ELUCIDATING PSYCHOLOGICAL AND NEURAL MECHANISMS ASSOCIATED WITH RISK FOR ANXIETY AND DEPRESSION

BY

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DISSERTATION

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ABSTRACT

Anxiety and depressive disorders are associated with significant social and occupational impairments and lead to considerable emotional, economic, and societal burden. Trait negative affect (NA) is a crucial factor associated with increased likelihood of developing anxiety and depression, as well as vulnerability to comorbidity and relapse. However, little is known about how trait NA fosters anxiety and depression. The present dissertation aimed to clarify possible psychological and biological mechanisms through which trait NA leads to the development and maintenance of anxiety and depressive disorders in order to develop interventions that more effectively prevent their onset and recurrence. A series of studies tested the overarching hypothesis that one possible route is through triggering maladaptive cognitive and motivational processing. Trait NA appears to foster risk through dysfunction in brain regions that implement top-down attentional control in the presence of distracting information that is both emotional and nonemotional in nature. It is also associated with problems integrating motivational processes with emotional and cognitive processes. Trait NA does not appear to alter behavior, rather individuals high in trait NA are able to recruit compensatory strategies, particularly in rewarding contexts. In addition, trait NA interacts with deficits in executive function, specifically updating and shifting, to predict depressive symptoms. Present results may lead to the identification of early markers of risk for anxiety and depression that are not necessarily observable via behavior or self-report. This may foster the development of prevention strategies aimed at addressing dysfunctional processing in those individuals identified as being at risk.
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CHAPTER 1

GENERAL 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). With low rates of complete recovery (Fricchione, 2004; Kessler & Wang, 2009), it is crucial to identify and address risk factors associated with anxiety and depression in order to prevent their onset and recurrence. Research has shown that trait negative affect (NA) is a crucial factor associated with increased likelihood of developing anxiety and depression, as well as vulnerability to comorbidity and relapse (Clark, 2005; Krueger, Caspi, Moffitt, Silva, & McGee, 1996).

Trait NA is a relatively stable disposition (Watson & Walker, 1996), though not immutable (see Roberts, 2009), that has been discussed as a dimension of both temperament (i.e., negative affectivity or negative temperament) and personality (i.e., neuroticism or negative emotionality; see Clark, Watson, & Mineka, 1994; Watson & Clark, 1984). For present purposes, personality traits are defined in accord with Roberts (2009, pg. 140) as “relatively enduring patterns of thoughts, feelings, and behaviors that are reflect the tendency to respond in certain ways under certain circumstances.” Trait NA is associated with the tendency to experience negative mood states (e.g., worry, anger), as well as poor self-esteem, pessimism, and a propensity to dwell on failures, mistakes, and disappointments (Watson & Clark, 1984). Individuals high in trait NA are more likely to report that they are less satisfied with themselves and describe themselves more negatively than individuals low in trait NA (Watson & Clark, 1984). In addition, they are more likely to have deficient mood-regulation skills (Costa,

At present, we do not know how trait NA fosters anxiety or depression. The primary goal of the present series of studies was to clarify psychological and biological mechanisms through which trait NA may lead to the development and maintenance of anxiety and depressive disorders. The present research tested the overarching hypothesis that one possible route is through triggering maladaptive cognitive and motivational processing that ultimately leads to some of the deficits that are characteristic of these mood and anxiety disorders. However, dysfunction in these processes may not manifest in behavior because individuals high in trait NA frequently develop compensatory strategies. Neuroimaging methods were used to reveal the nature of these deficits and their associated neural mechanisms, which may be otherwise unattainable via behavioral measures or self-report. This line of research has the potential to lead to the identification of early risk factors for anxiety and depression that can be targets for prevention strategies and aid in tailoring cognitive therapies toward more specific processing deficits in order to reduce the occurrence, duration, and chance of relapse of these disorders.

The first study (chapter 2) will examine the hypothesis that trait NA fosters risk through a deficit in attentional control that is present across attentionally demanding contexts, regardless of whether distracting information is emotional in nature or not. The second study (chapter 3) investigated relationships among specific executive function (EF) domains and dimensions of anxiety, depression, and trait NA in order to test the hypothesis that EF deficits contribute to the cognitive dysfunction, negative biases, and emotion regulation problems observed in anxiety, depression, and trait NA. The third study (chapter 4) extended this research by examining how
trait NA modulates brain regions involved in integrating motivational processes with emotional and cognitive processes, given that motivational dysfunction is present in both anxiety and depression. Such research can inform our understanding of the mechanisms through which trait NA and motivational dysfunction contribute to the development and maintenance of anxiety and depression. The final chapter provides a general discussion that reviews the implications of these findings and future directions for research. Notably, chapters 2, 3, and 4 are written in the form of manuscripts ready to submit for publication.
CHAPTER 2

NEURAL CORRELATES OF TRAIT AND STATE NEGATIVE AFFECT: ATTENTIONAL CONTROL DURING NON-EMOTIONAL DISTRACTION

The literature has increasingly argued that a dimensional rather than categorical approach may provide a more veridical understanding the etiology of mental disorders (Hyman, 2010; Krueger & Piasecki, 2002; Widiger & Gore, 2011). In line with this, NIMH recently developed the Research Domain Criteria (RDoC) initiative to encourage researchers to use a dimensional framework, aiming to better foster the translation of basic science into the prevention and treatment of mental disorders (Morris & Cuthbert, 2012). A focus of the initiative is to improve understanding of how dysfunction in neural networks contributes to symptoms of psychopathology. One of the domains highlighted in the RDoC initiative is negative valence. This domain contributes to constructs such as fear, anxiety, and loss, all of which share a core feature of negative affect (NA). Negative affective states are present in most psychological disorders, and trait NA conveys risk for their development and maintenance (for a review, see Clark, 2005).

The main focus of research regarding trait NA has been on its correlates that are emotional in nature, particularly given its role in mood and anxiety disorders. In addition to being associated with a tendency to experience negative mood states, trait NA has been linked to a negative attributional style, ruminative style of thinking, and negative biases in attention, memory, and interpretation (Haney, 1973; Larsen, 1992; Luten, Ralph, & Mineka, 1997; Martin, 1985). Similarly, state NA has been associated with biases in attention and memory for negative information (Chepenik, Cornew, & Farah, 2007) as well as a processing strategy that focuses on
immediate situational details rather than pre-existing knowledge (for reviews, see Schwarz & Clore, 1996; Heller & Nitschke, 1997).

Although not always distinguished in research, trait and state NA appear to play important yet distinct roles in psychopathology (Crocker et al., 2012). Confounding their effects in studies prevents the elucidation of the unique mechanisms by which they may contribute to the causes and consequences of mental health disorders, as well as the role their interaction may play. Trait and state NA may ultimately contribute to similar behavioral outcomes (e.g., anxiety and depressive symptoms). However, research suggests that they are associated with distinct types of cognitive dysfunction and patterns of brain activity (Crocker et al., 2012).

