BAD MOODS AND ATTITUDES: NEURAL CORRELATES OF STATE AND TRAIT NEGATIVE AFFECT

BY

LAURA DIANNA CROCKER

THESIS

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Master’s Committee:

Professor Gregory A. Miller
Professor Wendy Heller
ABSTRACT

Trait and state negative affect contribute to the development and maintenance of psychopathology, though the mechanisms through which they exert their effects remain unclear. The present study was motivated by the hypothesis that attentional-control deficits will help to understand the biological and psychological mechanisms involved in the potentially distinct contributions that trait and state NA make in initiating and maintaining mental disorders. Brain activation associated with trait and state negative affect was measured by fMRI during performance of an emotion-word Stroop task. Trait negative affect was associated with reduced activity in areas involved in top-down, goal-directed attentional control. In contrast, state negative affect was associated with more activity in regions involved in bottom-up, stimulus-driven attentional control. Present results suggest that these two emotional facets are associated with distinct attentional control deficits, which has implications for the prevention and treatment of psychological disorders.
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INTRODUCTION

Anxiety and depressive disorders, two of the most common classes of mental health disorders, are associated with significant social and occupational impairments and lead to considerable emotional, economic, and societal burden (Kessler & Greenberg, 2002; Wang, Simon, & Kessler, 2003). Anxiety and depression frequently co-occur (Brown, Campbell, Lehman, Grisham, & Mancill, 2001; Kessler et al., 1994; Sanderson, DiNardo, Rapee, & Barlow, 1990), with comorbidity present in approximately one-half of those diagnosed with an anxiety or depressive disorder (for reviews, see Breier, Charney, & Heninger, 1985; Clark, 1989; Gersh & Fowles, 1979). The co-occurrence of these disorders has an even greater impact than either alone, leading to greater impairments in psychosocial function, greater severity of disorder, elevated rates of suicidality and morbidity, increased health service use, increased treatment resistance, and poorer short- and long-term outcomes (Judd et al., 1998; Lydiard & Brawman-Mintzer, 1998). Therefore, it is crucial to identify risk factors associated with anxiety and depression in order to prevent the onset and recurrence of these disorders.

In order to identify risk factors shared by anxiety and depression, it is necessary to explore their overlap. Research indicates that anxiety and depression share a general distress factor, negative affect (NA), which was initially conceptualized as reflecting the negative mood states that characterize these disorders, including worry, nervousness, anger, fear, guilt, and sadness (Clark & Watson, 1991a). Further theorizing extended the conceptualization of the overlap between anxiety and depression to the stable personality dimension of negative temperament or neuroticism (Clark, Watson, & Mineka, 1994), which has since received an abundance of empirical support (for review, see Clark, 2005). Thus, both state and trait negative affect are associated with the development and maintenance of clinically significant anxiety and depression.

Although trait negative affect is associated with a disposition to experience negative mood states (Costa & McCrae, 1980; Watson & Clark, 1984), research indicates that it has other important facets that persist even outside of negative mood states. Trait NA is linked to poor self-esteem, pessimism, and a propensity to make somatic complaints (Clark, Watson, & Mineka, 1994; Watson & Clark, 1984; Watson & Pennebaker, 1989). Individuals high in trait NA report that they are less satisfied with themselves and describe
themselves more negatively than individuals low in trait NA (for review, see Watson & Clark, 1984). Furthermore, individuals high in trait NA often dwell on failures, mistakes, and disappointments (Watson & Clark, 1984) and have deficient mood-regulation skills (Costa, Somerfield, & McCrae, 1986; Kokkonen & Pulkkinen, 2001). Trait NA has significant implications for psychopathology, as it is a risk factor that predicts the impact of life stress, as well as the onset and outcome of affective disorders (for review, see Ormel, Rosmalen, & Farmer, 2004).

Recent research in the anxiety and depression literature has shown that another crucial risk factor is cognitive dysfunction, including deficits in executive functions and biased processing of negative information (Clark & Beck, 2010; Gotlib & Joorman, 2010; Mathews & MacLeod, 2005). Unsurprisingly, trait and state NA are also associated with biased cognitive processing, which likely perpetuates them and leads to the development and maintenance of anxiety and depression. Trait NA is associated with biases in perception, memory, and interpretation, such that high trait NA individuals recognize and recall negative information more readily than do low trait NA individuals (Larsen, 1992, Martin, 1985, for review, see Watson & Clark, 1984), interpret ambiguous information in a more negative manner (Haney, 1973), and appraise situations as more stressful and threatening (Gallagher, 1990; Hemenover & Dienstbier, 1996; Oliver & Brough, 2002). Furthermore, trait NA is associated with a negative attributional style, negative self-referential thinking, and dysfunctional judgments and beliefs about oneself, others, and the world (Luten, Ralph, & Mineka, 1997; Clark & Watson, 1991b; Watson & Clark, 1984). Therefore, negative affect on a trait level appears to exert top-down influence on the perceptions and interpretations of sensory events, social interactions, and other data about the environment, in turn influencing beliefs, attitudes, and expectations.

Research indicates that mood states, like personality traits, also influence various cognitive processes (for review, see Silvia & Warburton, 2004). Negative mood states narrow attention to focus on local details, restrict the range of thoughts and actions that come to mind, and bias perception and memory toward negatively-valenced words (Chepenik, Cornew, & Farah, 2007; Clore & Huntsinger, 2007; Fredrickson & Branigan, 2005; Gable & Harmon-Jones, 2010; Niedenthal, Halberstadt, & Setterlund, 1997). Negative moods can also affect judgments about various things, including life satisfaction,
likelihood of events, and morality of actions (Clore & Huntsinger, 2007). Additionally, negative moods are associated with a systematic processing strategy that relies on bottom-up processing and attention to situational details, with little reliance on pre-existing knowledge (for reviews, see Heller & Nitschke, 1997; Schwarz & Clore, 1996). Emotional states evoke emotion knowledge that is experiential and context-dependent (Robinson & Clore, 2002). Conversely, it has been proposed that emotional traits are based on an individual’s stable beliefs about their emotions in general, which may or may not be activated by certain situations (Robinson & Clore, 2002). Emotion knowledge associated with traits appears to be somewhat context-independent. Therefore, it seems likely that in emotional contexts certain cognitive processes are modulated differentially by transient emotional states and enduring traits. Thus, the present study aims to disentangle the correlates of trait and state NA, given that many studies confound their effects and preclude understanding potentially unique cognitive mechanisms through which they serve as risk factors for psychological disorders.

The anxiety and depression literatures provide some clues to the specific cognitive mechanisms associated with trait and state NA that lead to the development and maintenance of psychopathology. This literature suggests that deficits in attentional control may underlie the cognitive dysfunction and biases observed in both anxiety and depression (e.g., Derakshan & Eysenck, 2009; Engels et al., 2010; Eysenck, Derakshan, Santos, & Calvo, 2007; Gotlib & Joorman, 2010). For anxiety, two pervasive cognitive findings are 1) an early attentional bias to threatening stimuli and 2) difficulty ignoring salient distracting information, which interferes with task-relevant processing (for reviews, see Bar-Haim et al., 2007; Sass et al., 2010). It has been suggested that these problems reflect a disruption in the balance between two attentional systems, such that anxiety decreases the influence of a goal-directed, top-down attentional system and increases the influence of a stimulus-driven, bottom-up attentional system (Bishop, 2007; Derakshan & Eysenck, 2009; Eysenck et al., 2007).

