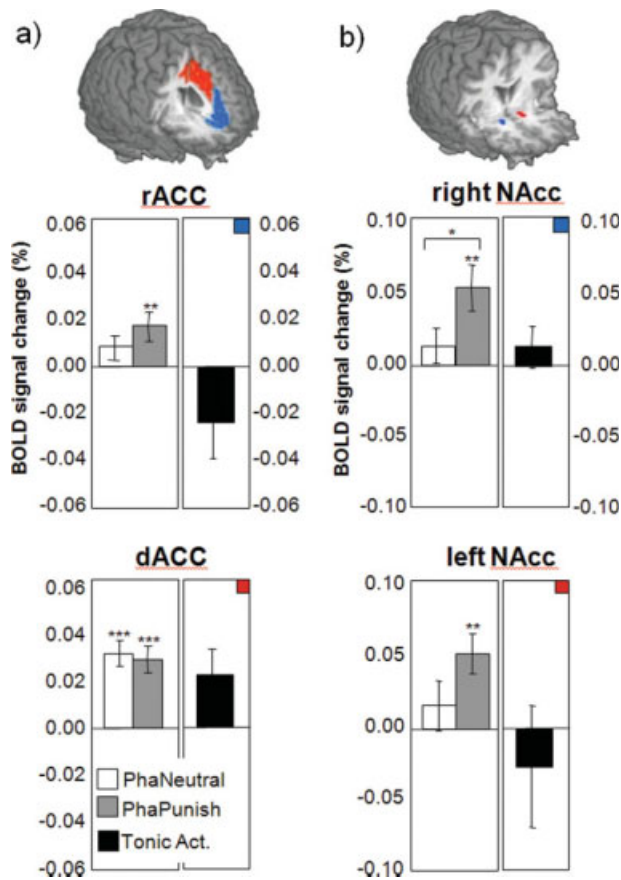
Finally, the discrepancy between the results observed in the dACC for the whole brain analysis vs. the ROI analysis (i.e., the fact that the dACC activation in the ROI analysis does not reach significance as opposed to a significant activation in the whole brain analysis) is likely to be due to differences of volume in the different regions. In the whole brain analysis for errors and inhibitions, the size of the functionally-defined dACC ROI is substantially smaller than the cluster considered in the ROI analysis (whole brain analysis: errors 2,656 μl; inhibitions 457 μl; ROI analysis: 11,791 μl); it is likely that the nonresponsive voxels of the larger volume serve to dampen effects present in a subset of that volume.

### Phasic Activity

One of the main results of the present study was the insensitivity of the event-related error activity in the dACC to the punishment manipulation. This could be considered a surprising result given the extensive literature reporting modulation of ACC error-related activity with reward/punishment manipulations with both fMRI [Breiter and Rosen, 1999; Knutson et al., 2001a, 2005; O'Doherty et al., 2001; Taylor et al., 2006] and electrophysiology [Gehring and Willoughby, 2002; Holroyd et al., 2004]. It might be argued that the lack of a significant effect in the dACC in the present study may be due to an insensitivity of our methods to detect what might be a small effect, but this concern is offset somewhat by the fact that (a) significant phasic effects in this region were detected when the block regressor was removed and (b) that with the block regressor included significant effects were detected in other regions (e.g., the rACC).

Differences in experimental design may be responsible for these discrepant findings. Many of the fMRI tasks containing reward/punishment manipulations present a cue to the subject indicating that a cash amount can soon be won or lost. As previously reported, activity in the ACC is





**Figure 4.**

ACC and NAcc analysis. (a) The clusters represent the dorsal ACC (red) and the rostral ACC (blue) according to Vogt et al. [1995]. (b) The figure shows the left and right NAcc according to the Talairach and Tournoux brain Atlas. In both figures the white and grey bars represent the BOLD signal change for the phasic event-related activity elicited by the errors in the neutral and the punishment conditions -PhaNeutral and PhaPunish, respectively. The BOLD signal change elicited by the tonic activity (the difference between tonic levels of activity in the punishment and neutral conditions) for the ACC clusters was calculated and is represented by the black bars (\* $P < 0.05$ ; \*\* $P < 0.001$ ; \*\*\* $P < 0.001$ ).

modulated by the expectancy of reward [Knutson et al., 2001a]. Consequently, if a shifting baseline of activation is not taken into account when computing the ACC activity due to wins/losses, this could lead to an erroneous attribution of activation changes to the win/loss event rather than to the processes that precede the event. A similar result was recently observed by Locke and Braver [2008]. In a task designed to look at the effect of motivation in cognitive control, they observed that reward incentives were associated with increased levels of tonic activity and not with transient trial-by-trial activity.