Based on the hypothesis that trait and state NA would be associated with dysfunction in distinct attentional control networks (top-down vs. stimulus driven), Crocker and colleagues (2012) examined brain activity during an attentionally demanding task involving distracting emotional information (emotion-word Stroop task). Trait NA was associated with decreased activation in a network of brain areas that implement top-down attentional control to facilitate the ability to ignore task-irrelevant information and focus on the task at hand. Specifically, trait NA was associated with less activation for high arousing than neutral words in posterior dorsolateral prefrontal cortex (DLPFC), rostral anterior cingulate cortex (rACC), and precuneus. Drawing on the cascade-of-control model (Banich, 2009) and research on two attentional systems (top-down and stimulus-driven systems; Corbetta & Shulman, 2002; Corbetta, Patel, & Shulman, 2008), Crocker et al. suggested that individuals high in trait NA have difficulty exerting top-down control to maintain task goals in the presence of salient, distracting information. Posterior DLPFC failed to bias posterior cortex toward task-relevant features of
stimuli and away from irrelevant aspects. Further, it failed to recruit rACC to compensate for impaired attentional control, which in turn led to behavioral interference from arousing words.

In contrast, state NA was associated with increased activation in mid-DLPFC, medial frontal cortex, rACC, dorsal anterior cingulate cortex (dACC), posterior dACC, and precuneus. Crocker et al. (2012) suggested that individuals in negative moods engage in excessive processing of salient, emotionally-arousing stimuli, as evidenced by hyperactivity in regions involved in stimulus-driven attentional control and processing of emotional material. Mid-DLPFC plays a key role in detecting salient, behaviorally-relevant stimuli in the environment and interrupting top-down attentional processes to reorient attention to these stimuli. This constant interruption of goal-directed, top-down control appears to lead to decrements in behavior (increased RT interference and task errors) when the emotional material is not pertinent to the task at hand. Increased activity in regions of ACC was interpreted as reflecting failed attempts to compensate for weak top-down control as well as unsuccessful attempts to signal DLPFC to exert stronger control in future trials to override stimulus-driven processing.

Crocker et al. (2012) also examined the interaction of trait and state NA to determine whether the relationship between trait NA activation in certain areas depended on the level of state NA. Co-occurring high levels of trait and state NA were associated with decreased activation in lateral middle frontal gyrus (MFG), medial superior frontal gyrus (SFG), bilateral superior parietal cortex, bilateral middle temporal gyrus (MTG), and occipital cortex. Importantly, none of these regions overlapped with those exhibiting main effects for trait and state NA. Decreased activity in this network of areas was thought to reflect difficulty maintaining a goal-congruent task set in the context of irrelevant emotional information, leading to an increase in task errors. Hypoactivity in MFG and SFG in combination with hypoactivity in
parietal, temporal, and occipital regions suggested that these frontal regions were not effectively modulating the latter regions in order to bias processing of the appropriate stimulus representations. The interaction between trait and state NA appears to contribute uniquely to attentional control deficits, above and beyond their main effects.

Although these results shed light on the mechanisms by which trait NA, state NA, and their interaction may uniquely contribute to symptoms of psychopathology, it is not clear whether emotional contexts are necessary to elicit the observed attentional control deficits or whether such deficits are present in other contexts. There is some evidence that individuals high in trait NA exhibit attentional control deficits that are not specific to emotional information. Wallace and Newman (1998) demonstrated that females high in neuroticism were more impaired by distracters during a visual search task than females low in neuroticism. Trait NA has also been linked to larger attentional blink (AB) magnitudes during rapid serial visual presentation (RSVP) tasks, indicating difficulty disengaging attention from an initial target in order to process a second target in a rapid stream of stimuli (MacLean & Arnell, 2010; MacLean, Arnell, & Busseri, 2010). It was suggested that increased AB magnitudes in individuals high in trait NA reflected decreased or less efficient cognitive control, resulting in prolonged disengagement from the first target. Bredemeier and colleagues (2011) provided further support for the hypothesis that individuals high in trait NA exhibit deficits in attentional control in non-emotional contexts. They employed a single-target RSVP task involving salient, non-emotional distracters and found that trait NA was associated with longer ABs, suggesting that individuals high in trait NA have difficulty disengaging attention from distracters regardless of whether they are emotional in nature.
Research examining whether state NA is associated with deficits in attentional control in non-emotional contexts is mixed. Compton (2000) found that individuals who were the slowest to disengage their attention from invalid cues during an attentional orienting task showed the greatest increase in state NA following a negative film. In contrast, Chepenik and colleagues (2007) found that a sad mood did not affect performance for attentionally demanding tasks that were not emotional in nature; only performance for emotional tasks was affected. None of the studies described above investigating the relationship between NA and attentional control examined both trait and state NA, so it is unclear whether the results described could be accounted for by the unmeasured construct. It may be the case that trait but not state NA is associated with broad attentional control deficits across contexts, and the results from studies examining only state NA actually reflect the effects of trait NA, given that individuals high in trait NA are more susceptible to negative moods. Even if it is the case that both trait and state NA are associated with attentional deficits in non-emotional contexts, these deficits may be different in nature. Neuroimaging methods can be used to address this empirical question, since they can provide information inaccessible though self-report and behavioral assessment and may reveal when divergent processing strategies are being engaged.

The purpose of the present study was to determine whether the attentional control deficits associated with trait and state NA observed in Crocker et al. (2012) are specific to distracting emotional information or extend to task-irrelevant, non-emotional information. It was hypothesized that the results of Crocker et al. (2012) would be replicated for trait NA, given the expectation that trait NA is associated with broad attentional control impairments that occur across contexts. Specifically, trait NA was hypothesized to be associated with decreased activation in posterior DLPFC, as well as in other areas involved in top-down attentional control.
including ACC and parietal cortex, in the context of non-emotional, distracting information. In contrast, it was expected that the results of Crocker et al. (2012) would not be replicated for state NA. Given that increased activation in mid-DLPFC, medial frontal cortex, rACC, and parietal cortex associated with state NA during the emotion-word Stroop was thought to reflect enhanced processing of emotionally arousing, salient information, it was hypothesized that state NA would not be associated with increased activation in these areas when ignoring non-emotional, distracting information. These outcomes would support the view that state NA is associated with hyperactive stimulus-driven processing only when emotional information is present.

The interaction of trait and state NA may further contribute to difficulty maintaining a top-down, goal-congruent task set when in the presence of distracting information. Thus, the present study also explored the hypothesis that individuals high in both trait and state NA exhibit decreased activity in MFG, medial SFG, and parietal regions in non-emotional contexts, similar to results obtained in Crocker et al. (2012). A well-established, attentionally-demanding task (color-word Stroop) was employed in order to examine study hypotheses regarding trait NA, state NA, and their interaction.

**Method**

**Participants**

Participants were recruited from the local community via advertisements and gave written informed consent prior to participation in the study, which was approved by the Institutional Review Board of the University of Illinois at Urbana-Champaign. All participants were right-handed, native speakers of English with self-reported normal color vision and no reported neurological disorders or impairments. Participants were excluded if they had a history of mania or psychosis or met criteria for current substance abuse or dependence as assessed by
the Structured Clinical Interview for the DSM-IV. Participants were given a laboratory tour, informed of the procedures of the study, and screened for claustrophobia and other contraindications for MRI participation. Twenty-eight 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 were defined as greater than 3 standard deviations from the sample mean), or error rates exceeding 15%. The final sample included 103 paid participants (64 females, age \( M = 34.19, SD = 9.21 \)). Participants were the same as those in Crocker et al. (2012), which examined a separate task (emotion-word Stroop), although the overlap is \( N = 98 \) because the exclusion criteria listed above were applied separately to each task.

