Psychophysiology, 44 (2007), 343–351. Blackwell Publishing Inc. Printed in the USA.

DOI: 10.1111/j.1469-8986.2007.00515.x

Differential engagement of anterior cingulate cortex subdivisions for cognitive and emotional function

APRAJITA MOHANTY,[a,b,c] ANNA S. ENGELS,[b,c] JOHN D. HERRINGTON,[b,c,d] WENDY HELLER,[b,c] MOON-HO RINGO HO,[e,f] MARIE T. BANICH,[g] ANDREW G. WEBB,[h] STACIE L. WARREN,[b,c] AND GREGORY A. MILLER[b,c,i]

[a]Institute for Neuroscience and Cognitive Neurology and Alzheimer's Disease Center, Northwestern University, Evanston, Illinois, USA
[b]Beckman Institute Biomedical Imaging Center, University of Illinois at Urbana-Champaign, Urbana, Illinois, USA
[c]Department of Psychology, University of Illinois at Urbana-Champaign, Urbana, Illinois, USA
[d]Yale University School of Medicine, New Haven, Connecticut, USA
[e]Department of Psychology, McGill University, Montreal, Quebec, Canada
[f]Department of Psychology, Nanyang Technological University, Singapore
[g]Department of Psychology and Institute of Cognitive Science, University of Colorado at Boulder, Boulder, Colorado, USA
[h]Department of Bioengineering, Pennsylvania State University, University Park, Pennsylvania, USA
[i]Department of Psychiatry, University of Illinois at Urbana-Champaign, Urbana, Illinois, USA

Abstract

Functional differentiation of dorsal (dACC) and rostral (rACC) anterior cingulate cortex for cognitive and emotional function has received considerable indirect support. Using fMRI, parallel tasks, and within-subject analysis, the present study directly tested the proposed specialization of ACC subdivisions. A Task × Region interaction confirmed more dACC activation during color-word distractors and more rACC activation during emotion-word distractors. Activity in ACC subdivisions differentially predicted behavioral performance. Connectivity with prefrontal and limbic regions also supported distinct dACC and rACC roles. Findings provide direct evidence for differential engagement of ACC subdivisions in cognitive and emotional processing and for differential functional connectivity in the implementation of cognitive control and emotion regulation. Results point to an anatomical and functional continuum rather than segregated operations.

Descriptors: fMRI, Anterior cingulate, Functional connectivity, Cognition, Emotion, Stroop

In recent years neuroimaging data have often been interpreted as evidence for a fundamental, qualitative differentiation of cognition and emotion, emphasizing that particular brain regions are specialized for either cognition or emotion and that this specialization is anatomically segregated and often functionally reciprocal (Drevets & Raichle, 1998). Although such a strict distinction between cognition and emotion is probably not viable (Miller, 1996), considerable data are compatible with the specialization of brain structures for cognitive versus emotional processing. Anterior cingulate cortex (ACC) is a prominent example of a brain region suggested as reflecting such a fractionation of cognitive and emotional processing. Based on indirect but impressive evidence from a variety of hemodynamic neuroimaging studies, the ACC has been divided into "cognitive"/dorsal and "affective"/rostral subdivisions (Bush, Luu, & Posner, 2000; Devinsky, Morrell, & Vogt, 1995). However, no direct statistical test of this specialization has been published.

The logic of such a test is based on the concept of double dissociation. As implemented in functional brain specialization studies, if performance on task A is associated with increased neural activity in region X but not brain region Y, and if in addition performance on task B is associated with increased neural activity in region Y and not brain region X, then region X is specialized for task A and region Y is specialized for task B (Gray, Braver, & Raichle, 2002). Using the same group of participants, two studies reported activation of the "cognitive"/dorsal ACC during a nonemotional counting Stroop task (Bush

This research was supported by the National Institute of Drug Abuse (R21 DA14111), the National Institute of Mental Health (R01 MH61358, T32 MH14257, T32 MH19554), and the University of Illinois Beckman Institute and Intercampus Research Initiative in Biotechnology. Anna S. Engels was a predoctoral trainee in the Cognitive Psychophysiology training program of the Department of Psychology, University of Illinois at Urbana–Champaign, under NIMH Grant T32 MH19554. John D. Herrington was a predoctoral trainee in the Quantitative Methods training program of the Department of Psychology, University of Illinois at Urbana–Champaign, under NIMH Grant T32 MH14257.

The authors thank Emily Cahill, Nancy Dodge, Rebecca Levin, Sarah Sass, Brad Sutton, Holly Tracy, and Tracey Wszalek for their contributions to this project.

Address reprint requests to: Gregory A. Miller, Department of Psychology, University of Illinois at Urbana–Champaign, 603 E. Daniel Street, Champaign, IL 61820, USA. E-mail: gamiller@uiuc.edu

et al., 1998) or "affective"/rostral-ventral ACC during an emotion-word counting Stroop task (Whalen et al., 1998). However, this apparent difference in functional localization was not tested statistically. A meta-analysis also made a strong case for the functional differentiation of the two ACC subregions (Bush et al., 2000), but a decisive test would strengthen the case. The present study is the first direct test, via parallel tasks and within-subject ANOVA, of the proposed specialization of ACC subdivisions for particular aspects of emotional and cognitive processing.

Dorsal ACC (dACC) occupies Brodmann areas (BA) 24b′–c′ and 32′ (Figure 1) and shows extensive connectivity with prefrontal cortex (Barbas & Pandya, 1989; Paus, 2001). dACC has extensive connections with dorsolateral prefrontal cortex (DLPFC, BA 46/9) as well as primary, premotor, and supplementary motor areas, making it an ideal candidate for cognitive–motor mechanisms (Paus, 2001). dACC is believed to play an important role in attention and executive function. One view suggests that dACC detects conflict occurring between incompatible streams of information that create the potential for erroneous task performance (Carter et al., 1998). According to this model, following detection of conflict, dACC recruits DLPFC and inferior parietal cortex to exert attentional control and reduce conflict (Banich et al., 2000b; Carter et al., 1998; Kerns et al., 2004; MacDonald, Cohen, Stenger, & Carter, 2000). Another viewpoint proposes a functional differentiation within dACC (Milham & Banich, 2005), with more posterior portions involved in late-stage attentional processes, which are usually response-related (Milham et al., 2001; Milham, Banich, & Barad, 2003), and anterior portions showing involvement in response evaluation (Milham & Banich, 2005).