Similarly, depressed individuals also selectively attend to negative stimuli (when given sufficient time to elaborate on such stimuli) and have difficulty disengaging from this information (for review, see Gotlib & Joorman, 2010). Individuals who depressively ruminate about negative moods and their implications appear to have deficits in cognitive
control mechanisms, such that they have difficulty removing irrelevant information from working memory and flexibly switching attention to focus on the task at hand (see Banich et al., 2009; Engels et al., 2010). Therefore, impairments in attentional control, particularly in the face of emotional information, characterize both depression and anxiety.

Importantly, attentional control deficits have also been associated with trait and state NA (Bredemeier, Berenbaum, Most, & Simons, 2011; Compton, 2000; Derryberry & Reed, 1994), a link that may constitute one mechanism through which trait and state NA trigger and maintain serious psychological symptoms.

Research on attentional control deficits in anxiety and depression has utilized neuroimaging methods in order to identify neural mechanisms associated with dysfunction in attentional systems. Biological measures are particularly valuable in that they can provide information inaccessible though self-report and behavioral assessment (Miller & Keller, 2000). They have the potential to identify individuals at risk for developing an initial or co-occurring psychological disorder or relapsing after recovery before other markers of vulnerability manifest in behavior or become accessible to awareness and hence reportable. Additionally, they can elucidate when individuals are using alternate processing strategies that are maladaptive and may eventually break down in more challenging contexts or when additional brain areas are being recruited to compensate for dysfunction in others.

Neuroimaging work examining the successful implementation of attentional control in the context of emotional distracters has implicated several key areas, including the dorsolateral prefrontal cortex (DLPFC) and the anterior cingulate cortex (ACC; Banich et al., 2009; Compton et al., 2003; Herrington et al., 2010; Mohanty et al., 2007; Whalen et al., 1998). Not surprisingly, research in clinical neuroscience has found that these areas function abnormally in anxiety and depression, such that dysfunction in the DLPFC, as well as in both dorsal and rostral portions of the ACC, has been associated with difficulty ignoring distracting emotional information (e.g., Bishop, 2008; Engels et al, 2007; 2010; Herrington et al., 2010). Additionally, various parts of the parietal cortex, including the precuneus and superior and inferior parietal lobules, play a role in attentional control in both emotional and nonemotional contexts (Banich et al., 2000b; Compton et al., 2003; Corbetta, Patel, & Shulman, 2008) and are disrupted in anxiety and depression (Bruder et
Given that anxiety and depression are both associated with dysfunction in the DLPFC, ACC, and parietal cortex, it seems likely that trait and state NA are linked to disruption in those areas as well, leading to attentional-control problems that may predispose individuals to develop psychological disorders, as well as maintain them.

We propose that state and trait negative affect differentially impact the two systems implementing attentional control (i.e., bottom-up and top-down systems; Corbetta & Shulman, 2002; Corbetta et al., 2008). According to Corbetta et al. (2008), the dorsal frontoparietal network (or top-down system) includes posterior portions of middle frontal gyrus (MFG) extending into premotor areas, frontal eye fields (FEF), and dorsal parietal cortex (particularly intraparietal sulcus and superior parietal lobule), whereas the ventral frontoparietal network (or bottom-up system) includes anterior parts of MFG, inferior frontal gyrus (IFG), and temporal parietal junction (TPJ). Given that trait NA is associated with a reliance on beliefs and knowledge that is somewhat context-independent, we propose that it is associated with dysfunction in the goal-directed top-down attentional system, which is influenced by current goals, expectations, and pre-existing information. Furthermore, we expect that negative mood states will be associated with disrupted function in the stimulus-driven, bottom-up attentional system, given that negative moods are related to a systematic, bottom-up processing strategy and attending to contextual details. Some neuroimaging support for this proposal comes from a study that distinguished between state and trait anxiety effects in attentional control (Bishop, 2007). Trait anxiety disrupted function in top-down attentional areas, including the DLPFC and ACC, whereas state anxiety negatively impacted function in the amgydala, which has been linked to bottom-up processing. The present study is based on theorizing that extends this research to examine emotional traits and states more broadly (i.e., negative affect). Furthermore, broader attentional networks are also considered in the present study, including those proposed by Corbetta and Shulman (2002), as well as Banich (2009, discussed below). These networks include parietal areas as well as specific areas of the DLPFC that are involved in bottom-up processing (and not just top-down-control processing that is typically assumed to be the main role of the DLPFC).
The cascade-of-control model (Banich, 2009) proposes that distinct areas of the DLPFC implement different functions necessary for attentional control. It posits that posterior DLPFC is involved in imposing a top-down attentional set that maintains overall task goals and biases posterior brain regions (e.g., parietal cortex) toward processing task-relevant information and away from task-irrelevant information (which can occur even before stimuli are received), whereas mid-DLPFC is involved stimulus processing such that it selects and maintains the most relevant aspects of stimuli that have been received (Banich, 2009). Herrington et al. (2010) supported this distinction in terms of emotion-modulated attentional processing. Individuals selected for high trait-like levels of anhedonic depression exhibited reduced posterior DLPFC activity in response to negative stimuli. In contrast, mid-DLPFC was more active for positive stimuli, regardless of levels of anhedonic depression. It was proposed that posterior DLPFC imposes more static, persistent, context-insensitive aspects of an affective set and is associated with trait affect and top-down processes, whereas mid-DLPFC imposes aspects of an affective set that are more transient, stimulus-driven, context-dependent, and related to state affect and bottom-up processes. The cascade-of-control model also includes areas of the ACC that are involved in response selection and response evaluation. The model asserts that there is a temporal cascade of processing such that DLPFC comes online first and in turn influences later ACC activity. When incorrect responses are made during a task, anterior regions of the ACC signal the posterior DLPFC to assert stronger top-down control on future trials.

Most work in the psychopathology literature investigating cognitive control deficits in emotional contexts has focused on negative stimuli. Excluding positive stimuli leaves unclear whether the observed attentional problems are valence-specific, or are actually driven by highly arousing stimuli. There is some evidence that anxious individuals selectively attend to both positive and negative stimuli, supporting the possibility that anxiety is associated with enhanced processing of emotionally arousing, salient information, not just negative stimuli (Becker, Rinck, Margraf, & Roth, 2001; Martin, Williams, & Clark, 1991; Sass et al., 2010). Similarly, the depression literature has focused primarily on the role of negative stimuli in triggering and perpetuating depressive symptoms. However, when positive stimuli were included in studies, they were rarely equated with negative stimuli on arousal levels. The inclusion of positive stimuli is
important for understanding cognitive and emotional dysfunction in depression because evidence suggests that depressed individuals exhibit reduced emotional reactivity to both negative and positive stimuli (Rottenberg, Kasch, Gross, & Gotlib, 2002; Rottenberg, Gross, & Gotlib, 2005) and allocate insufficient attentional resources to pleasant stimuli (Gilboa & Gotlib, 1997; Gotlib, McLachlan, & Katz, 1988; McCabe & Gotlib, 1995; McCabe, Gotlib, & Martin, 2000). The present study included both positive and negative stimuli matched on arousal in order to avoid the potential confound between valence and arousal, as well as to explore the possibility that trait and state NA are associated with difficulties disengaging attention from salient, distracting information (which has received some empirical support; e.g., Bredemeier et al., 2011; Compton, 2000).