**Questionnaires**

During the laboratory tour, participants completed the 28-item Negative Temperament scale of the General Temperament Survey (GTS-NT) to assess trait NA (Watson & Clark, 1993). Participants were instructed to decide whether each statement mostly described them and to rate each item as 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.” Past research suggests that the GTS-NT has excellent test-retest reliability and good convergent and discriminant validity (Watson & Clark, 1993). State NA was measured using the Negative Affect scale from the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988), which was administered immediately before participants performed the emotion-word Stroop task during fMRI. Participants indicated the extent to which they were feeling each of 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"). The PANAS also has been found to have good psychometric properties (Watson & Clark, 1999; Watson et al., 1988). Internal consistencies (measured using Cronbach’s alpha) for the GTS-NT and PANAS NA scales in the present sample were .81 and .75, respectively. Measures for trait and state NA were correlated, $r = .21, p < .05$, consistent with previous research indicating that state and trait measures of NA typically exhibit moderate correlations (in the .20 to .50 range, Watson & Clark, 1992).

**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 color-word Stroop task are reported here; fMRI data from the emotion-word Stroop task are reported in Crocker et al. (2012). The order of the Stroop tasks within session and the order of fMRI and EEG sessions were counterbalanced. The color-word Stroop task consisted of blocks of color-congruent or color-incongruent words alternating with blocks of neutral words. Half of the trials in the congruent and incongruent blocks were neutral 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., 2000a, 200b; Milham & Banich, 2005). There were eight orders of stimulus presentation blocks that were counterbalanced across subjects (each participant received one out of eight possible orders). In addition to the word blocks, there were four fixation blocks (one at the beginning, one at the end, and two in the middle of the session) and five rest blocks (one at the beginning, one at the end, and one between each word block). In the fixation condition, a fixation cross intensified in place of word presentation, and in the rest condition the subject was instructed to rest and keep their eyes open while the screen was blank.
Each trial consisted of one word presented in one of four ink colors (red, yellow, green, blue) on a black background, with each color occurring equally often with each word type. The 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” printed 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 on word frequency and length. Participants responded to the color of the ink with their middle and index fingers using left- and right-hand response boxes.

Participants received 256 trials presented in 16 blocks (4 congruent, 4 incongruent, and 8 neutral) of 16 trials each, with a variable ITI (±225 ms) averaging 2000 ms between trial onsets. A trial began with the presentation of a word for 1500 ms, followed by a fixation cross for an average of 500 ms. Participants completed 32 practice trials during a low-resolution anatomical scan. No participants failed to understand the task instructions or the mapping between colors and buttons after completing practice trials. Stimuli, 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 2000 ms, TE 25 ms, flip angle 80°, FOV 22 cm). Thirty-eight 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 axial 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 analyses**

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/). All participants demonstrated less than 3.3 mm absolute motion or 2 mm relative motion (participants with motion exceeding this threshold were excluded from analyses, leaving N = 103). 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 data were then intensity-normalized, temporally filtered with a high-pass filter, and spatially smoothed using a 3D Gaussian kernel (FWHM = 5 mm).

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 were created for each condition (incongruent, congruent, 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-level-dependent (BOLD) hemodynamic response function. Each explanatory variable yielded a per-voxel effect-size parameter estimate ($\beta$) map representing the magnitude of activation associated with that explanatory variable. In order to create comparisons of interest, $\beta$ values for the relevant parameters were contrasted. The contrast of particular interest for this study is the incongruent versus neutral contrast, because incongruent trial performance requires executive function to exert top-down attentional control and resolve conflict. For each participant, the functional activation maps were warped into a common stereotaxic space (the 2009 Montreal Neurological Institute [MNI] 152 symmetrical 1 mm x 1 mm x 1 mm template; Fonov, Evans, McKinstry, Almli, & Collins, 2009) using FMRIB’s Non-Linear Image Registration Tool, FNIRT (Andersson, Jenkinson, & Smith, 2007).

Cross-subject inferential statistical analyses of brain activation were carried out using FLAME (FMRIB’s Local Analysis of Mixed Effects). The incongruent versus neutral contrast was entered as a dependent variable (DV) in a multiple regression analysis with questionnaire scores (GTS-NT scale for trait NA and PANAS-NA scale for state NA) entered simultaneously into a higher-level regression analysis to predict activation voxel-by-voxel. The resulting $\beta$ map for each predictor reflected the unique variance associated with that predictor. The results of this analysis were consistent with analyses where each questionnaire was entered separately into a regression (without the shared variance from the other questionnaire removed). The interaction between trait and state NA was added as a third independent variable (IV) to this 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 $\beta$s maps that were converted to z-scores. All hypotheses were directional,
justifying one-tailed tests for these analyses, consistent with the approach taken in Crocker et al., 2012. 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 provided the appropriate cluster size to give an overall family-wise error rate of $p \leq 0.05$.

To limit the number of voxels under consideration, a priori regions of interest were examined using masks of the frontal cortex, ACC, and parietal cortex that were created using 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. An individual voxel level 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$^3$, and parietal cortex = 780 mm$^3$. All analyses were also conducted using two-tailed tests, and in no case did a two-tailed test result in significant clusters in the direction opposite to hypotheses.

**Behavioral data**

Average reaction time (RT) was computed separately for incongruent and neutral conditions. An interference score was calculated by subtracting each participant’s average neutral-word RT from their average incongruent-word RT. Positive interference scores indicate that participants took longer to respond to incongruent words than neutral words. To examine the relationship between RT interference and trait and state NA, RT interference was entered as a DV in regression analyses with the questionnaires entered simultaneously as predictors. The interaction between trait and state NA was then added to this latter analysis to examine whether the relationship between trait NA and RT interference depended on the level of state NA.

**Results**
Behavioral performance

Trait NA, state NA, and the interaction between trait and state NA did not predict behavioral interference for incongruent versus neutral words ($\beta = -0.14, p = 0.17; \beta = -0.01, p = 0.93; \beta = -0.16, p = 0.76$ respectively).

Brain regions uniquely associated with trait negative affect

Table 1 lists the brain regions that were correlated with trait NA. All correlations were negative. Higher levels of trait NA were associated with less activation in bilateral posterior DFPFC (MFG extending into precentral gyrus), right inferior frontal gyrus (IFG), right anterior-middle orbitofrontal cortex (OFC), left anterior-lateral OFC, left posterior-middle OFC, right anterior insula, and right angular gyrus (see Figure 1). There were no significant clusters positively correlated with trait NA.

Brain regions uniquely associated with state negative affect

Table 1 lists the regions that were correlated with state NA. All correlations were positive. Higher levels of state NA were associated with more activation in anterior-medial OFC, left lateral frontal pole, and left postcentral gyrus (see Figure 1). There were no significant clusters negatively correlated with state NA.

The interactive effects of trait and state negative affect

Table 1 lists the three regions significantly associated with the interaction between trait and state NA. These regions include left DLPFC (lateral MFG), left lateral frontal pole, and left anterior supramarginal gyrus (see Figure 2). Graphing the interaction showed that increased trait NA was associated with decreased left MFG activation, but only when state NA is high (see Figure 2). Tests of simple slopes showed that this was the only significant slope [$t(99) = -4.56, p \leq 0.001$]. Tests of simple slopes for left frontal pole and left supramarginal gyrus showed that,
similar to the left MFG, increased trait NA was associated with decreased activation at high levels of state NA \[ t(99) = -2.73, p \leq .01 \text{ and } t(99) = -2.70, p \leq .01 \text{ respectively} \], but with increased activation at low levels of state NA \[ t(99) = 3.42, p \leq .001 \text{ and } t(99) = 1.94, p = .05 \text{ respectively}; \text{ see Figure 2} \]. No regions were positively correlated with the interaction between trait and state NA.