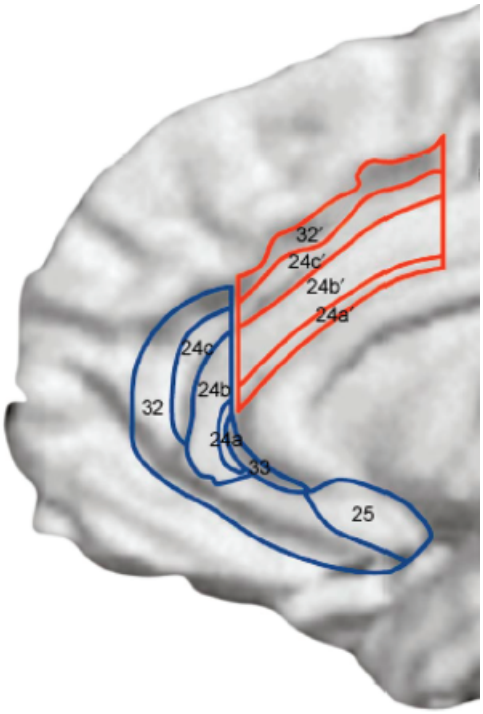

Figure 1. Cytoarchitectural subregions of anterior cingulate cortex (ACC) per Brodmann system (dACC subregions in red and rACC subregions in blue). These localizations are approximate and for illustrative purposes. From "Cognitive and Emotional Influences in Anterior Cingulate Cortex," by G. Bush, P. Luu, and M. I. Posner, 2000, *Trends in Cognitive Neuroscience*, p. 216. Copyright (2000) by Elsevier Science Ltd. Adapted with permission of the author and publisher.

In contrast to dACC's role in cognitive processing, considerable evidence implicates rostral ACC (rACC) in the assessment of emotional information as well as the regulation of emotional responses. rACC occupies Brodmann areas 24a–c, 32, 25, and 33 (Figure 1) and projects directly to amygdala, nucleus accumbens, hypothalamus, hippocampus, and orbitofrontal cortex (Devinsky et al., 1995). Studies show rACC involvement in emotional processing in normal individuals and in symptom provocation in anxiety disorders (e.g., Bush et al., 2000; Devinsky et al., 1995; Drevets & Raichle, 1998; Whalen et al., 1998). Rather than being specialized distinctly for emotion, rACC may play an important role in tasks requiring cognitive control in the presence of emotional stimuli. Most studies of cognitive control have employed stimuli and tasks lacking an explicit affective component. However, cognitive control is equally important when task-irrelevant emotional stimuli interfere with task-relevant processing. Initial evidence supports the involvement of rACC in implementation of this control and evaluation of interference from emotionally salient but task-irrelevant stimuli. For example, increased rACC activity has been observed in neuroimaging studies examining interference in task-relevant processing due to task-irrelevant emotional information, such as fearful faces and negatively valenced words (Bishop, Duncan, Brett, & Lawrence, 2004; Mohanty et al., 2005; Vuilleumier, Armony, Driver, & Dolan, 2001; Whalen et al., 1998).

Functional connectivity studies provide additional support for the functional differentiation of rACC and dACC. For example, dACC and DLPFC coactivation has been observed during the performance of a variety of cognitive tasks (Paus, 2001), and transcranial magnetic stimulation of DLPFC results in increased blood flow in dACC (Paus, Castro-Alamancos, & Petrides, 2000). dACC is also believed to recruit DLPFC to implement strategic processes involved in exerting attentional control and reduction of conflict (Kerns et al., 2004). In contrast, rACC is believed to be involved in emotion regulation via modulation of amygdala (Ochsner, Bunge, Gross, & Gabrieli, 2002).

Although studies indicate differential involvement of dACC and rACC in cognitive and emotional function, respectively, evidence also suggests that the roles of these two regions are not so distinct. For example, increases in rACC activity are associated with decreased amygdala activity, but both dACC and rACC negatively modulate the thalamus–amygdala relationship (Das et al., 2005; Ochsner et al., 2002; Petrovic, Carlsson, Petersson, Hansson, & Ingvar, 2004). There is also evidence indicating dACC involvement in emotional processing. For example, attention-demanding tasks involving emotional content can alter the firing rate of dACC neurons (Davis et al., 2005), and emotional processing appears to foster increased dACC activity particularly in the context of concomitant cognitive demands (Phan, Wager, Taylor, & Liberzon, 2002). dACC's involvement in cognitive and emotional processes may reflect its more general role in modulation of autonomic responses related to adaptive behavioral control (Critchley et al., 2003). Beyond its putative role as the "affective" subdivision, rACC has been implicated in a variety of cognitive functions, particularly in monitoring of errors. Functional magnetic resonance imaging (fMRI) studies have localized error-related activity in rACC (Kiehl, Liddle, & Hopfinger, 2000). rACC has also has been implicated in the generation of two error-related ERP components, error-related negativity (Luu, Tucker, Derryberry, Reed, & Poulsen, 2003)

and error positivity (Van Veen, & Carter, 2002). Because both components vary with negative affect (Hajcak, McDonald, & Simons, 2004), rACC may be involved in the affective evaluation of errors (Van Veen, & Carter, 2002). Thus, some degree of functional specialization need not mean that each function unfolds, or that each region is active, in isolation. For example, the portion of anterior dACC that abuts rACC is involved in affective processes associated with the evaluation of responses (Gehring & Knight, 2002), indicative of involvement in an integration of emotional and cognitive processing. Rather than supporting distinct processes, the expanse of ACC extending from dorsal to ventral may implement a continuum of processing that blends putatively cognitive and emotional features.

It is clear that the ACC is not functionally monolithic. A variety of indirect observations have been interpreted to favor a rather stark specialization of ACC subdivisions for cognitive versus emotional processing, but no studies have investigated this functional differentiation using appropriate ANOVA designs that examine the interaction between ACC subdivision and cognitive versus emotional task. Most studies have used only voxel-by-voxel statistics (rather than cluster-level or region-of-interest statistics) focusing solely on whether activity in each subdivision met a particular statistical threshold in separate tasks, without evaluating the relative magnitude of the apparently differential activity or evaluating a continuum model of functional differentiation.

To directly investigate the functional differentiation of dACC and rACC in cognitive versus emotional processing, the present investigation examined ACC activation using both voxel-wise and region-of-interest (ROI) analyses for two attentionally demanding tasks, one considered more cognitive, the classic color-word Stroop task, and one with similar task demands but involving emotional processing, the emotional Stroop task. Both tasks involve the simultaneous presentation of task-relevant (ink color of letters) and task-irrelevant (word meaning) attributes. In both tasks, the task-irrelevant word causes interference, leading to a slowed response, because word reading is a partially automatic process. The manner in which the word interferes differentiates the two tasks. In the incongruent condition of the color-word Stroop (e.g., the word "BLUE" written in red ink), interference occurs because the word's meaning or the response to which it leads conflicts with the task-relevant ink color. In the emotional Stroop task, interference occurs because of attentional capture by emotional or threatening information (e.g., the word "KILL" written in red ink). Less interference is predicted for neutral conditions (e.g., the word "LAMP" written in red ink) in which the word does not capture attention as automatically.