The present study was motivated by the possibility that attentional-control deficits will help to understand the nature and mechanisms involved in potentially distinct contributions that trait and state NA make in initiating and maintaining mental disorders. Trait NA was hypothesized to be associated with decreased activation in posterior DLPFC, as well as other areas involved in top-down attentional control, in the context of emotionally arousing, distracting information. In contrast, state NA was expected to facilitate the processing of emotionally arousing, salient stimuli and thus to be linked to increased activation in mid-DLPFC as well as other areas involved in bottom-up processing. Additional, exploratory analyses examined the neural correlates of the interactive effects of trait and state NA, given that many individuals high in trait NA are also likely to experience frequent negative mood states and that behavioral research has found that the interaction between traits and states has important implications for understanding their impact on cognitive processing and behavior (e.g., MacLeod & Mathews, 1988; MacLeod & Rutherford, 1992; Tamir & Robinson, 2004).
METHOD

Participants

One hundred and one paid participants (62 females, age $M_{age} = 34.57$, $SD_{age} = 9.27$) were recruited from the local community. All participants were right-handed, native speakers of English with self-reported normal color vision, and no reported neurological disorders or impairments. Participants were given a laboratory tour, informed of the procedures of the study, and screened for claustrophobia and other contraindications for MRI participation. Thirty additional participants were excluded from analyses for a variety of reasons, including excessive motion in the scanner, technical errors during fMRI acquisition, loss of questionnaire or reaction time data, outliers on the questionnaires or in reaction time (outliers are defined as greater than 3 standard deviations from the mean), or error rates exceeding 15%.

Questionnaires

During the laboratory tour, participants completed the General Temperament Survey (GTS) to assess trait negative affect using the Negative Temperament scale (Watson & Clark, 1993). The Negative Temperament scale includes 28 items describing attitudes, feelings, interests, and other characteristics. Participants were instructed to decide if each statement mostly described them or not and rate each item as either true or false. Sample items include “I often have strong feelings such as anxiety or anger without really knowing why,” “I sometimes get all worked up as I think about things that happened during the day,” and “Often life feels like a big struggle.” State NA was measured using the Negative Affect scale from the Positive and Negative Affect Schedule-Expanded Form (PANAS-X; Watson & Clark, 1994), which was administered immediately before participants performed the task during fMRI. Participants indicated the extent to which they were feeling 10 negative emotions (e.g., afraid, nervous, irritable, upset) that day on a scale from 1 (“very slightly or not at all”) to 5 (“extremely”).
Stimuli and Experimental Design

Participants performed two tasks, a color-word Stroop and an emotion-word Stroop, during the fMRI session and also in a similar EEG session. Only fMRI data from the emotion-word Stroop task are reported here. The order of the Stroop tasks within session and the order of fMRI and EEG sessions were counterbalanced. The emotion-word Stroop task consisted of blocks of positive or negative emotion words alternating with blocks of neutral words. Each participant received one of eight orders designed to ensure that the blocks of emotional and neutral words preceded each other equally often. There was a brief rest period after every fourth block. Additionally, there were four fixation blocks (one at the beginning, one at the end, and two in the middle) in which a brighter fixation cross was presented for 1,500 ms, followed by a dimmer fixation cross for an average of 500 ms.

Participants received 256 trials in 16 blocks (4 positive, 8 neutral, 4 negative) of 16 trials, with a variable ITI (±225 ms) averaging 2,000 ms between trial onsets. A trial began with the presentation of a word for 1,500 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). Participants were instructed to press one of four buttons to indicate the color in which the word appeared on the screen, while ignoring the word meaning (thus making it irrelevant to the task). Each color occurred equally often with each word type (positive, neutral, negative), and trials were pseudorandomized such that no more than two trials featuring the same color appeared in a row. Participants completed 32 practice trials prior to the task to ensure they understood the task instructions and the mapping between colors and buttons.

The 256 emotion-word stimuli were selected from the Affective Norms for English Words (ANEW) set (Bradley & Lang, 1999). Sixty-four positive (e.g., birthday, laughter), 64 negative (e.g., suicide, war), and two sets of 64 neutral (e.g., hydrant, moment) words were carefully selected on the basis of established norms for valence, arousal, word length, and frequency of use in the English language (Bradley & Lang, 1999). Both positive and negative words were selected to be highly arousing, whereas the neutral words were selected to be low in arousal (see Herrington et al., 2010, for detailed stimulus characteristics). Stimuli were displayed using back projection, and
word presentation and reaction-time measurement were controlled by STIM software (James Long Company, Caroga Lake, NY).

Image Acquisition

MR data were collected using a 3T Siemens Allegra scanner. Gradient field maps were collected to correct for geometric distortions in the functional data caused by magnetic field inhomogeneity (Jezzard & Balaban, 1995). Three hundred and seventy functional images were acquired using a Siemens gradient-echo echo-planar imaging sequence (TR 2,000 ms, TE 25 ms, flip angle 80°, FOV 22 cm). Thirty-eight contiguous oblique axial slices (slic thickness 3 mm, in-plane resolution 3.4375 mm x 3.4375 mm, .3 mm gap between slices) were acquired parallel to the anterior and posterior commissures. After the functional acquisition, an MPRAGE structural sequence was also acquired (160 slices, slice thickness 1 mm, in-plane resolution 1 mm x 1 mm) for registering each participant's functional data to standard space.

fMRI Data Reduction and Analysis

Image processing and statistical analyses were implemented primarily using the FSL analysis package (http://www.fmrib.ox.ac.uk/fsl). Functional data for each participant were motion-corrected using rigid-body registration via FMRIB's linear registration tool MCFLIRT (Jenkinson, Bannister, Brady, & Smith, 2002). Spikes or sudden intensity shifts were corrected using AFNI's 3dDespike program (http://afni.nimh.nih.gov/). The time series of 1 participant was truncated due to excessive motion only at the end of the scan. All other participants demonstrated less than 3.3 mm absolute motion or 2 mm relative motion (the participants with motion exceeding this threshold were excluded from analysis as discussed above, leaving N=101). After motion correction and despiking, each time series was corrected for geometric distortions caused by magnetic field inhomogeneity. Remaining preprocessing steps, single-subject statistics, and higher-level regression analyses were done with FEAT (FMRI Expert Analysis Tool, FMRIB's Software Library, http://www.fmrib.ox.ac.uk/analysis/research/feat/). The first three fMRI volumes of each time series were discarded in order to allow the MR signal to reach a steady state. The
Regression analyses were then performed on each participant's time series using FILM, FMRIB’s Improved Linear Model with autocorrelation correction (Woolrich, Ripley, Brady, & Smith, 2001). Statistical maps were generated via multiple regression computed for each intracerebral voxel. Four explanatory variables (EV) were created for each condition (positive, neutral, negative, and rest) and included in the regression model, with fixation left as the unmodeled baseline. Each explanatory variable was convolved with a gamma function to approximate the temporal course of the blood-oxygen-dependent (BOLD) hemodynamic response function. Each explanatory variable or regressor yielded a per-voxel effect-size parameter estimate ($\beta$) map representing the magnitude of activation associated with that explanatory variable. In order to create the comparison of interest, $\beta$ values for the relevant parameters were contrasted. The contrast of interest was the arousal contrast (positive and negative words jointly compared with neutral words).