**Discussion**

The results of the present study in conjunction with those from Crocker et al. (2012) indicate that trait NA, state NA, and their interaction have different neural correlates during attentionally-demanding tasks, highlighting the importance of considering trait and state NA separately, as well as their interaction. Most relevant to present hypotheses, trait NA and its interaction with state NA were associated with disrupted patterns of activity in regions implicated in attentional control across emotional and non-emotional contexts. In contrast, state NA was associated with hyperactive stimulus-driven processing only when distracting information was emotional in nature. When distracters are non-emotional, state NA was instead associated with increased activity in lateral frontal pole, medial OFC, and postcentral gyrus.

**Trait NA**

As hypothesized, trait NA was associated with decreased activation in posterior DLPFC, the same region that exhibited decreased activation during an emotion-word Stroop task. This region has consistently been implicated in top-down attentional control in order to maintain task goals in the presence of salient, distracting information (Banich, 2009; Banich et al., 2000a, 2000b; Compton et al., 2003). Research also supports its role in proactive control, the effortful control exerted in anticipation of upcoming challenges by selecting and actively maintaining task-relevant contextual information across time (for a review, see Braver, Gray, & Burgess,
Similarly, Corbetta and colleagues (2008) proposed that posterior DLPFC is a key node of a dorsal frontoparietal attentional network that selects stimuli and responses that are goal-relevant and congruent with expectations based on previous experiences.

In addition, this posterior frontal region influences a separate ventral attentional network, biasing it to detect stimulus features that are consistent with task goals. Thus, decreased activity in posterior DLPFC associated with trait NA indicates that individuals high in trait NA have difficulty sustaining top-down attention when salient distracters are present in the environment, as well as problems anticipating and preparing for future tasks. Repeated difficulty attaining goals over time may ultimately contribute to the development of pessimism and poor self-esteem, which are characteristic of trait NA. Further, deficits in attentional control likely contribute to other types of cognitive dysfunction observed in these individuals, including negatively-biased attention, interpretations, and judgments.

In addition, trait NA was associated with decreased activity in right IFG, a region recruited across a range of inhibition tasks requiring the resolution of interference from conflicting information (Jonides & Nee, 2006; Nelson, Reuter-Lorenz, Sylvestre, Jonides, & Smith, 2003). Although it is been asserted that right IFG plays a key role in inhibiting dominant or incorrect responses (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; Aron, Robbins, & Poldrack, 2004), others have proposed that it is involved in context monitoring to detect salient, goal-related environmental cues and switching/reorienting attention to focus on these cues (Chatham et al., 2012; Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010). In addition to IFG, decreased activity was observed in right anterior insula and right angular gyrus (a region at the temporoparietal junction). Similar to IFG, research has implicated anterior insula and angular gyrus in salience processing and the reorienting of attention (Seeley et al., 2007; Seghier, 2013).
Together, all three regions are part of the stimulus-driven attentional system that identifies salient stimuli that are behaviorally relevant or unexpected and interrupts top-down processing to shift attention to these objects (Corbetta & Shulman, 2002; Corbetta et al., 2008). This system is also involved in shifting attention from internally-driven representations to external stimuli.

Given that one of the roles of posterior DLPFC is to bias this ventral network toward processing only stimuli deemed to be important or behaviorally relevant, it appears that for individuals high in trait NA this stimulus-driven network was not receiving the appropriate top-down modulation in order to successfully persist in goal achievement. Although Crocker et al. (2012) did not report decreased activation in any of these nodes of the stimulus-driven network, a further examination of clusters of voxels meeting a lower z threshold (z = 1.64) than the z threshold reported in the paper (z = 2.05) revealed that the cluster in bilateral DLPFC extended into IFG during an emotion-word Stroop task. Thus, it appears that individuals high in trait NA not only exhibit weak top-down control, leaving them vulnerable to distraction, but have difficulty reorienting attention to information that is more consistent with goals once they are distracted. Importantly, these attentional deficits are not specific to emotional information but are present across contexts involving salient distracters.

Finally, trait NA was also associated with decreased activity in three regions of OFC, right anterior-middle OFC, left anterior-lateral OFC, and left posterior-middle OFC. Research suggests that OFC evaluates and maintains the motivational value of stimuli and communicates this information to DLPFC to be used to determine whether stimuli are consistent with current goals (for a review, see Spielberg et al., 2012). It has been hypothesized that the relationship between DLPFC and OFC is bidirectional, such that DLPFC in turn biases OFC to maintain the value of stimuli that are goal-congruent. There is some research to support the role of left middle
and left lateral OFC in maintaining the value of unpleasant/punishing stimuli, whereas bilateral medial and right lateral OFC are involved in maintaining the value of pleasant/rewarding stimuli (Wager et al., 2008). In connectivity analyses, it was found that regions in DLPFC associated with approach and avoidance motivation exhibited increased connectivity with clusters in OFC in the face of distracting information (Spielberg et al., 2012). Decreased activity in regions in both DLPFC and OFC in the present study indicates that individuals high in trait NA have difficulty integrating motivational information and top-down control to execute goal-directed behavior. This is consistent with dysfunctional interactions between cognitive and motivational processes observed in disorders which share a core feature of trait NA (e.g., depression and anxiety; for a review, see Crocker et al., 2013).

Although trait NA was associated with decreased activity in several regions integral to implementing attentional control and goal pursuit, trait NA was not associated with behavioral interference (i.e., longer RT for incongruent vs. neutral words). The combination of dysfunction in brain networks and intact behavioral performance suggests that trait NA disrupts efficiency of processing but not effectiveness of performance. This is consistent with the assertion that high trait NA/neuroticism is associated with inefficient executive function, reflected in increased reaction time variability (Robinson & Tamir, 2005). Although in some cases individuals high in trait NA may be able to compensate and perform adequately, it is possible that they are unable to do so in contexts that are particularly cognitively demanding, and their performance declines. Future research will benefit from examining trait NA across a range of contexts that vary in task difficulty.

**State NA**
In contrast to trait NA, brain regions associated with state NA in the present study did not overlap with any of those observed during an emotional task. Instead, state NA was associated with increased activity in left lateral frontal pole, anterior-medial OFC, and left postcentral gyrus during a color-word Stroop task. The main effect of state NA in the left lateral frontal pole was qualified by an interaction between trait and state NA, as this region overlapped with the frontal pole region that was associated with the interaction (see below for discussion). Increased activity in anterior-medial OFC likely indicates increased attempts to monitor outcomes and/or maintain the reward value of stimuli that are more attentionally demanding (i.e., incongruent words; Elliot, Dolan, & Frith, 2000; Wager et al., 2008). Individuals high in state NA may be ramping up their focus on the outcome of trials that are more difficult in nature in order to maintain their behavioral performance, even when no explicit reward is at stake, in order to overcome being distracted by their own task-irrelevant thoughts (indicated by increased frontal pole activity, see below).