The primary hypothesis was that activation of dACC would be driven more by interference from color-incongruent stimuli, whereas activation of rACC would be driven more by interference from negatively valenced stimuli. The strongest form of these hypotheses, in which both are true, represents a double dissociation between putatively emotional and nonemotional processing and the two ACC regions.

Secondarily, it was hypothesized that the degree of interference observed behaviorally would support the distinction in function between these regions. Thus, increased dACC activity would be associated with greater interference from color-incongruent words, whereas increased rACC activity would be associated with greater interference from negative emotional words.

As a further test of the potentially distinct roles of dACC and rACC, the third goal was examination of functional connectivity among dACC, DLPFC, rACC, and amygdala during these Stroop tasks. DLPFC is important for top-down attentional biasing in the face of competing information (Banich et al., 2000a). Because both color-word and emotion-word Stroop tasks depend on selective attention to the task-relevant ink color in the face of interference from word meaning, a significant functional relationship between dACC and DLPFC was predicted for both tasks. In contrast, a relationship between rACC and amygdala was predicted only during the emotional Stroop task: Attentional control in the presence of task-irrelevant emotional stimuli would be implemented through rACC modulation of emotional-stimulus-induced activity in the amygdala.

Method

Participants

Participants were 14 paid volunteers (6 women; mean/*SD* age = 18.57/0.94 years) recruited from the university community. Participants were screened for a history of neurological insult, color blindness, claustrophobia, anxiety, and depression (because they affect cognitive and affective function) or contraindications for fMRI participation and gave informed consent prior to participation.

Experimental Tasks

Participants completed two tasks, an emotion-word Stroop and a color-word Stroop. The order of presentation of the two tasks was counterbalanced across participants. The emotion-word Stroop task was implemented as blocks of positively or negatively valenced words alternating with blocks of neutral words. Pilot studies for this project as well as published work show that a valence-blocked design is more effective in eliciting emotion-word Stroop interference than mixing positive and negative words in the same block (Compton et al., 2003). In the color-word Stroop task, blocks of color-congruent or color-incongruent words alternated with blocks of neutral words. Additional neutral trials were intermixed 50:50 in congruent and incongruent blocks to prevent the development of word-reading strategies. This type of blocked-design color-word Stroop task has been shown to effectively elicit Stroop interference (Banich et al., 2000b; Milham & Banich, 2005; Milham et al., 2003). The order of presentation of blocks in the present investigation was counterbalanced for each participant. In addition to the 16 word blocks, there were four fixation blocks—one at the beginning, one at the end, and two in the middle of the session. In the fixation condition, a fixation cross was presented for 1500 ms.

Each task consisted of 256 trials in 16 blocks (four positive and four negative valence, or four congruent and four incongruent, and eight neutral) of 16 trials, with a variable ITI (2000 ± 225 ms) between trial onsets. A trial began with presentation of a word for 1500 ms, followed by a fixation cross for an average of 500 ms. Each trial consisted of one word presented in one of four ink colors (red, yellow, green, blue), each color occurring equally often with each word type. The color-word task consisted of congruent trials in which the word named the ink color in which it was printed (e.g., the word "RED" printed in red ink), incongruent trials in which the word named a color incongruent with the ink color in which it was printed (e.g., "GREEN" in red ink), and neutral trials in which the word was unrelated to color (e.g., "LOT" in red ink). Neutral words were

matched with color words for word frequency and length. The 256 word stimuli included in the emotion-word Stroop task were selected from the Affective Norms for English Words set (Bradley & Lang, 1998). Sixty-four were pleasant (e.g., birthday, ecstasy, laughter), 64 were unpleasant (e.g., suicide, war, victim), and two sets of 64 were neutral (e.g., hydrant, moment, carpet). The words were carefully selected on the basis of established norms for valence, arousal, frequency of usage in the English language (Bradley & Lang 1998), and number of letters. Words ranged from three to eight letters. Each word (visual angle 7–14°) was centered on a black background and presented through a goggle system (Resonance Technology, Inc., Northridge, CA). Participants responded with their index and middle fingers using a four-button response box (James Long Company) under each hand, with the emotion-word and color-word tasks using the same mapping of color to button for a given subject.

fMRI Data Collection

The fMRI data were 370 three-dimensional (3D) images acquired using a Siemens gradient-echo echo-planar imaging sequence (TR 2000 ms, TE 25 ms, flip angle 60°, FOV = 24 cm) on a Siemens Allegra 3T scanner. Each image consisted of 20 contiguous oblique axial slices (slice thickness 7 mm, no gap, in-plane resolution 3.75 × 3.75 mm) acquired parallel to the anterior and posterior commissures. After the fMRI acquisition, a 128-slice MPRAGE structural sequence was acquired (spatial resolution 1 × 1 × 1.3 mm) and used to register the participant's functional data into standard space.

fMRI Data Reduction and Initial Analysis

Image processing and statistical analyses were implemented primarily using FEAT (FMRI Expert Analysis Tool, FMRIB's Software Library, http://www.fmrib.ox.ac.uk/analysis/research/feat/), part of the FSL analysis package (http://www.fmrib.ox.ac.uk/fsl). Additional analyses were carried out using locally written Matlab programs.

The first three time points (fMRI volumes) of the data set corresponding to each task for each subject were discarded to allow the MR signal to reach a steady state. Functional data for each participant were motion corrected using FMRIB's linear registration tool, MCFLIRT (Jenkinson, Bannister, Brady, & Smith, 2003), intensity normalized, temporally filtered with a nonlinear high-pass filter, and spatially smoothed using a 3D Gaussian kernel (FWHM = 7 mm). MCFLIRT effectively adjusts for motion up to one voxel (Jenkinson et al., 2003); no participants exceeded this criterion for head motion.