For each participant, the functional activation maps were warped into a common stereotaxic space (the 2009 Montreal Neurological Institute 152 symmetrical 1mm x 1mm x 1mm template; Fonov, Evans, McKinstry, Almli, & Collins, 2009) using FMRIB’s Non-Linear Image Registration Tool, FNIRT (Andersson, Jenkinson, & Smith, 2007). First, the middle volume of the functional scan was registered to the structural scan using rigid-body registration (only allowing xyz translation and rotation). Next, the structural scan was registered to the MNI template using a two-step process. First, a linear registration was carried out, allowing xyz translation, rotation, zoom, and shear. Finally, a non-linear registration using cubic b-spline basis functions was carried out, using the results of the linear registration as a starting point. The three registration steps (rigid-body function to structural, affine structural to MNI, & non-linear structural to MNI) were concatenated to create a warp mapping functional to MNI space and then applied to the $\beta$ maps.

Cross-subject inferential statistical analyses of brain activation were carried out using FLAME (FMRIB’s Local Analysis of Mixed Effects). The arousal contrast was entered as a dependent variable into a multiple regression analysis with questionnaire
scores (GTS Negative Temperament scale for trait NA and PANAS-X NA scale for state NA) entered as continuous predictors to predict activation voxel-by-voxel. Two different higher-level analysis approaches served to identify (1) brain areas associated with both trait and state NA and (2) brain areas showing distinct relationships to them. First, separate regressions were performed for each questionnaire (without the shared variance from the other questionnaire removed). These essentially provided zero-order correlations between trait or state NA and each brain voxel. These were followed by a conjunction analysis to reveal areas in common for trait and state NA (Nichols, Brett, Andersson, Wager, & Poline, 2005). A conjunction z map was created by comparing the z value of each voxel in the trait NA map with the z value in the state NA map. If the z scores were of opposite signs, the value for the voxel in the conjunction z map was set to zero. If the z scores were in the same direction, the value for the voxel in the conjunction z map was assigned to the z value with the weaker significance. The conjunction z map was then thresholded to identify significant clusters, using the thresholded method described below. Second, the GTS NT and PANAS-X NA scores were entered as predictors into a higher-level regression analyses that included both predictors. The resulting β map for each predictor reflected the unique variance associated with that predictor. Because the conjunction analyses identified no shared brain regions, and results for the zero-order correlations in the first set of analyses generally resembled results from the second set of analyses, the latter are reported below. The interaction between trait and state NA was added as a third IV to this latter analysis to examine regions where the relationship between trait NA and brain activation depended on the level of state NA.

Significantly activated voxels were identified via thresholding of per-voxel t-tests conducted on contrast βs maps that were converted to z-scores. All hypotheses regarding the main effects of trait and state NA were directional, justifying one-tailed tests for these analyses. Monte Carlo simulations via AFNI’s AlphaSim program were used to estimate the overall significance level (probability of a false detection) for thresholding the 3D functional z-map image (Ward, 2000). The simulations were conducted for several individual voxel z-threshold values, providing the appropriate cluster size giving an overall family-wise error rate of $p \leq 0.05$ (although all clusters reported here survived a more stringent family-wise error rate of $p = .01$).
To limit the number of voxels under consideration and examine a priori regions of interest, masks for the frontal cortex, anterior cingulate cortex, and parietal cortex were created based on the Harvard-Oxford probabilistic atlas available with FSL. For each of these masks, a cluster-size threshold was computed and used only for voxels within the mask. A threshold z-value of 2.0537 was used for all masks. The minimum cluster sizes for the masks were: frontal cortex = 702 mm$^3$, ACC = 351 mm$^3$, parietal cortex = 780 mm$^3$. A whole-brain gray-matter mask was used to examine areas not involved in a priori hypotheses (cluster size threshold = 1,170 mm$^3$). All analyses were also conducted using two-tailed tests, with results largely in line with the planned one-tailed tests. In no case did a two-tailed test result in significant clusters in the direction opposite to hypothesis. Two-tailed results for these analyses are thus not reported here. Because the analysis examining the interaction between trait and state NA was exploratory, two-tailed tests using the whole-brain gray-matter mask were conducted (cluster size threshold = 2,340 mm$^3$).

**Lateralization Analyses**

Research supports important distinctions in functional specialization of the two hemispheres, particularly the frontal cortex (e.g., Engels et al., 2007; 2010; Herrington et al., 2005; 2010, Spielberg, et al., 2010; for reviews, see Heller, Nitschke, & Miller, 1998; Herrington, Koven, Heller, Miller, & Nitschke, 2009). Therefore, analyses were conducted for the clusters that emerged in the frontal cortex to determine whether they were significantly lateralized. Lateralization was tested using a locally written Matlab program. This program implemented a repeated-measures homogeneity of slopes General Linear Model, with hemisphere as the repeated measure, trait and state NA scores as continuous predictors, and fMRI activation for the arousal contrast as the dependent variable. This ANCOVA was conducted on a per-voxel basis, and the resultant $\beta$ maps were thresholded as described above, with the exception that F-tests were used. Because testing laterality determines whether the beta in a voxel in the right hemisphere is significantly different from the beta in the homologous voxel in the left hemisphere, half as many tests are conducted as in a full-brain analysis. Therefore, a mask containing only the right frontal hemisphere was created.
Behavioral Data

Average RTs were computed for each condition (positive, neutral, and negative), and an arousal interference score was calculated by subtracting each participants’ average neutral-word RT from the mean of their positive-word and negative-word RT averages. Higher interference scores indicated that participants took longer to respond to emotionally arousing words than neutral words. To examine the relationship between trait and state NA and arousal interference, arousal RT interference was entered as a dependent variable in regression analyses first with each questionnaire entered separately and second with the questionnaires entered simultaneously as predictors. The interaction between trait and state NA was added to this latter analysis to examine whether the relationship between trait NA and arousal interference depended on the level of state NA. The same regression analyses were repeated, except with overall number of task errors as the dependent variable.

Analysis of Brain Activation and Behavior Relationships

In order to explore the relationship between behavioral performance and neural activation in the clusters associated with trait and state NA, β values were averaged across all voxels in each cluster to create a single score for each participant. Correlations between arousal RT interference and cluster scores, as well as number of task errors and cluster scores, were calculated using PASW Statistics (SPSS) 18.
RESULTS

Behavioral data

Table 1 lists the results of the regression analyses for the behavioral data. State NA was associated with arousal-related RT interference and total number of task errors, such that higher levels of state NA were associated with 1) responding more slowly to emotionally arousing words than to neutral words and 2) committing more errors. Trait NA was not associated with arousal RT interference or errors. The interaction between trait and state NA predicted task errors, such that high state NA was associated with committing more task errors when co-occurring trait NA was high.