In addition to its role in maintaining stimulus values and monitoring outcomes, OFC receives input from various sensory and visceral regions, including the somatosensory cortex, located in postcentral gyrus. Thus, OFC is also involved in integrating sensory and bodily information in order to influence behavior and guide decision-making (Kringelbach, 2005). Therefore, increased activity in postcentral gyrus in conjunction with increased OFC activity suggests that individuals high in state NA attend to their physical sensations more during challenging conditions in order use this information to guide their behavior.

**Interaction between trait and state NA**

The present study also examined the interaction between trait and state NA and found that it was associated with decreased activity in left MFG, left lateral frontal pole, and left
supramarginal gyrus. Thus, the relationship between trait NA and activation in these regions depended on the level of co-occurring state NA. The left MFG region observed in the present study overlapped with the left MFG region that was associated with the interaction between trait and state NA during an emotion-word Stroop task. An examination of the interaction revealed that co-occurring high levels of trait and state NA were associated with decreased activity in this region, similar to the pattern observed previously. Crocker and colleagues (2012, p. 10) interpreted this pattern to indicate that individuals high in both trait and state NA have “difficulty maintaining a top-down, goal-congruent task set while dealing with distracting emotional information.” Extending this interpretation, present results suggest that the problem maintaining task sets is not specific to emotional material and is present across contexts, regardless of the nature of the distracting information.

Examining the interaction pattern for left lateral frontal pole and left supramarginal gyrus indicated that being high or low in both trait and state NA was associated with decreased activation in these regions, whereas being high in only one dimension was associated with increased activity. The left frontal pole region overlapped with the region associated with the main effect of state NA. The lateral frontal pole has been associated with stimulus-independent attending, which encompasses focusing on internally-generated thoughts that may be task-irrelevant (e.g., mind-wandering, day-dreaming), as well as thoughts that are maintained in the absence of the external stimuli that provoked them (Burgess, Dumontheil, & Gilbert, 2007). Further, it supports switching between stimulus-independent and stimulus-oriented attention. It also appears to play an integral role in multitasking and maintaining more than one goal/plan at a time (Koechlin & Hyafil, 2007).
In the present study, individuals high in trait NA or state NA alone may have been focusing on task-irrelevant thoughts, possibly ruminative in nature or related to their current affective state/emotional experience. Thus, increased frontal pole activity may reflect attempts by these individuals to switch their attention back to the task at hand, away from internally-generated thoughts and goals. In contrast, individuals high in both trait and state NA appear to have difficulty switching their focus to pertinent external stimuli, reflected in decreased activity in the frontal pole.

The supramarginal gyrus plays a role in the reorienting of attention as a node of the stimulus-driven attentional network (Corbetta et al., 2008). Further, Rushworth and colleagues (2001a, 2001b, 2003) implicated it in "motor attention" more specifically, given that it is activated during the preparation and redirection of motor movements of the hand. Thus, decreased activity in this region suggests that individuals high in both trait and state NA have difficulty redirecting attention away from an incorrect motor response to the correct one, given that incongruent words activate conflicting motor responses (one associated with the ink color and one with the word meaning).

In summary, results for trait NA suggest that individuals high in trait NA have difficulty engaging top-down attentional control in order to persist in goal achievement in the presence of salient, irrelevant information. Importantly, these deficits exist across distracting contexts, regardless of whether they are emotional in nature. Further, the top-down attentional system in these individuals fails to bias a separate attentional system involved in the detection of behaviorally-relevant stimuli, suggesting that they also have difficulty reorienting attention to goal-consistent information once they are distracted. Such difficulties may contribute to the
development of core features of trait NA, including pessimism, poor coping skills, and negatively-biased attention.

In contrast, results for state NA suggest that individuals high in state NA do not exhibit hyperactivity of the stimulus-driven attentional system in the presence of non-emotional, distracting material. Rather, when confronted with non-emotional information that is not pertinent to their current goals, they increase their efforts to maintain the reward value of stimuli that are more attentionally-demanding and/or increase their focus on the outcomes of difficult trials. In addition, they incorporate more sensory information to influence their behavior and decisions. Their performance was not disrupted in the presence of non-emotional, distracting information, in contrast to the interference they demonstrated when it was emotional in nature. The interaction of trait and state NA appears to be associated with difficulty maintaining task sets in the presence of distracting information across emotional and non-emotional contexts. In conjunction with the findings of Crocker et al. (2012), the present study highlights the importance of distinguishing between trait NA, state NA, and their interaction in order to better understand their neural correlates and the distinct role that each may play in the development and maintenance of psychopathology.
CHAPTER 3
RELATIONSHIPS AMONG EXECUTIVE FUNCTION, TRAIT NEGATIVE AFFECT, AND PSYCHOPATHOLOGY

A growing literature has provided evidence that both anxiety and depression are accompanied by cognitive biases and dysfunction that appear to contribute to the emotional problems observed in these classes of disorders. For example, individuals with anxiety and depression exhibit an attentional bias such that they preferentially process threat-related information (for a review, see Crocker et al., 2013). In addition, anxiety has been associated with a bias to interpret ambiguous information more negatively (for reviews, see Mathews & MacLeod, 2005; Zinbarg & Yoon, 2008), whereas depression has been linked to a memory bias to preferentially recall negative over positive information (for reviews, see Gotlib & Joormann, 2010; Mathews & MacLeod, 2005). Recent theorizing and investigating have suggested that at least some of the cognitive biases and impairments associated with anxiety and depression are due to specific executive function (EF) deficits (Austin, Mitchell, & Goodwin, 2001; Levin, Heller, Mohanty, Herrington, & Miller, 2007; Pizzagalli, Pecoraro, Davidson, & Cohen, 2006).

In terms of proposed EF deficits associated with anxiety, the attentional control theory asserts that anxiety (specifically worry) impairs the central executive of the working memory system and consequently is accompanied by deficits in inhibition and shifting functions (Eysenck, Derakshan, Santos, & Calvo, 2007). In support of this assertion, Airaksinen et al. (2005) and Johnson (2009) reported that anxiety was associated with deficits in shifting between mental sets, although Castaneda et al. (2010) did not replicate this finding. In addition, anxiety has been linked to working memory problems (Derakshan & Eysenck, 1998; Eysenck, Payne, & Derakshan, 2005; MacLeod & Donnelan, 1993), particularly under stressful conditions (Eysenck
et al., 2007). Bredemeier and Berenbaum (2013) found that poorer working memory was associated with increases in worry over time. Two recent reviews of behavioral and neuroimaging studies provided further evidence that anxiety is associated with inhibition and shifting deficits (see Derakshan & Eysenck, 2009; Eysenck & Derakshan, 2011).

Similar to anxiety, it has been hypothesized that depression is associated with deficits in inhibition, such that individuals with depression have problems disengaging from mood-congruent information, which leads to further elaboration of the negative information (for a review, see Gotlib & Joorman, 2010). Although some evidence suggests that these inhibition difficulties are specific to negatively-valenced material (e.g., Goeleven, De Raedt, Baert, & Koster, 2006), other research indicates that individuals with depression have problems ignoring distracting information regardless of whether it is emotional or non-emotional in nature (Gotlib & Joormann, 2010; Snyder, 2013). In addition, depression has been associated with deficits in updating and removing previous task-relevant information from working memory and flexibly switching attention to the task at hand (Banich et al., 2009; Joormann, 2010; Joormann & Gotlib, 2008; Warren, Heller, & Miller, in preparation). A recent meta-analysis provided support that major depressive disorder is associated with impairments on a range of neuropsychological measures of EF, including inhibition, updating, and shifting (Snyder, 2013).