Regression analyses were performed on the processed functional time series of each participant using FILM, FMRIB's Improved Linear Model (Woolrich, Ripley, Brady, & Smith, 2001). Four explanatory variables, one for each word type block, were included in the regression model for each task. For each explanatory variable, the vector of assigned weights corresponding to word type was convolved with a gamma function to better approximate the temporal course of the blood-oxygen-dependent (BOLD) hemodynamic response function. Each explanatory variable yielded a per-voxel effect-size parameter estimate (β) map representing the magnitude of activation associated with that explanatory variable. The β values for the incongruent word condition in the color-word Stroop task or the negative word condition in the emotion-word Stroop task were contrasted with the corresponding neutral word condition, resulting in per-voxel contrast parameter estimate maps (incongruent minus neutral = INC and negative minus neutral = NEG contrast β maps). For each subject, these functional activation maps as well as the corresponding structural MRI map were registered into a common stereotaxic space (Talairach & Tournoux, 1988) using FMRIB's Linear Image Registration Tool, FLIRT (Woolrich et al., 2001). Finally, MEDx v3.4.1 (Medical Numerics, Inc., Virginia) was used to create per-voxel paired *t* test group statistical maps for INC and NEG comparisons. These maps were thresholded using an overall significance level (probability of a false detection) estimated using Monte Carlo simulations implemented via AFNI's AlphaSim program (http://afni.nimh.nih.gov/pub/dist/doc/manual/AlphaSim.pdf). These simulations showed that a threshold z-value of ± 2.5 with a cluster size of 151 provided an overall family-wise error rate of .05. Clusters of activity meeting this threshold within hypothesized regions were used to define ROIs (Figure 2B, C) for further analyses. The mean β value across voxels was calculated for each ROI, for each subject. ROI activation was averaged across the two hemispheres (separate analyses within hemisphere yielded results essentially identical to results from averaging reported here). Hypotheses regarding task-related differences in dACC and rACC activation as well as differential relationships of dACC and rACC to DLPFC and amygdala were tested using these ROIs. In addition, spatially averaged β values for INC and NEG contrasts were also extracted from a priori ROIs (4-mm diameter sphere) for each subject. A priori coordinates for dACC (4 14 36) and rACC

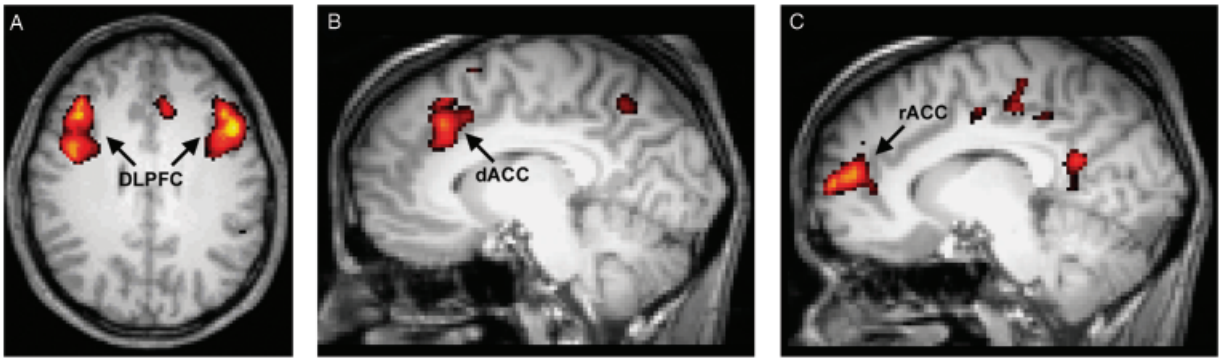

Figure 2. Differences in brain activity between the INC (incongruent-minus-neutral) and NEG (negative-minus-neutral) contrasts in hypothesized regions. A: More bilateral DLPFC activation for the INC contrast (displayed at slice z = 28; left side of brain is on left side of figure). B: More dACC (displayed at slice x = 8) activation for the INC contrast. C: More rACC activation for the NEG contrast (displayed at slice x = − 10).

(− 2 44 20) ROIs in the present study were derived from a meta-analysis (Bishop et al., 2004; Bush et al., 2000). Left and right ACC regions were not distinguished in those studies or here. Coordinates for spherical DLPFC and amygdala ROIs were (± 40 18 24; Milham et al., 2003) and (± 24 − 4 − 16; Hamann, Ely, Hoffman, & Kilts, 2002), respectively. Results for a priori ROIs were virtually identical to those for data-driven ROIs, so the latter are emphasized here.

To examine differential functional relationships of dACC and rACC with DLPFC and amygdala, six sets of hierarchical regressions, using spatially averaged β values in ACC regions as predictors and averaged β values in DLPFC or amygdala as the dependent variable, were conducted across subjects. In each set of regressions, dACC activation was entered alone as a predictor, then rACC activation was entered alone, and finally both dACC and rACC activation were entered together. Unique variance contributed was represented by the increment in variance accounted for (ΔR^2) by a predictor when added second.

Results

Behavioral Performance

Every participant's accuracy in identifying the ink color of an item was at least 80%. Incongruent color-word and negative-word Stroop interference scores (INC_RT, and NEG_RT, respectively) were calculated as the difference in RT for incongruent or negative words minus RT for same-block neutral words. INC_RT was in the predicted direction, with incongruent ($M = 761.4$ ms, $SD = 87.6$) trials slower than neutral trials ($M = 652.1$ ms, $SD = 65.1$), $t(13) = 8.06$, $p < .001$, effect size = 2.15 *SD*. NEG_RT was in the expected direction, with negative trials ($M = 696.4$ ms, $SD = 79.4$) slower than neutral trials ($M = 685.7$ ms, $SD = 79.1$), but did not approach significance, $t(13) = .82$, effect size = .22 *SD*.

Task Modulation of dACC and rACC Activation

As discussed in the Introduction, differential functional specialization of dACC and rACC for aspects of cognitive and emotional function can be demonstrated if (a) incongruent words, relative to neutral words, are associated with more activation of dACC than rACC and (b) negative words, relative to neutral words, are associated with more neural activation in rACC than dACC (Gray et al., 2002). Figure 2 illustrates DLPFC and dACC activation for the incongruent-minus-neutral comparison (INC) and rACC activation for the negative-minus-neutral comparison (NEG). To examine specialization of ACC regions for aspects of cognitive and emotional processing, an ANOVA with task condition (INC, NEG) and ACC region (dACC, rACC ROIs) as within-subject factors was conducted. Figure 3 illustrates a Task × Region interaction, $F(1,13) = 70.95$, $p < .001$, with significant simple effects and nonsignificant main effects of task and region, confirming differential ACC engagement, with more task-related dACC activation during incongruent than during neutral trials (INC) and more task-related rACC activation during negative than during neutral trials (NEG). A parallel analysis using a priori ACC ROIs confirmed these results, again yielding a Task × Region interaction, $F(1,13) = 5.95$, $p = .030$. Thus, in line with the first hypothesis, results indicated differential involvement of dACC and rACC in cognitive and emotional processing, respectively.