Brain regions uniquely associated with trait negative affect

Table 2 lists the four regions that were negatively correlated with trait negative affect. In line with hypotheses, higher levels of trait NA were associated with less brain activation in areas involved in attentional control: left posterior DFPFC (middle frontal gyrus extending into precentral gyrus), rostral anterior cingulate cortex (rACC), and precuneus (see Figure 1). In addition, a cluster emerged in left caudate when using the whole-brain gray-matter mask. As mentioned above, there were no significant clusters positively correlated with trait negative affect.

Brain regions uniquely associated with state negative affect

Table 2 lists the regions that were positively correlated with state negative affect. In line with hypotheses, higher levels of state NA were associated with more activation in mid-DLPFC (middle frontal gyrus, extending into inferior frontal gyrus), ACC, and precuneus (see Figure 1). Three separate clusters emerged in the ACC: rACC, dorsal ACC (dACC), and posterior dACC. In addition to mid-DLPFC, a second cluster emerged using the frontal cortex mask: left medial frontal cortex. Finally, when using the whole-brain gray-matter mask, two additional clusters emerged: one in left parahippocampal gyrus and one spanning left and right nucleus accumbens/caudate. There were no significant clusters negatively correlated with state negative affect.
The interactive effects of trait and state negative affect

Table 3 lists the seven regions significantly negatively correlated with the interaction between trait and state NA. These regions include left DLPFC (lateral middle frontal gyrus), medial superior frontal gyrus, bilateral superior parietal cortex (extending into occipital cortex), bilateral middle temporal gyrus, and occipital cortex (spanning intracalcarine cortex/lingual gyrus/occipital fusiform gyrus; see Figure 2). Graphing the interaction showed that increased trait NA was associated with decreased activation in these areas at high levels of state NA. No regions were positive correlated with the interaction between trait and state NA.

Lateralization analyses

Lateralization analyses were conducted to explore whether the three left frontal clusters (posterior DLPFC associated with trait NA, mid-DLPFC/IFG associated state NA, and lateral MFG associated their interaction) were significantly lateralized. Only the lateral MFG cluster associated with the interaction between trait and state NA was left lateralized.

Correlations between brain activation and behavior

As presented in Table 2, all clusters associated with trait and state NA were positively correlated with reaction time to high-arousing versus neutral stimuli. These positive correlations indicate that as activation in these areas increased, participants were more distracted by the emotional nature of the words. Furthermore, as seen in Table 3, five of the seven clusters associated with the interaction between trait and state NA were also positively correlated with RT interference for arousing words, including left DLPFC (middle frontal gyrus), medial superior frontal gyrus, left superior parietal cortex, and left and right middle temporal gyrus. Only the cluster located in mid-DLPFC (positively associated with state NA) was marginally correlated with error rate (r = .17, p = .08). As activation in this area increased, participants made more errors during the task.
Mediation analyses

Less activation in posterior DLPFC for higher levels of trait NA was consistent with hypotheses. However, it was expected that less activation in this region would be associated with decrements in performance, such that individuals with high levels of trait NA would have more difficulty ignoring the arousing nature of the stimuli given their difficulty recruiting posterior DLPFC to implement top-down attentional control. However, the positive correlation between brain activation in this area and RT interference indicated that less activation in posterior DLPFC was associated with better performance (less distraction by the emotional words). A multiple mediation analysis was conducted to investigate the possibility that the impact of posterior DLPFC activation on behavioral performance is actually mediated by other brain areas (see Figure 3). This hypothesis is in line with the cascade-of-control model, which posits that the ACC comes online after the DLPFC in order to implement response-related attentional processes, such as evaluating responses.

The multiple mediation model involves an independent variable (IV), \( j \) possible mediators (M), and a dependent variable (DV). In the present model, the IV was left posterior DLPFC, the DV was arousal RT interference, and the possible mediators were the rACC, precuneus, and caudate clusters that emerged from the trait NA analysis. The multiple mediation model allows for the testing of several potential mediators simultaneously and has several advantages over testing separate simple mediation models. It can be used to determine 1) whether an overall effect exists (analogous to conducting a regression analyses with multiple predictors and evaluating total \( R^2 \)) and 2) whether specific variables mediate the direct effect (conditional on other mediators being included in the model). It also reduces the likelihood of parameter bias due to omitted variables (see Preacher & Hayes, 2008, for discussion). Furthermore, it is more convenient, precise, and parsimonious to examine all possible mediators in the same model.

Following the recommendation of Preacher and Hayes (2008), mediation (examined via significance of the indirect effect \( a_j \times b_j \)) was determined by using bootstrapped confidence intervals rather than the Sobel (1982) test. The bootstrap method is preferred over the Sobel test because the former does not require the
assumption of a normal distribution. The indirect effect has an asymmetrical distribution in finite samples and is normal only in large samples (Preacher & Hayes, 2004, 2008). Furthermore, simulations have shown that bootstrapping methods have higher power while still performing well regarding Type I error rates (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002; MacKinnon, Lockwood & Williams, 2004). The SPSS macro script of Preacher and Hayes (2008) was used to conduct multiple mediation analyses by calculating 95% bias-corrected and accelerated bootstrap confidence intervals for the indirect effect involving 5000 repetitions.

The results of the mediation analyses are presented in Table 4. The total indirect effect was significant, as was each of the specific indirect effects, indicating that the rACC, precuneus and caudate clusters mediated the relationship between posterior DLPFC activation and RT interference. As shown in the table, the effect of posterior DLPFC on RT interference was reduced from .67 to .06 by the three mediators, going from a significant (p = .0001) to nonsignificant (p = .84) relationship, indicating full mediation. Consistent with the cascade-of-control model, rACC mediated the relationship between DLPFC and RT interference. Importantly, when the other areas were in the model, the effect of rACC on RT interference (path b) was negative, indicating that less activation in the rACC is associated with more interference from arousing stimuli (when partialling out the effect of the posterior DLPFC). Thus, less activation in posterior DLPFC is associated with less activation in rACC, which is in turn associated with difficulties ignoring emotionally arousing stimuli.
DISCUSSION

Trait negative affect

The present study tested hypotheses about relationships between self-reported trait and state negative affect (NA) and activity in specific brain regions supporting control of attention during emotional challenge. As hypothesized, trait NA was associated with less activation in areas involved in attentional control, including posterior DLPFC, precuneus, and rACC, during an emotion-word Stroop task. Studies of healthy individuals have found that posterior DLPFC plays a key role in successfully implementing top-down control in order to ignore distracting information and focus on the task at hand (Banich, 2009; Banich et al., 2000a, 2000b, 2009; Compton et al., 2003; Milham, Banich, & Barad, 2003). The present finding that trait NA is negatively related to posterior DLPFC activation supports the contention that individuals high in trait NA have difficulty engaging top-down aspects of attentional control and maintaining task goals (Banich, 2009; Herrington et al., 2010). Less activation in left posterior DLPFC in individuals high in trait NA is consistent with studies that examined individuals high in anhedonic depression and found less activity in this area following negative than following neutral words (Engels et al., 2010; Herrington et al., 2010). The present study extends these findings by demonstrating that abnormal processing in this area is not specific to depression but is associated with trait NA, a more general risk factor for developing and maintaining various forms of psychopathology, particularly anxiety and depression (Ormel et al., 2004). Furthermore, present results indicate that individuals high in trait NA have difficulty ignoring salient, arousing information (both positively and negatively valenced), suggesting that their attentional deficit is not specific to negative stimuli. This finding is consistent with research showing that neuroticism is associated with difficulty ignoring salient distracters during a non-emotional task (Bredemeier et al., 2011).