A pervasive view in the literature is that these EF deficits are due to symptoms of anxiety and depression (e.g., Eysenck et al., 2007; Williams et al., 2000) and resolve when symptoms remit. However, several studies have demonstrated that individuals in remission from depression still exhibit various EF deficits (e.g., set-shifting, inhibition; Austin, et al., 2001; Beats, Sahakian, & Levy, 1996; Paradiso, Lamberty, Garvey, & Robinson, 1997; Snyder, 2013), suggesting that these EF deficits are not simply be the result of current psychopathology (e.g.,
Austin et al., 2001). Given that executive dysfunction persists even when symptoms improve, it is highly plausible that these EF deficits play a role in the onset, maintenance, and relapse of anxiety and depression and are at least partly responsible for the biases, cognitive dysfunction, and impaired emotion-regulation abilities associated with these disorders (for a review, see Crocker et al., 2013). For example, bias to attend to negative information may be driven by difficulties inhibiting distracting information and/or shifting attention to relevant aspects of tasks, leading to prolonged processing of negative stimuli and sustained negative affect (e.g., Joormann, 2010).

However, various issues in the literature have made it difficult to determine the relationship between psychopathology and EFs. For example, the literature is riddled with variability and imprecision in EF definitions, and there are a multitude of ways to conceptualize EFs (Martin & Failows, 2010). For present purposes, EFs will be defined as the set of abilities that organize and integrate multiple cognitive processes (e.g., visuospatial processing, object perception, word recognition) in order to effortfully guide behavior and perform complex, goal-directed tasks (Banich 2009; Miyake et al., 2000). There has been some debate as to the structure of EF, including whether there is one central EF responsible for all of the higher-order processes that are considered to be executive in nature (e.g., planning, updating, switching, inhibiting, sequencing) and/or whether these processes are separable and contribute differentially to EF tasks. Often researchers have measured EF using a single task that involves several component executive processes (e.g., Wisconsin Card Sorting Task [WCST]), thus making it difficult to determine which EF(s) contributed to poor task performance. This uncertainty, in turn, complicates efforts to identify EF problems in psychopathology.
Miyake and colleagues (2000) used a latent-variable approach and found that specific component EFs – shifting, updating, and inhibition – were in fact separable and contributed differentially to performance on complex tasks (WCST, Tower of Hanoi), supporting the multiple-component EF model. Miyake and colleagues selected shifting, updating, and inhibition because they were 1) the ones most often proposed in the literature as being important, 2) relatively confined functions that could be operationally defined in a narrow way (compared to other EFs such as planning), 3) easily measured by several available tasks that predominately tap these specific EFs, and 4) hypothesized to contribute significantly to the successful performance of complex EF tasks. According to their conceptualization, shifting between tasks or mental sets involves disengaging from an irrelevant task set in order to engage a new task-relevant set. Updating involves directly monitoring and manipulating the contents of working memory (as opposed to simply storing or maintaining it), such that old, irrelevant information is discarded and replaced with newer incoming information that is task-relevant. Lastly, inhibition is defined as the ability to suppress automatic or prepotent responses.

An abundance of evidence from neuropsychological and neuroimaging studies suggests that successful implementation of all three EFs involves intact function of the frontal cortex, particularly dorsolateral prefrontal cortex (DLPFC). Although DLPFC has been the brain area most focused on in the EF literature, it is clear that EFs recruit a distributed network of areas that interact with each other. Shifting and updating tasks have implicated anterior cingulate cortex (ACC) and parietal regions (e.g., superior parietal cortex; Colletta et al., 2005; Collette, Hogge, Salmon & Van der Linden, 2006; Miyake et al., 2000; Wager, Jonides, & Reading, 2004). In addition, shifting tasks recruit occipital regions, whereas updating tasks appear to involve other frontal areas, including frontopolar cortex, middle frontal gyrus (MFG), inferior frontal gyrus
(IFG), and orbitofrontal cortex (OFC; Collette et al., 2005, 2006). Tasks involving inhibition recruit right IFG, ACC, superior parietal cortex, and other parietal and temporal areas (Aron, Robbins, & Poldrack, 2004; Collette et al., 2005, 2006). Anxiety and depression have been associated with dysfunction in several nodes of these EF networks, including DLPFC, IFG, ACC, and parietal regions (for a review, see Crocker et al., 2013).

A risk factor common to anxiety and depression, trait negative affect (NA), also appears to be associated with biases and dysfunction in various cognitive processes, as well as hypoactivity in EF-related brain regions (DLPFC, ACC, parietal cortex; see Crocker et al., 2012). Trait NA is associated with a bias to interpret ambiguous information in a more negative manner (Haney, 1973) and make negative appraisals, judgments, and attributions (e.g., Clark, et al., 1994; Watson & Clark, 1984). Similar to anxiety and depression, trait NA has been associated with attention and memory biases for negative information (Derryberry & Reed, 1994; Larsen, 1992; Martin, 1985), self-reported difficulties in shifting attention (Derryberry & Rothbart, 1988), and difficulty disengaging from salient, distracting stimuli both emotional and non-emotional in nature (Bredemeier, Berenbaum, Most, & Simons, 2011; Crocker et al., 2012, in preparation; Wallace & Newman, 1998).

Research has yet to determine whether trait NA is associated with objective EF deficits in specific domains (updating, shifting, inhibition) that may contribute to cognitive dysfunction. Further, despite evidence that anxiety and depression, as well as trait NA, are characterized by EF deficits, the precise nature of these deficits remains unclear. Recent work by Warren and colleagues (in preparation) examined relationships among self-reported EF impairments in updating, shifting, and inhibition and dimensions of psychopathology (anxious apprehension, anxious arousal, and anhedonic depression). Anxious apprehension was associated only with
shifting impairments, whereas anxious arousal and anhedonic depression were associated with broad impairments in EF (shifting, updating, and inhibition). However, these relationships have not yet been examined using neuropsychological measures of EF, an important avenue of research since behavioral measures may provide information unavailable to self-report and may not be susceptible to the same biases.

Thus, one goal of the present research was to clarify the relationships among specific EF domains as measured by neuropsychological tasks and dimensions of anxiety and depression, as well as trait NA, a shared risk factor. This may help provide a mechanistic account of how specific EF deficits contribute to the cognitive dysfunction, negative biases, and emotion dysregulation observed in anxiety, depression, and trait NA. Furthermore, understanding the nature of EF deficits may inform psychological interventions, given evidence that their effectiveness depends on adequate EF (Crocker et al., 2013). It was expected that dimensions of anxiety and depression would be associated with distinct patterns of EF deficits, given differences in the nature of cognitive biases associated with them. Specifically, the present study examined whether the patterns of EF deficits (as measured by neuropsychological tasks) would replicate those observed by Warren and colleagues (as measured by self-report). In terms of trait NA, it was hypothesized that it would be associated with impairments in inhibition, given that it is a common factor shared by anxiety and depression and both have been most consistently associated with inhibition deficits.