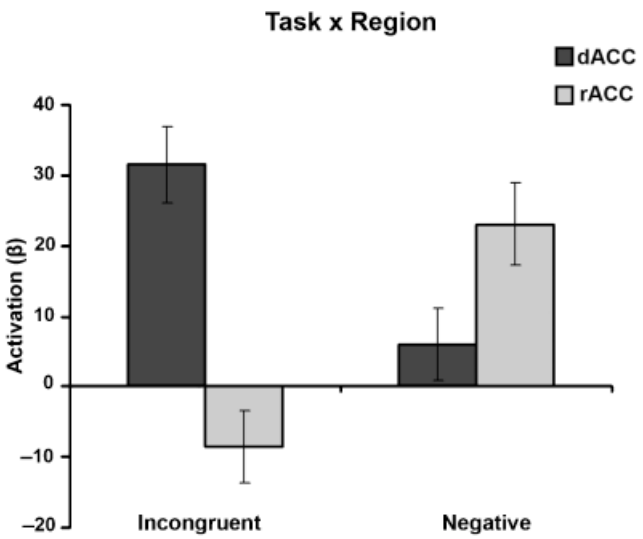

Figure 3. Modulation of dACC and rACC activity by color-word and emotion-word Stroop tasks. Error bars represent one standard error of the mean. A Task (INC, NEG) × Region (dACC, rACC) interaction ($p < .001$) confirmed greater task-related dACC activation in the color-word task and greater rACC activation in the emotion-word task. One-tailed simple-effects tests showed that (1) dACC was more active for INC than NEG ($p < .001$), (2) rACC was more active for NEG than INC ($p < .001$), (3) for INC dACC was more active than rACC ($p < .001$), and (4) for NEG rACC was more active than dACC ($p = .045$).

Relationship between Brain Activity and Behavioral Performance

The second hypothesis was that, during the color-word Stroop task, increased interference (manifested as a larger value for the INC_RT comparison) would correlate positively with dACC activation and that, during the emotion-word Stroop task, increased interference (manifested as a larger value for the NEG_RT comparison) would correlate positively with rACC activation. Regressions tested these predictions, with dACC and rACC activation predicting INC_RT or NEG_RT. Increased dACC but not rACC activation was uniquely associated with increased INC_RT (Figure 4A). INC_RT was also associated with unique DLPFC activation, $\Delta R^2 = .402$, $p = .015$. For NEG_RT, in contrast, increased rACC but not dACC activation uniquely predicted increased NEG_RT (Figure 4B). These results were replicated using the a priori ROIs. Thus, results indicate that activation of dACC is more related to attentional control exerted for incongruent words, whereas rACC activation is more related to attentional control exerted for negative words.

Task Modulation of dACC and rACC Connectivity

The third prediction was that, in the INC comparison, dACC and not rACC would be associated with DLPFC activation and that neither ACC region would be associated with amygdala activation. As shown in Table 1, dACC and rACC together accounted for 74% of the variance in DLPFC activation. As hypothesized, dACC predicted DLPFC activation even after removing the variance associated with rACC. Also as predicted, rACC was not uniquely associated with DLPFC activation. In contrast, dACC and rACC, tested jointly or incrementally, did not account for significant variance in amygdala activation.

The third hypothesis also stated that the NEG comparison would show a complementary pattern of connectivity, with rACC and not dACC predicting variance in amygdala activation. Together dACC and rACC activation predicted

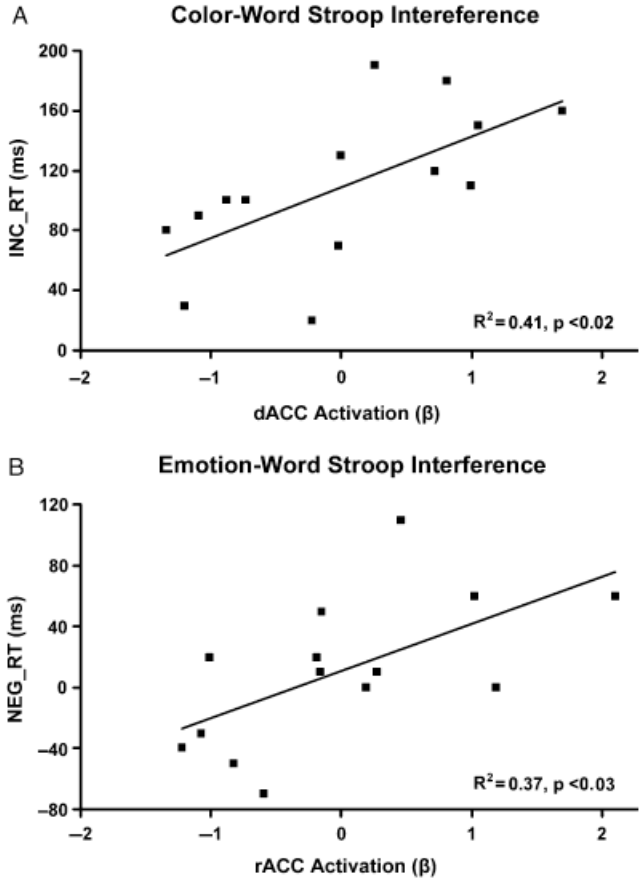

Figure 4. Relationship of dACC and rACC activity to RT interference. A: More dACC activation (with rACC variance removed) associated with increased incongruent-word RT interference (INC_RT) in the color-word Stroop task. B: More rACC activation (with dACC variance removed) associated with increased negative-word RT interference (NEG_RT) in the emotion-word Stroop task.

78% of amygdala activation (Table 1). As predicted, rACC contributed significant unique variance. However, dACC did as well. Together dACC and rACC accounted for 80% of the variance in DLPFC activation. Once again, dACC predicted DLPFC activation after removing the variance associated with rACC, whereas rACC was not uniquely associated with DLPFC activation. This pattern was replicated using the a priori dACC and rACC ROIs. Thus, results indicate differential functional connectivity of dACC and rACC.

Discussion

The present study used parallel tasks and a within-subjects design to demonstrate a task (color-word/emotion-word Stroop) by region (dACC/rACC) interaction, providing direct evidence that dACC and rACC are differentially engaged in attentional control. dACC appears to become active when task-irrelevant information is distracting due to cognitive content. In contrast, rACC appears to become active when task-irrelevant information is distracting because it interferes due to emotional content. The differential sensitivity of ACC subdivisions for addressing different kinds of interference was confirmed by behavioral findings. RT interference due to incongruent color-word stimuli was associated with increased dACC activity, whereas interference

Table 1. *dACC and rACC Activation Predicting DLPFC or Amygdala Activation for Color-Word and Emotion-Word Stroop Tasks*

DV	Predictors	R^2	ΔR^2	F or t	p
Color-word Stroop: INC comparison					
DLPFC	Full Model	.742		15.835	.001
	dACC added		.703	5.476	.000
	rACC added second		.011	−0.694	.502
	Full Model	.171		1.136	.356
	dACC added		.027	0.595	.564
	rACC added second		.157	1.441	.177
Emotion-word Stroop: NEG comparison					
DLPFC	Full Model	.799		21.812	.000
	dACC added		.682	6.104	.000
	rACC added second		.003	0.370	.719
	Full Model	.776		19.062	.000
	dACC added		.761	6.116	.000
	rACC added second		.237	3.412	.006

Note. DV: dependent variable. Numerator degrees of freedom = 2 for full model and 1 for testing dACC or rACC when added second. Denominator degrees of freedom = 13.

due to emotional stimuli was associated with increased rACC activity. Functional connectivity analyses further supported the differential roles of dACC and rACC. dACC but not rACC activity predicted DLPFC activity during incongruent and negative word conditions. In addition, dACC and rACC activity each uniquely predicted increased amygdala activity during the negative word condition.