Electrophysiological studies have reported error-related negativity following both an error of commission [Falkenstein et al., 1990; Gehring et al., 1993] and feedback indicating errors or monetary losses [e.g., Gehring and Willoughby, 2002; Hajcak et al., 2006; Holroyd and Coles, 2002]. It has been widely reported that the ERN following feedback is larger for negative feedback (e.g., monetary losses) than positive feedback, although very few studies have looked at the effect of the monetary loss on the response locked ERN (RL-ERN). In two different studies Hajcak et al. [2005] and Dunning and Hajcak [2007] showed that the RL-ERN was larger for errors associated with larger losses even before the feedback was presented.

The increased phasic ACC response observed in both EEG and fMRI studies could be driven by a separate contribution from rACC. A regional analysis of the dorsal and rostral ACC activation after a commission error revealed no difference between the two conditions in the dACC but stronger activity in the rACC for errors during the punishment condition. This result is in line with Taylor et al. [2006] who also reported activity in rACC for monetary losses and may reflect an affective response to the financially consequential error given this region's role in affective processes.

Although the right DLPFC (BA 10) did not show tonic activation during the punishment condition, it had more phasic activity for errors occurring during the punishment condition. The DLPFC is more active for errors that subjects are aware of, relative to unaware errors [Hester et al., 2005], which may suggest that the greater activity for errors in the punishment condition reflects the heightened salience of financially consequential errors. BA10 is part of a fronto-striatal loop with projections to the ventral striatum [Alexander et al., 1986], and has been reported to be part of a network processing monetary reward in the human brain [Elliott et al., 2000; Thut et al., 1997]. This dopaminergic dependency might explain the heightened phasic response of this brain region to the consequential errors of the punishment condition.

The thalamus and fusiform gyrus were also more active for errors in the punishment condition. Both these areas, previously reported to be active during error processing [Garavan et al., 2002; Hester et al., 2004; Ullsperger and von Cramon, 2001], have recently been reported to underlie the alerting component of attention [Fan et al., 2005] and their activity may also reflect the increased salience of financially consequential errors.

Significant event-related activity was also observed in the right NAcc for errors in the punishment condition and in both right and left NAcc for correct inhibitions in the punishment condition. There was no tonic activity difference in the NAcc between conditions. Increased NAcc activity for errors during the punishment condition are consistent with the reward prediction error theory [Schultz et al., 1997] according to which unexpected events increase dopaminergic activity. If the monitoring state of the subject is higher during the punishment condition with the

result that there is a lower expectation of errors, then an error might produce a greater prediction error signal as indexed by greater NAcc activity. However, greater NAcc activity was also observed for successful inhibitions during the same punishment condition, the condition in which they were more frequent.

More recent theories have reported that NAcc activity may not only mediate the anticipation of reward [Knutson et al., 2001a, 2005], but also the anticipation of aversive stimuli [Jensen et al., 2003; Seymour et al., 2007] and the salience of a stimulus [Berridge and Robinson, 1998]. For example, during a visual task where subjects were presented with nonrewarding flickering visual distracters, Zink et al. [2003] observed that when the distracters were infrequent (more salient) NAcc was activated more than if the distracters were frequent (less salient). In the present task, NoGo stimuli are salient events since they require a different behavioral response than the more frequent GO stimuli. The positive NAcc activity for both errors and inhibitions in the punishment condition would suggest that salience rather than reward valence is the stimulus attribute processed by this structure, an interpretation that is consistent with theories proposing a “salience system” involved in all motivated behaviors elicited by both rewarding and aversive stimuli [Jensen et al., 2003; Seymour et al., 2007].

Finally, the activation profile of rACC and NAcc were similar as both were more active for errors in the punishment condition. This reflects that both regions receive similar dopaminergic inputs and underscores the functional distinction between rACC and dACC as has also been revealed by distinct patterns of rostral and dorsal interregional correlations [Magno et al., 2008; Margulies et al., 2007]. Although it has been shown that there are no sex differences in ACC and insula during the Go-NoGo task [Hester et al., 2004], it would be interesting to determine if this also applies for the reward-related areas shown in this study, i.e., rACC and NAcc.

### Inhibitory Control

During the neutral condition, when there was a relative lack of tonic activity compared to the punishment condition, there was greater transient activity for successful inhibitions. Greater phasic activity for successful inhibitions may result from reduced tonic performance monitoring throughout the neutral condition. Another articulation of this dynamic between “proactive” and “reactive” processes is that the reduced tonic monitoring of performance in the neutral condition resulted in less cautious performance (e.g., faster responses) thereby requiring greater neuronal “effort” to inhibit responding on neutral NOGO trials and increased reactive performance evaluation processes. These tonic-phasic interactions are supported by an observed correlation between the increased tonic dACC activity during the punishment block and the difference in

phasic activity for inhibitions between the neutral and the punishment conditions ( $R = 0.53$ ,  $P < 0.05$ ). That is, across subjects, the greater the increase in proactive monitoring functions across conditions the smaller the additional phasic activity necessary in the punishment condition for successful inhibitions.

### ACKNOWLEDGMENTS

The authors thank Jennifer Montesi and Raj Sanjoi for assistance with data acquisition. This work was presented in abstract form at the 2006 Human Brain Mapping Meeting in Florence, Italy.

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