Corbetta et al. (2008) have also asserted that posterior portions of the frontal cortex (extending into the frontal eye fields and premotor areas) are part of a dorsal frontoparietal network involved in the top-down selection of stimuli that are congruent with goals as well as expectations based on previous experiences. Furthermore, posterior
DLPFC appears to feed top-down signals to a separate ventral attentional network involved in detecting salient stimuli in order to bias processing of the appropriate stimulus features (Corbetta et al., 2008). As reviewed above, individuals high in trait NA tend to ignore meaningful contextual details and rely excessively on pre-existing, context-independent knowledge. Dysfunction in a key node of the dorsal attentional network may explain why these individuals have difficulty appropriately integrating pre-existing information with current goals in order to attend to the information in their environment that is most relevant. Functional impairments in posterior DLPFC also perturb activity in other areas, particularly parietal regions that receive top-down modulation from it. In the present study, less activation in a cluster in the parietal cortex associated with trait NA, the precuneus, suggests that this area fails to receive top-down signals from posterior DLPFC that bias processing toward task-relevant aspects of stimulus representations (color information) and away from irrelevant features (word information; Banich et al., 2000). Additionally, the precuneus appears to be a central “hub” linking the frontal cortex with other parietal areas (Bullmore & Sporns, 2009). Thus, dysfunction in the precuneus may also prevent the successful modulation of other key parietal areas by frontal regions.

High trait NA was also associated with decreased activation in rACC, a region involved in evaluating interference from emotionally salient distracters and implementing attentional control to ignore these task-irrelevant stimuli (Mohanty et al., 2007; Vuilleumier, Armony, Driver, & Dolan, 2001; Whalen et al., 1998). The cascade-of-control model (Banich, 2009), based on a series of studies examining the color-word Stroop task and variants of it, asserts that attentionally demanding tasks first recruit the DLPFC, which in turn influences later ACC activity, specifically the dorsal portion of this region. However, in the present study, the cluster that was significantly associated with trait NA was located in the rostral portion of the ACC. This is consistent with work that found rACC engaged during attentional control tasks involving emotional information (e.g., emotion-word Stroop), whereas dACC was engaged during non-emotional attentionally demanding tasks (e.g., color-word Stroop; Bush et al., 2000; Mohanty et al., 2007). The combination of hypoactivity in both posterior DLPFC and rACC regions in individuals high in trait NA suggests they have difficulty exerting top-
down control to handle conflict from emotional distracters. Furthermore, the finding that, for the sample as a whole, rACC activation mediated the relationship between posterior DLPFC activation and RT interference suggests that DLPFC failed to recruit rACC to compensate for poor attentional control, thus leading to increased distraction from emotionally arousing stimuli. Similar deficits in the frontocingulate network have been observed in anxious individuals and may be related high levels of trait NA rather than anxiety-specific symptoms (Bishop et al., 2004; Engels et al., 2007).

State negative affect

In contrast to trait NA, state NA was associated with increased activation in areas involved in attentional control, including mid-DLPFC, precuneus, rACC, and dACC. Previous studies support the role of mid-DLPFC in the selection and processing of specific aspects of stimuli in the environment (Banich, 2009; Engels et al., 2007; Herrington et al., 2005; 2010). Successful implementation of attentional control is associated with engaging mid-DLPFC to select the most pertinent features and ignore irrelevant ones. Mid-DLPFC (an anterior portion of middle frontal gyrus) has been proposed to be part of the stimulus-driven ventral attentional network, functionally and anatomically separate from the top-down dorsal attentional network described above (Corbetta et al., 2008). In the present study, the cluster in mid-DLPFC extended ventrally into inferior frontal gyrus (IFG), another key node in the ventral attentional network. This network is involved in detecting salient stimuli in the surroundings and determining their behavioral relevance (Corbetta et al., 2008). This network interrupts top-down processing in order to reorient attention to stimuli that have been determined to be “important” or relevant. Hyperactivity in mid-DLPFC has been linked to too much engagement with irrelevant features of stimuli (the meaning of threat words in the emotion-word Stroop), interfering with processing task-relevant features (word color; Engels et al., 2010). In the present study, individuals high in state NA appear to have been paying too much attention to the emotional aspects of the words, which impeded their ability to focus on the color of the words. This explanation is supported by the significant relationship between increased activity in mid-DLPFC and greater behavioral
(RT) interference for emotionally arousing than for neutral words. Mid-DLPFC activation was also marginally positively correlated with overall task errors.

State NA was also associated with three clusters in the anterior cingulate cortex: one in the anterior portion of dACC, one in the posterior portion of dACC, and one in rACC. Whereas previous work has highlighted the key role dACC plays in implementing attentional control during non-emotional tasks, evidence suggests that it is also recruited in contexts involving emotional distracters (Mohanty et al., 2007). The anterior portion of dACC appears to be involved in response evaluation, with activity increasing when the likelihood of making errors during a task is greater (Banich, 2009; Milham & Banich, 2005). The posterior portion of dACC is engaged during late-stage attentional processing, such that it determines what information to use to guide response selection (Banich, 2009; Milham et al., 2001, 2003). Additionally, if DLPFC function earlier in the processing stream is problematic, posterior dACC must deal with unresolved selection issues. In the present study, increased activation in both portions of the dACC was associated with increased interference from emotional stimuli. Given that high state NA individuals engage in excessive processing of salient stimuli, increased dACC activity appears to reflect 1) unsuccessful attempts to compensate for dysfunctional DLPFC control and 2) attempts to signal the DLPFC to engage stronger top-down control in the future, in order to override bottom-up processing (Banich, 2009; Milham et al., 2003).

A third cluster in the anterior cingulate was located in the rostral portion, overlapping with the cluster that emerged in the trait NA analysis. However, the relationship between state NA and rACC was in the direction opposite that of trait NA, such that increased levels of state NA were associated with increased activation in rACC. In addition to being involved in attentional control during emotional tasks, rACC has been implicated in regulating emotional states and responses to emotional material (Bush et al., 2000). Increased rACC activation has also been linked to symptom provocation in individuals with anxiety disorders (Bush et al., 2000; Devinsky, Morrell, & Vogt, 1995; Drevets & Raichle, 1998; Whalen et al., 1998). A cluster in medial frontal cortex also emerged in the state NA analysis. Similar to rACC, this region has also been implicated in various functions related to affective states, including negative emotional responses to
pictures, as well as making attributions about emotional states (Lane & McRae, 2004; Ochsner et al., 2004; 2009). Increased activation in both rACC and medial frontal cortex in the present study for individuals high in state NA suggests that they were overly involved in attending to the emotional content of the stimuli and/or their own mood states.