Increased dACC response to incongruent color-word stimuli is consistent with the role of this region in late-stage selection, as there are two competing sources of task-related information on which one could base a response, the information contained in the word and the information contained in the ink color (Milham & Banich, 2005). Increased rACC response to emotional stimuli cannot arise from ''conflict'' per se, as the emotional word does not provide a conflicting semantic or response-related representation. Rather, the word captures attention due to its salience. The increased rACC activity might occur for either of two reasons, both of which are related to emotional processing. One possibility is that, because the emotional word captures attention, it diverts attention from the task-relevant attribute of ink color. rACC may be involved in recruiting greater attentional control required to focus attention on task-relevant aspects in the presence of emotional distractors. This suggestion is consistent with studies demonstrating greater recruitment of rACC in the presence of competing task-irrelevant emotional information (Bishop et al., 2004; Compton et al., 2003; Mohanty et al., 2005; Whalen et al., 1998). Another possibility is that it is the emotional nature of the word, in and of itself, that engages rACC.

The differential roles of dACC and rACC were further confirmed by connectivity analyses. dACC but not rACC activation predicted DLPFC activation during both the incongruent and negative word conditions. One view of the relationship between dACC and DLPFC is that lateral PFC maintains online information required for the choice of an appropriate response, whereas ACC facilitates implementation of response selection (Milham & Banich, 2005; Milham et al., 2001; Paus, 2001; Paus et al., 2000). Thus, DLPFC is involved in preparation of ''attentional set,'' whereas ACC is involved later during the response selection stage, dealing with any remaining attentional control that is required before the response is emitted. Transcranial

magnetic stimulation of DLPFC results in increased blood flow in dACC, indicating such a causal relationship (Paus et al., 2000).

An alternative view of the dACC/DLPFC relationship posits that ACC is primarily responsible for conflict monitoring, not conflict resolution at the response level. The conflict monitoring hypothesis (Carter et al., 1998; Kerns et al., 2004) states that dACC detects conflict and recruits DLPFC to implement control processes required for overcoming the conflict. Because task-irrelevant information in both color-word and emotion-word Stroop tasks is effective in interfering with task-relevant processing, there is an increased need for cognitive control to select the information that should be used to guide performance. Present findings of a dACC/DLPFC relationship may be interpreted in line with a recent report of a strong association between dACC activity on conflict and error trials and DLPFC activity and behavioral adjustments on subsequent trials (Kerns et al., 2004). However, present dACC/DLPFC connectivity findings do not provide information about how the relationship is mediated. An examination of the influence of DLPFC over ACC or vice versa would enhance present findings by illuminating causal relationships (Stephan, 2004).

Connectivity results also showed that dACC and rACC activity each uniquely predicted amygdala activity during the negative word condition. At first blush, these findings appear contrary to prior studies showing that rACC down-regulates amygdala activity (Ochsner et al., 2002). This apparent contradiction may be resolved when considering findings about the regulation of PFC by amygdala. Single-cell studies show that facilitation of PFC responses occurs only if amygdala is activated between 7 and 30 ms prior to PFC stimulation (Grace, 2000). Researchers have hypothesized that both hippocampus and amygdala can modulate PFC, with hippocampus providing general, context-dependent modulation and amygdala providing event-related modulation by which salient emotional stimuli can override an otherwise context-limited response system (Williams et al., 2006). It is possible that, in the emotional Stroop task, salient emotional stimuli elicit responses in amygdala, which attempts to override PFC-implemented task-relevant processing, resulting in increased interference. Detecting the interference, rACC activates dACC, which recruits DLPFC to implement cognitive control. The relationship between these regions can be better elucidated by examining its temporal dynamics. For example, a recent study showed that earlier, more subliminal processing of fear stimuli involves rostral-ventral ACC and amygdala, whereas later, more conscious elaboration of fear signals involves the dACC-amygdala pathway (Williams et al., 2006).

Although it is tempting to interpret present ANOVA findings as showing a double dissociation, with dACC involved specifically in cognitive processing and rACC involved specifically in emotional processing, regression analyses indicated otherwise. The strong connectivity between dACC and DLPFC in the negative-word condition demonstrates that dACC plays an important role in the implementation of attentional control in the presence of emotional distractors. Furthermore, the dACC-amygdala relationship during the emotional Stroop task suggests that it plays a role in emotional regulation.

The present study made use of two tasks that require selective attention in the presence of competing emotional or color-related information. Although the color-word Stroop task produced a robust interference effect, the weakness of the interference effect in the emotional task may reflect use of carefully screened subjects low in both anxiety and depression, which have been shown to modulate emotional Stroop performance. A larger study including anxious participants as well as the present nonclinical sample demonstrated a significant interference effect (Engels et al., 2007). Furthermore, a behavioral study using a larger, unselected sample in a nearly identical paradigm found significant interference (Koven, Heller, Banich, & Miller, 2003), confirming the present experimental manipulation. The behavioral Stroop effect is the end result of many different brain processes. It is possible that the confluence of these processes might not produce a net behavioral effect. Conversely, however, the absence of an overt effect does not indicate that components of these processes are not active and not detectable by brain imaging. For example, we have been able to detect differences in brain activation between a color-word and emotion-word Stroop task even when the behavioral interference in emotion-word task did not reach significance (Compton et al., 2003). Furthermore, the same pattern of brain activation is noted across numerous color-word Stroop tasks, even though in some studies the pattern does not reach behavioral significance (e.g., Liu, Banich, Jacobson, & Tanabe, 2006).