There has been much recent attention in the literature on emotion-cognition interactions and their role in psychopathology (for a review, see Crocker et al., 2013), but relationships between certain emotional and cognitive risk factors, including trait NA and EF deficits, have yet to be considered. Thus, a second goal was to better understand the mechanisms through which
emotion-cognition interactions may contribute to development and maintenance of psychopathology by testing the hypothesis that interactions between trait NA and EFs would predict symptoms of anxiety and depression. Like Warren and colleagues (in preparation), the present study considered dimensions of anxious apprehension, anxious arousal, and anhedonic depression. An abundance of research has demonstrated that these two dimensions of anxiety are distinct yet cut across DSM-defined anxiety disorders (Engels et al., 2007; 2010; Heller, Nitschke, Etienne, & Miller, 1997; Nitschke, Heller, Imig, McDonald, & Miller, 2001; Nitschke, Heller, Palmieri, & Miller, 1999). Anxious apprehension is characterized by worry and verbal rumination (Andrews & Borkovec, 1988; Barlow, 1991), whereas anxious arousal is associated with somatic tension and sympathetic hyperarousal (Watson, Clark et al., 1995; Watson, Weber et al., 1995). Anhedonic depression is characterized by low positive affect (Clark & Watson, 1991).

Following the approach of Miyake and colleagues, three exemplar tasks primarily tapping each component EF process (updating, shifting, inhibition) were selected, and factor analyses were conducted to identify latent factors. Recent empirical work and theorizing led Miyake and Friedman (2012) to update their 3-component EF model. The inhibition factor appears to be subsumed by a general EF factor that captures what is common across all EF measures and is thought to reflect the ability to “actively maintain task goals and goal-related information and use this information to effectively bias lower-level processing” (Miyake & Friedman, 2012, pg. 11). In light of this reconceptualization, the present study examined multiple EF models when determining the best-fitting latent factor structure for the data, including Miyake and colleagues’ original and updated 3-factor models. Relationships among EF factor scores and measures of psychopathology, as well as their role in emotion-cognition interactions, were then examined in
order to better understand the mechanisms by which EFs may contribute to symptoms of anxiety and depression.

**Method**

**Participants**

Participants were recruited from a large pool of undergraduates who were enrolled in a psychology course. During group screening sessions, potential participants completed a series of questionnaires, including the Negative Affect (NA) and Positive Affect (PA) subscales of the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988). Participants were instructed to rate the extent to which they felt 10 positive and 10 negative emotions during the past few weeks. Participants received course credit for completing questionnaires and were selected to have a range of NA and PA scores to allow both categorical and dimensional analytic strategies. Specifically, participants were contacted to participate in the present study (1) if they scored at or above the 80th percentile (≥ 29) on the NA subscale of the PANAS and at or below the 50th percentile (≤ 34) on the PA subscale; (2) if they scored at or above the 80th percentile (≥ 41) on the PA subscale and at or below the 50th percentile (≤ 22) on the NA subscale; (3) if they scored at or below the 50th percentile (≤ 22 on the NA subscale and ≤ 34 on the PA subscale) on the NA and PA subscales. Percentile cutoff scores were determined using a large sample of college students (N = 600). The present investigation utilized a dimensional analytic approach.

Individuals who agreed to participate were given a laboratory tour, during which they completed various questionnaires. A total of 96 participants completed the neuropsychological test protocol (50% female, M age = 19.32, SD = 1.06).

**Neuropsychological Tasks**
The order of the neuropsychological tasks was counterbalanced across subjects by domain (inhibition, shifting, updating tasks) as well as within domain as a function of verbal versus visuospatial tasks. All tasks were administered according to a standardized protocol by individuals who completed at least a year of training in neuropsychology.

**Updating tasks**

*Keep track task.* The keep track task was adapted from Miyake et al. (2000), originally based on Yntema (1963). On each trial, participants were shown two to five target categories out of six possible (animals, colors, countries, distances, metals, and relatives) at the bottom of the computer screen. The target categories remained on the screen while individual words belonging to the six possible categories were presented serially for two seconds each. Trials ranged in length from 15 to 24 words. Participants were instructed to recall the last word from each of the target categories shown on the bottom of the computer screen and state them out loud at the end of the trial. Thus, they had to closely attend to the words in order to update their working memory representations for the specified categories. Participants performed two practice trials and then 16 task trials, recalling a total of 56 words. The dependent measure was the proportion of words recalled correctly for the task trials.

*Letter memory task.* The letter memory task was adapted from Miyake et al. (2000), originally based on Morris and Jones (1990). Each trial consisted of 9, 11, or 13 letter strings presented individually and serially on the computer screen for three seconds each. The task was to recall the last four letters presented in the list in the proper sequential order. Participants were instructed to continually rehearse out loud the last four letters by adding the most recent letter and dropping the fifth letter back and then saying the new string of four letters until the end of the list. The number of letters presented (9, 11, or 13) on each trial varied randomly so that
participants did not know how long each list was and had to continuously update their working memory representation until the end of each trial. After three practice trials, participants performed 12 task trials for a total of 48 letters recalled. The dependent measure was the proportion of letters recalled correctly.

**Spatial updating task.** The spatial updating task was developed in the laboratory (Warren, Towers, Miller, & Heller, unpublished) as a visuospatial analog of the letter memory task. Participants viewed a screen with a spatial array of 21 small boxes in which 9, 11, or 13 boxes were sequentially darkened in a random order. Participants were instructed to indicate the last four boxes that darkened in the proper sequential order using the mouse to click the boxes until the end of the trial. Similar to the letter memory task, participants had to update their working memory representations to add the most recent box and drop the fifth box back. After two practice trials, participants performed 12 task trials for a total of 48 boxes recalled (the last four boxes for each trial). The dependent measure was the proportion of boxes recalled correctly.

**Shifting tasks**

**Trail-making task.** The trail-making test from the Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan & Kramer, 2001) is a visual-motor sequencing task used to assess the ability to flexibly shift between sets (e.g., number-letter sequencing). Prior to the main switching task, participants completed two baseline conditions of simple number sequencing and simple letter sequencing. All three conditions consisted of two pages of circles containing numbers and letters. During the first baseline task, participants were instructed to connect just the numbers in sequential order. During the second baseline task, participants were instructed to connect just the letters in alphabetical order. During the switching condition, participants were instructed to switch between connecting the numbers and letters in the appropriate order (A-1-B-
2, etc.). The dependent measure was the cost of shifting between numbers and letters, computed by subtracting the average of the times to complete the simple number and letter sequencing conditions from the time to complete the switching condition.

**Plus-minus task.** The plus-minus task was adapted from Miyake et al. (2000), originally based on Jersild (1927) and Spector and Biederman (1976). Participants were presented with three lists of 30 two-digit numbers (the numbers 10-99 prerandomized without replacement). They were instructed to add one to each number for the first list, subtract one from each number for the second list, and alternate between adding one to and subtracting one from the numbers for the third list. For each list, participants wrote down their answers. Participants were told to complete each list quickly and accurately, and the time to complete each list was measured with a stopwatch. The dependent measure was the cost of shifting between the operations of addition and subtraction, computed by subtracting the average of the times to complete the addition and subtraction lists from the time to complete the alternating list.