State NA was also associated with activation in the precuneus and parahippocampal gyrus. As described above, activation in the precuneus is linked to the strengthening of particular aspects of stimulus representations over other features. Given that precuneus activation was associated with difficulty ignoring the emotional content of the words, it is likely that individuals high in state NA were biasing the processing of word meaning instead of word color. Previous studies using the Stroop task found that decreased parahippocampal activity was associated with the successful implementation of attentional control (Compton et al., 2003). Since this area is associated with the binding together of information, deactivation in this area during the Stroop was thought to reflect inhibiting the binding of ink color and word meaning in order to facilitate task performance. Increased activation in the hippocampal gyrus in the present study may indicate that individuals high in state NA were binding together this information, which contributed to detriments in their performance.

As reviewed above, individuals in negative moods tend to engage in a systematic processing strategy that relies on bottom-up processing and attention to situational details. Instead of relying on pre-existing information, they utilize knowledge that is context-dependent. The pattern of brain activity associated with high state NA suggests that, when individuals are in negative moods, they engage in excessive bottom-up processing of salient stimuli. This is problematic when these stimuli are not behaviorally relevant for the task at hand. In effect, these individuals are constantly interrupting top-down processing in order to reorient attention to focus on irrelevant contextual information, which penalizes their performance during tasks involving salient distracters.

Interactive effects of trait and state negative affect

The results of the present study indicate that individuals who have high levels of both trait and state NA exhibit a distinct pattern of brain activation in the context of
emotional distraction, beyond the additive effects of trait and state NA. The clusters that emerged for the interaction analysis of trait and state NA did not overlap with any of the clusters associated with the main effects, highlighting the importance of considering the interactive effects of these emotional facets. Relative to individuals high in only trait or state NA, individuals high in both showed less activation in lateral middle frontal gyrus and medial superior frontal gyrus, indicating difficulty maintaining a top-down goal-congruent task set while dealing with conflicting emotional information (Ferstl, Rinck, & Cramon, 2005; Schirmer, Zysset, Kotz, & Yves von Cramon, 2004; Spielberg et al., 2010).

Individuals high in trait and state NA also exhibited decreased activation in several areas early in the dorsal processing stream, including occipital cortex, bilateral middle temporal gyrus, and bilateral superior parietal areas. Hypoactivation in visual and temporal areas in conjunction with hypoactivation in frontal areas indicates that these regions were not receiving modulation from the prefrontal cortex to bias processing of the appropriate sensory representations (Banich et al., 2000b). Given that the superior parietal cortex is part of the dorsal top-down attentional network, decreased activation in this region suggests that these individuals have more difficulty allocating attentional resources in a top-down manner than do individuals high in only trait or state NA (Corbetta, Patel, & Shulman, 2008; Husain & Nachev, 2007).

**Conclusion**

Overall, results of the present study indicate that trait NA, state NA, and their interaction have unique neural correlates. High levels of trait NA negatively impact top-down attentional processing, such that static aspects of attentional control that maintain goals across time are compromised. Specifically, individuals high in trait NA have difficulty sustaining attention and persisting in goal achievement in environments involving salient distractions. Given that the top-down attentional system is also involved in anticipating and preparing for upcoming tasks (Corbetta et al., 2008), the dysfunction in this system observed in these individuals suggest that they experience deficits related to these functions as well. Present results are consistent with research indicating that high trait anxious individuals exhibit problems engaging proactive control,
or “sustaining representation of task requirements or goals throughout periods of high control demand” (p. 240, Fales et al., 2008; though present results suggest such deficits are not specific to anxiety). Difficulty implementing top-down attentional control in the face of distracting emotional information likely leads to the negative correlations associated with high levels of trait NA, including biased expectations, interpretations, and attributions of environmental information. High trait NA individuals appear to rely excessively on (potentially inappropriate) knowledge based on previous experiences, failing to integrate it with pertinent information in current context in order to respond adaptively.

In contrast to trait NA, high levels of state NA are associated with an over-reliance on more transient aspects of attentional control and excessive bottom-up processing of salient information. Hyperactivity of the stimulus-driven attentional network leads to repeated interruption of top-down processing in order to focus on contextual details that often turn out to be irrelevant to the task at hand. Whereas individuals high in trait NA appear to be ineffective at incorporating information from their immediate environment, those high in state NA appear to have the opposite problem, such that they have difficulty appropriately attending to ongoing goals. The present findings support the assertion that trait NA is not simply the tendency to experience negative moods; rather it has correlates that are dissociable from state NA. Furthermore, present results contribute to the understanding of the likely psychological and biological mechanisms through which trait and state NA differentially trigger and maintain symptoms associated with anxiety and depression. Importantly, these two emotional facets are associated with distinct attentional control deficits.

Present results have implications for the prevention and treatment of psychological disorders. Intervention methods should target maladaptive aspects of both bottom-up and top-down processing, such that individuals learn to engage the two attentional systems flexibly and strike an appropriate balance between them. It has been suggested that deficits in bottom-up processing may be modified through behavioral reinforcement methods, whereas top-down problems can be addressed using a cognitive restructuring approach (see Ochsner et al., 2009). Future work should determine whether
the combination of these methods will effectively target the additional attentional deficits that individuals high in both trait and state NA exhibit.
Table 1

Regression analyses for behavioral data

<table>
<thead>
<tr>
<th>Mediators</th>
<th>Beta(^1)</th>
<th>p</th>
<th>R(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entered separately:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait NA (GTS NT)</td>
<td>-.04</td>
<td>.70</td>
<td>.00</td>
</tr>
<tr>
<td>State NA (PANAS NA)</td>
<td>.20</td>
<td>.04</td>
<td>.04</td>
</tr>
<tr>
<td>Entered simultaneously:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 1:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GTS NT</td>
<td>-.10</td>
<td>.32</td>
<td>.05</td>
</tr>
<tr>
<td>PANAS NA</td>
<td>.23</td>
<td>.03</td>
<td></td>
</tr>
<tr>
<td>Step 2:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GTS NT x PANAS NA</td>
<td>-.28</td>
<td>.62</td>
<td>.05</td>
</tr>
</tbody>
</table>

DV = Arousal RT interference

DV = Total task errors

Entered separately:

| GTS NT                  | .11 | .27 | .01 |
| PANAS NA                | .22 | .03 | .05 |

Entered simultaneously:

| GTS NT                  | .06 | .59 | .05 |
| PANAS NA                | .20 | .05 |     |

Step 2:

| GTS NT x PANAS NA       | 1.18 | .04 | .09 |

\(^{\text{Note.}}\) \(t\) = standardized betas, GTS NT = General Temperament Survey, Negative Temperament scale, PANAS NA = Positive and Negative Affect Schedule, Negative Affect scale
Table 2
*Brain areas moderated by trait and state negative affect and correlations with behavior*