A recent study argued that the emotional Stroop task measures an automatic (in the sense of being preattentive), threat-related, generic slowdown as opposed to attentional selection (Algom, Chajut, & Lev, 2004). That study highlighted a distinction between the color-word Stroop and the emotion-word Stroop, in that there is no direct overt conflict between the dimension to be ignored and the dimension to be attended. However, the case has not been established that the emotional Stroop effect is ''automatic'' in the sense of being preattentive. On the contrary, what may be obligatory is the capture of attention by potent emotional stimuli, necessitating the same type of attentional control to perform the designated task as in the color-word Stroop. Dalgleish (2005) argued compellingly that Algom et al. did not provide compelling evidence supporting the unrelatedness of the two Stroop variants, nor did they question the central role of attention selection and control in the two tasks. Prior neuroimaging work from our laboratory (Compton et al., 2003) indicates that at least some degree of cognitive control is required during the emotion-word Stroop task, as this task, like the color-word Stroop task, engages overlapping regions of DLPFC. It can be argued that the critical feature defining any of these processes is not the nature of stimuli (e.g., congruence or incongruence) but competition among stimuli or among features of stimuli. In this view, the emotional Stroop task, which involves competition between processing the charged meaning of the emotional word and responding to the ink color, requires attention control (see Pessoa, 2005, for evidence against the complete automaticity of emotional processing). In support of this perspective, a key variable that determines response production and speed in the original connectionist model of the Stroop effect (Cohen, Dunbar, & McClelland, 1990) as well as in a revised connectionist model (Herd, Banich, & O'Reilly, 2006), which effectively models neuroimaging data unexplained by the original model, is not the nature of the input units. Rather, it is the ''strength of processing'' of competing pathways between word reading and ink color identification. Attention can be viewed as a modulator that interacts with strength of relationships in processing pathways to produce the pattern of interference seen in Stroop-like tasks. The recruitment of a similar dACC/DLPFC control mechanism in both emotional and color-word Stroop tasks in both Compton et al. (2003) and the present study (with different subjects,

different field strengths, and different analysis software) provides further evidence in favor of the view that the two tasks share fundamental cognitive processes.

In summary, the present investigation provides compelling evidence for the differential engagement of ACC subdivisions for cognitive and emotional function. Present psychophysiological data may be used to support either of two contrasting viewpoints regarding the relationship between cognitive and emotional processes. One view espouses the integrative and intertwined nature of the relationship (Gray et al., 2002; Heller & Nitschke, 1997; Miller, 1996). This view is supported by evidence that brain activity patterns associated with certain emotional states are intrinsically related to cognitive characteristics associated with these states (Heller & Nitschke, 1997; Levin, Heller, Mohanty, Herrington, & Miller, in press). According to a competing view, cognition and emotion are dissociable because they are implemented through two separable, reciprocal or even opposing systems (Drevets & Raichle, 1998). Present findings suggestive of a double dissociation can be interpreted as evidence of such a partition of cognitive and emotional function. However, this interpretation is based on several assumptions: Each task recruits one and only one function, activation in one brain region reflects one and only one brain function, and the functions are isolable from each other or show limited interactivity (Dunn & Kirsner, 2003). There is considerable evidence against each of these assumptions with regard to cognitive and emotional processing as well as the brain mechanisms that implement them (Compton et al., 2003; Frijda, 1994; Gray et al., 2002; Heller & Nitschke, 1997; Miller, 1996). Furthermore, double dissociations can exist even in fully interactive cognitive systems (Medler, Dawson, & Kingstone, 2005). However, even though an entire network may participate, different parts of the system may make distinct contributions and are differentially important for particular aspects of cognitive and emotional function (Mesulam, 1998). It is clear from present results that cognitive or emotional function may be best understood by examining how the properties of different brain regions implementing them are combined or aggregated, through interregional interactions rather than by the involvement of any specific region in isolation (McIntosh, 2000).

REFERENCES

Algom, D., Chajut, E., & Lev, S. (2004). A rational look at the emotional Stroop phenomena: A generic slowdown, not a Stroop effect. *Journal of Experimental Psychology—General*, *133*, 323–328.

Banich, M. T., Milham, M. P., Atchley, R., Cohen, N. J., Webb, A., Wszalek, T., et al. (2000a). fMRI studies of Stroop tasks reveal unique roles of anterior and posterior brain systems in attentional selection. *Journal of Cognitive Neuroscience*, *12*, 988–1000.

Banich, M. T., Milham, M. P., Atchley, R., Cohen, N. J., Webb, A., Wszalek, T., et al. (2000b). Prefrontal regions play a predominant role in imposing an attentional 'set': Evidence from fMRI. *Cognitive Brain Research*, *10*, 1–9.

Barbas, H., & Pandya, D. N. (1989). Architecture and intrinsic connections of the prefrontal cortex in the rhesus monkey. *Journal of Comparative Neurology*, *286*, 353–375.

Bishop, S., Duncan, J., Brett, M., & Lawrence, A. D. (2004). Prefrontal cortical function and anxiety: Controlling attention to threat-related stimuli. *Nature Neuroscience*, *7*, 184–188.

Bradley, M. M., & Lang, P. J. (1998). *Affective norms for English words (ANEW)*. Gainesville, FL: The NIMH Center for the Study of Emotion and Attention, University of Florida.

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., Whalen, P., Rosen, B., Jenike, M. A., McInerney, S. C., & Rauch, S. L. (1998). The counting Stroop: An interference task specialized for functional neuroimaging–validation study with functional MRI. *Human Brain Mapping*, *6*, 270–282.

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.

Cohen, J. D., Dunbar, K., & McClelland, J. L. (1990). On the control of automatic processes: A parallel distributed processing account of the Stroop effect. *Psychological Review*, *97*, 332–361.

Compton, R. J., Banich, M. T., Mohanty, A., Milham, M. P., Herrington, J., Miller, G. A., et al. (2003). Paying attention to emotion: An fMRI investigation of cognitive and emotional Stroop tasks. *Cognitive, Affective & Behavioral Neuroscience*, *3*, 81–96.

Critchley, H., Mathias, C. J., Josephs, O., O'Doherty, J., Zanini, S., Dewar, B., et al. (2003). Human cingulate cortex and autonomic control: converging neuroimaging and clinical evidence. *Brain*, *126*, 2139–2152.

Dalgleish, T. (2005). Putting some feeling into it—The conceptual and empirical relationships between the classic and emotional Stroop tasks: Comment on Algom, Chajut, & Lev (2004). *Journal of Experimental Psychology—General*, *135*, 585–591.

Das, P., Kemp, A. H., Liddell, B. J., Brown, K. J., Olivieri, G., Peduto, A., et al. (2005). Pathways for fear perception: Modulation of amygdala activity by thalamo-cortical systems. *NeuroImage*, *26*, 141–148.

Davis, K. D., Taylor, K. S., Hutchison, W. D., Dostrovsky, J. O., McAndrews, M. P., Richter, E. O., et al. (2005). Human anterior cingulate cortex neurons encode cognitive and emotional demands. *Journal of Neuroscience*, *25*, 8402–8406.

Devinsky, O., Morrell, M. J., & Vogt, B. A. (1995). Contributions of anterior cingulate to behavior. *Brain*, *118*, 279–306.

Drevets, W. C., & Raichle, M. E. (1998). Reciprocal suppression of regional cerebral blood flow during emotional versus higher cognitive processes: Implications for interactions between emotion and cognition. *Cognition and Emotion*, *12*, 353–385.

Dunn, J. C., & Kirsner, K. (2003). What can we infer from double dissociations? *Cortex*, *39*, 1–7.

Engels, A. S., Heller, W., Mohanty, A., Herrington, J. D., Banich, M. T., Webb, A. G., et al. (2007). Specificity of regional brain activity in anxiety types during emotion processing. *Psychophysiology*, *44*, 352–363.

Frijda, N. H. (1994). Emotions require cognitions, even if simple ones. In P. Ekman & R. J. Davidson (Eds.), *The nature of emotions: Fundamental questions* (pp. 197–202). New York: Oxford University Press.

Gehring, W. J., & Knight, R. T. (2002). Prefrontal-cingulate interactions in action monitoring. *Nature Neuroscience*, *3*, 516–520.

Grace, A. A. (2000). Gating of information flow within the limbic system and the pathophysiology of schizophrenia. *Brain Research Reviews*, *31*, 330–341.

Gray, J. R., Braver, T. S., & Raichle, M. E. (2002). Integration of emotion and cognition in the lateral prefrontal cortex. *Proceedings of the National Academy of Sciences, USA*, *99*, 4115–4120.

Hajcak, G., McDonald, N., & Simons, R. F. (2004). Error-related psychophysiology and negative affect. *Brain and Cognition*, *56*, 189–197.

Hamann, S. B., Ely, T. D., Hoffman, J. M., & Kilts, C. D. (2002). Ecstasy and agony: The human amygdala in positive and negative emotion. *Psychological Science*, *13*, 135–141.

Heller, W., & Nitschke, J. B. (1997). Regional brain activity in emotion: A framework for understanding cognition in depression. *Cognition and Emotion*, *11*, 637–661.

Herd, A., Banich, M. T., & O'Reilly, R. C. (2006). Neural mechanisms of cognitive control: An integrative model of Stroop task performance and fMRI data. *Journal of Cognitive Neuroscience*, *18*, 22–32.

Jenkinson, M., Bannister, P., Brady, M., & Smith, S. (2003). Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage*, *17*, 825–841.

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.

Koven, N., Heller, W., Banich, M. T., & Miller, G. A. (2003). Relationships of distinct affective dimensions to performance on an emotional Stroop task. *Cognitive Therapy and Research*, *27*, 671–680.

Levin, R. L., Heller, W., Mohanty, A., Herrington, J. D., & Miller, G. A. (in press). Cognitive deficits in depression and functional specificity of regional brain activity. *Cognitive Therapy and Research*.

Liu, X., Banich, M. T., Jacobson, B. L., & Tanabe, J. L. (2006). Functional dissociation of attentional selection within PFC: Response and non-response related aspects of attentional selection as ascertained by fMRI. *Cerebral Cortex*, *16*, 827–834.

Luu, P., Tucker, D. M., Derryberry, D., Reed, M., & Poulsen, C. (2003). Electrophysiological responses to errors and feedback in the process of action regulation. *Psychological Science*, *14*, 47–53.

MacDonald, A. W., 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.

McIntosh, A. R. (2000). Towards a network theory of cognition. *Neural Network*, *13*, 861–870.

Medler, D. A., Dawson, M. R. W., & Kingstone, A. (2005). Functional localization and double dissociations: The relationship between internal structure and behavior. *Brain and Cognition*, *57*, 146–150.

Mesulam, M. M. (1998). From sensation to cognition. *Brain*, *121*, 1013–1052.

Milham, M. P., & Banich, M. T. (2005). Anterior cingulate cortex: An fMRI analysis of conflict specificity and functional differentiation. *Human Brain Mapping*, *25*, 328–335.

Milham, M. P., Banich, M. T., & Barad, V. (2003). Competition for priority in processing increases prefrontal cortex's involvement in top-down control: An event-related fMRI study of the Stroop task. *Cognitive Brain Research*, *17*, 212–222.

Milham, M. P., Banich, M. T., Webb, A., Barad, V., Cohen, N. J., Wszalek, T., et al. (2001). The relative involvement of anterior cingulate and prefrontal cortex on attentional control depends on the nature of conflict. *Cognitive Brain Research*, *12*, 467–473.

Miller, G. A. (1996). Presidential address: How we think about cognition, emotion, and biology in psychopathology. *Psychophysiology*, *33*, 615–628.

Mohanty, A., Herrington, J. D., Koven, N. S., Fisher, J. E., Wenzel, E. A., Webb, A. G., et al. (2005). Neural mechanisms of affective interference in schizotypy. *Journal of Abnormal Psychology*, *114*, 16–27.

Ochsner, K. N., Bunge, S. A., Gross, J. J., & Gabrieli, J. D. E. (2002). Rethinking feelings: An fMRI study of the cognitive regulation of emotion. *Journal of Cognitive Neuroscience*, *14*, 1215–1229.

Paus, T. (2001). Primate anterior cingulate cortex, where motor control, drive and cognition interface. *Nature Reviews Neuroscience*, *2*, 417–424.

Paus, T., Castro-Alamancos, M., & Petrides, M. (2000). Cortico–cortical connectivity of the human mid-dorsolateral frontal cortex and its modulation by repetitive transcranial magnetic stimulation: A combined TMS/PET study. *NeuroImage*, *11*, S765.

Pessoa, L. (2005). To what extent are emotional visual stimuli processed without attention and awareness? *Current Opinion in Neurobiology*, *15*, 188–196.

Petrovic, P., Carlsson, K., Petersson, K. M., Hansson, P., & Ingvar, M. (2004). Context-dependent deactivation of the amygdala during pain. *Journal of Cognitive Neuroscience*, *16*, 1289–1301.

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.

Stephan, K. E. (2004). On the role of general system theory for functional neuroimaging. *Journal of Anatomy*, *205*, 443–470.

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

Van Veen, V., & Carter, C. S. (2002). The timing of action monitoring processes in the anterior cingulate cortex. *Journal of Cognitive Neuroscience*, *14*, 593–602.

Vuilleumier, P., Armony, J. L., Driver, J., & Dolan, R. J. (2001). Effects of attention and emotion on face processing in the human brain: An event-related fMRI study. *Neuron*, *30*, 829–841.

Whalen, P. J., Bush, G., McNally, R. J., Wilhelm, S., McInerney, S. C., Jenike, M. A., et al. (1998). The emotional Stroop counting paradigm: An fMRI probe of the anterior cingulate affective division. *Biological Psychiatry*, *44*, 1219–1228.

Williams, L. M., Liddell, B. J., Kemp, A. H., Bryant, R. A., Meares, R. A., Peduto, A. S., et al. (2006). Amygdala-prefrontal dissociation of subliminal and supraliminal fear. *Human Brain Mapping*, *27*, 652–661.

Woolrich, M. W., Ripley, B. D., Brady, M., & Smith, S. M. (2001). Temporal autocorrelation in univariate linear modelling of fMRI data. *NeuroImage*, *14*, 1370–1386.

(Received September 30, 2006; Accepted November 24, 2006)