<table>
<thead>
<tr>
<th>Region</th>
<th>Cluster Size mm$^3$</th>
<th>Direction of Relationship</th>
<th>Mean z-value</th>
<th>Location X</th>
<th>Location Y</th>
<th>Location Z</th>
<th>RT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trait Negative Affect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L middle frontal gyrus/precentral gyrus (posterior DLPFC)$^a$</td>
<td>3,200</td>
<td>Negative</td>
<td>-2.35</td>
<td>-34</td>
<td>16</td>
<td>39</td>
<td>.38**</td>
</tr>
<tr>
<td>Rostral anterior cingulate cortex$^b$</td>
<td>1,430</td>
<td>Negative</td>
<td>-2.41</td>
<td>-3</td>
<td>40</td>
<td>0</td>
<td>.27**</td>
</tr>
<tr>
<td>Precuneus$^c$</td>
<td>3,902</td>
<td>Negative</td>
<td>-2.36</td>
<td>-3</td>
<td>-60</td>
<td>22</td>
<td>.45**</td>
</tr>
<tr>
<td>L caudate$^d$</td>
<td>2,678</td>
<td>Negative</td>
<td>-2.29</td>
<td>-10</td>
<td>5</td>
<td>3</td>
<td>.43**</td>
</tr>
<tr>
<td><strong>State Negative Affect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L middle frontal gyrus/inferior frontal gyrus (mid-DLPFC)$^a$</td>
<td>1,182</td>
<td>Positive</td>
<td>2.35</td>
<td>-26</td>
<td>29</td>
<td>40</td>
<td>.37**</td>
</tr>
<tr>
<td>L medial frontal cortex$^a$</td>
<td>1,124</td>
<td>Positive</td>
<td>2.31</td>
<td>-6</td>
<td>52</td>
<td>-10</td>
<td>.42**</td>
</tr>
<tr>
<td>Rostral anterior cingulate cortex$^b$</td>
<td>547</td>
<td>Positive</td>
<td>2.28</td>
<td>0</td>
<td>39</td>
<td>2</td>
<td>.26**</td>
</tr>
<tr>
<td>Dorsal anterior cingulate cortex$^b$</td>
<td>390</td>
<td>Positive</td>
<td>2.30</td>
<td>-9</td>
<td>33</td>
<td>21</td>
<td>.36**</td>
</tr>
</tbody>
</table>
Table 2 (cont.)

<table>
<thead>
<tr>
<th>Region</th>
<th>Z</th>
<th>MNI Coordinates</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior dorsal anterior cingulate cortex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.33</td>
<td>-2, -3, 36</td>
<td>.26**</td>
</tr>
<tr>
<td>Precuneus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.48</td>
<td>-4, -62, 21</td>
<td>.46**</td>
</tr>
<tr>
<td>L parahippocampal gyrus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.42</td>
<td>-21, -14, -25</td>
<td>.24*</td>
</tr>
<tr>
<td>L&amp;R nucleus accumbens/caudate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.45</td>
<td>-1, 14, -2</td>
<td>.46**</td>
</tr>
</tbody>
</table>

Note. L = left. R = right. Location = Coordinates are for the center-of-mass in MNI152 2009a symmetrical space.

RT = Reaction time interference. * = Correction for only frontal cortex voxels. ** = Correction for only anterior cingulate cortex voxels. = Correction for only parietal cortex voxels. d = Correction for all gray-matter voxels.

* = p < .05, ** = p < .01.
<table>
<thead>
<tr>
<th>Region</th>
<th>Cluster Size mm³</th>
<th>Direction of Relationship</th>
<th>Mean z-value</th>
<th>Location X</th>
<th>Location Y</th>
<th>Location Z</th>
<th>RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>L lateral middle frontal gyrus&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2,828</td>
<td>Negative</td>
<td>-2.52</td>
<td>-44</td>
<td>16</td>
<td>37</td>
<td>.32**</td>
</tr>
<tr>
<td>Medial superior frontal gyrus&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2,750</td>
<td>Negative</td>
<td>-2.37</td>
<td>-1</td>
<td>44</td>
<td>38</td>
<td>.37**</td>
</tr>
<tr>
<td>L superior parietal cortex/occipital cortex&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2,594</td>
<td>Negative</td>
<td>-2.42</td>
<td>-26</td>
<td>-72</td>
<td>39</td>
<td>.12*</td>
</tr>
<tr>
<td>R superior parietal cortex/occipital cortex&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2,424</td>
<td>Negative</td>
<td>-2.38</td>
<td>33</td>
<td>-69</td>
<td>45</td>
<td>.14</td>
</tr>
<tr>
<td>L middle temporal gyrus&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7,422</td>
<td>Negative</td>
<td>-2.60</td>
<td>-61</td>
<td>-37</td>
<td>-4</td>
<td>.43**</td>
</tr>
<tr>
<td>R middle temporal gyrus&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6,990</td>
<td>Negative</td>
<td>-2.43</td>
<td>58</td>
<td>-46</td>
<td>-3</td>
<td>.22*</td>
</tr>
<tr>
<td>Occipital cortex (intracalcarine cortex/lingual gyrus/occipital fusiform gyrus)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>24,198</td>
<td>Negative</td>
<td>-2.43</td>
<td>-4</td>
<td>-74</td>
<td>-5</td>
<td>-.04</td>
</tr>
</tbody>
</table>

*Note.* L = left. R = right. Location = Coordinates are for the center-of-mass in MNI152 2009a symmetrical space.

RT = Reaction time interference. <sup>a</sup> = Correction for all gray-matter voxels 2-tailed test. * = p < .05, ** = p < .01.
Table 4

*Summary of multiple mediation analysis*

<table>
<thead>
<tr>
<th>Mediators (M)</th>
<th>IV = L posterior DLPFC</th>
<th>DV = Arousal RT interference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Path a (IV to M)</td>
<td>Path b (M to DV)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>rACC</td>
<td>1.29**</td>
<td>-.29*</td>
</tr>
<tr>
<td>Precuneus</td>
<td>1.06**</td>
<td>.51**</td>
</tr>
<tr>
<td>Caudate</td>
<td>1.34**</td>
<td>.33*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total Indirect Effect: .61*

Note.<sup>a</sup> = partialling out effects of IV, * = p ≤ 0.05, ** = p < .01.
Figure 1

Blue = negative correlation between brain activation and trait NA (panels A = D). Red = positive correlation between brain activation and state NA (panels E-K). L = Left. Clusters of activation in A = left posterior DLPFC, B = rostral anterior cingulate cortex (rACC), C = precuneus, D = left caudate, E = left mid-DLPFC, F = left medial frontal cortex, G = rACC and posterior dorsal ACC (dACC), H = dACC, I = precuneus, J = parahippocampal gyrus, K = bilateral nucleus accumbens/caudate.
Brain areas associated with the interaction between trait and state negative affect. Blue = Less activation when both dimensions are high than when one dimension is high. L = Left. Clusters of activation in A: left lateral middle frontal gyrus and medial superior frontal gyrus, B = bilateral parietal cortex/occipital cortex, C = bilateral middle temporal gyrus, D = occipital cortex.
Figure 3

The multiple mediation model
REFERENCES