**Verbal fluency task.** The verbal fluency task of the D-KEFS (Delis et al., 2001) was used to assess fluent productivity and shifting in the verbal domain. In the phonemic fluency condition, participants were instructed to generate words that began with a particular letter (F, A, S) as quickly as possible. In the semantic fluency condition, participants were instructed to generate words that belonged to specified categories (animals, boys’ names) as quickly as possible. In the category switching condition, participants were instructed to generate words, alternating between two different semantic categories (fruits and furniture) as quickly as possible. The dependent measure was the cost of shifting between categories, computed by subtracting letter and category fluency total number of words from switch accuracy.

**Inhibition tasks**
**Stop-signal task.** The stop-signal task was developed by van den Wildenberg and colleagues (2006) and used to measure an individual’s ability to suppress a dominant or automatic response. Participants were instructed to indicate the direction of a green arrow that appeared on a computer screen with corresponding arrow keys but withhold their response on trials in which the arrow changed from green to red (i.e., to inhibit a prepotent response). An initial block of 50 green arrow trials (i.e., go trials) was used to build up a prepotent response. The main task consisted of 48 practice trials and then 3 blocks of 80 trials in which 25% of the trials in each block were stop trials. Task instructions emphasized that the participants maintain a consistent response speed and not slow down to see if the arrow changed color. The time at which the arrow changed color was adjusted for each participant so that they were able to withhold a response on about 50% of the color-changing trials (40-60%). The inter-trial interval ranged from 750 to 1250 ms and participants were allowed up to 1000 ms to respond. Following van den Wildenberg et al. (2006), the dependent measure was the stop-signal reaction time (SSRT), calculated by subtracting the average stop-signal delay across the 3 blocks from the median of the distribution of reaction times for the correct go trials.

**Tower of London task.** The computerized version of the Tower of London (TOL) task was developed by W.K. Berg (Berg & Boyd, 2002) and customized with input from collaborators Warren, Heller, and Miller. At the beginning of each trial, participants viewed a target tower configuration at the top of the computer screen and a starting configuration at the bottom of the screen, each consisting of 3 pegs of different lengths and 3 colored balls placed on the pegs. Participants were instructed to move the colored balls across the bottom pegs with the mouse to make it look like the target configuration at the top in the fewest number of moves possible. When moving the balls, participants followed a set of rules typical for the TOL task.
(i.e., only one ball could be moved at a time, each ball had to be placed on one of the pegs, each peg had a maximum amount of balls it could hold [shortest peg = 1 ball, medium peg = 2 balls, tallest peg = 3 balls], and only the top ball could be moved if more than one ball was on a peg). Participants completed 2 practice trials and 13 task trials. The dependent measure was the time to the first move summed across all trials solved successfully, a measure commonly thought to reflect the inhibition of impulsive moves in order to deliberately plan a solution (Albert & Steinberg, 2011).

**Color-word interference task.** The color-word interference task from the D-KEFS (Delis et al., 2001) was used to assess inhibition of a prepotent verbal response. The baseline condition consisted of 50 colored squares (red, green, blue). Participants were instructed to name the colors of the squares as quickly and accurately as possible. The inhibition and inhibition/switching conditions consisted of 50 words naming colors (red, blue, green) printed in incongruent ink colors. In both conditions, participants were instructed to say the ink color the words were printed in, and not read the words, as quickly and accurately as possible. However, in the inhibition/switching condition, some of the words were printed inside boxes, and participants were instructed to read the words printed in the boxes but otherwise say the ink colors the words were printed in. The dependent measure was time to complete the inhibition/switching condition minus the time to complete the color naming condition. This measure was selected because it correlated with the dependent measures from the other two inhibition tasks, whereas the time to complete the inhibition only condition minus the time to complete the color naming condition did not.

**Questionnaires**
During a laboratory tour, participants completed the 28-item Negative Temperament scale of the General Temperament Survey (GTS-NT) to assess trait negative affect (Watson & Clark, 1993). Participants were instructed to decide whether each statement mostly described them and to rate each item as true or false. Past research suggests that the GTS-NT has excellent test-retest reliability and good convergent and discriminant validity (Watson & Clark, 1993). Internal consistency (measured using Cronbach’s alpha) for the GTS-NT in the present sample was .89.

Participants also completed measures of anxiety and depression. The 16-item Penn State Worry Questionnaire (PSWQ) was used to assess anxious apprehension or worry (Meyer, Miller, Metzger, & Borkovec, 1990; Molina & Borkovec, 1994). Participants rated how characteristic each statement was of them on a scale from 1 (“not at all typical”) to 5 (“very typical”). Participants also completed the Anxious Arousal and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (MASQ), rating how much they experienced each item during the previous week on a scale from 1 (“not at all”) to 5 (“extremely”; Watson, Clark et al., 1995; Watson, Weber, et al., 1995). The MASQ Anxious Arousal subscale (MASQ-AA) consists of 17 items, and the eight-item MASQ Anhedonic Depression subscale (MASQ-AD8) was used as it has been shown to reflect depressed mood (Nitschke, Heller, Imig, McDonald, & Miller, 2001) and to predict depressive disorders (Bredemeier et al., 2010). Past research indicates that the PSWQ and MASQ have good psychometric properties (Meyer et al., 1990; Nitschke et al., 2000; Watson, Clark et al., 1995; Watson, Weber, et al., 1995). Internal consistencies for the PSWQ, MASQ-AA, and MASQ-AD8 in the present sample were .68, .83, and .78, respectively.

**Transformations and Data Trimming**
In order to reduce skewness and kurtosis and improve normality, the neuropsychological data were transformed and trimmed following the general procedures of Miyake et al. (2000) and Friedman et al. (2008). An arcsine transformation was applied to the three proportion-correct measures (keep track, letter memory, spatial updating). For the tasks using RT measures and difference scores (trail-making, plus-minus, verbal fluency, TOL, and color-word inference), RTs for each condition were examined and trimmed such that RTs more than three standard deviations (SDs) from the mean were replaced with a value that was three SDs from the mean. These trimming procedures affected 1.04% to 4.21% of the observations for each of the measures. There were no outliers for the stop-signal task. Table 2 provides mean, standard deviation, skew, and kurtosis statistics for each measure after transformation and trimming procedures. Three subjects were missing TOL data, and one was missing color-word interference data. The directionality of the dependent measures was adjusted as needed so that larger numbers indicated better performance. Table 3 provides correlations between measures after transformations.

**Statistical analyses**

**Confirmatory factor analyses**

Multiple latent variable models were tested to examine the structure of EF. All confirmatory factor analyses were performed with the computer program Mplus 6.1 (Muthén & Muthén, 2010) using robust maximum-likelihood estimation, which is recommended for dealing with non-normality (MLM; Muthén & Muthén, 2007-2010). Model fit was evaluated using multiple fit indices: the mean-adjusted Satorra-Bentler chi-square goodness-of-fit test statistic which is robust to non-normality ($\chi^2$; Satorra & Bentler, 1988), the comparative fit index (CFI; Bentler, 1990), the Tucker-Lewis index (TLI; Tucker & Lewis, 1973), and the standardized root
mean-squared residual (SRMR). Smaller, nonsignificant $\chi^2$ values indicate that the model’s predictions do not deviate significantly from the observed pattern of the data. Following the recommendations of Hu and Bentler (1999), CFI > .95, TLI > .95, and SRMR < .08 were used as indications of good fit. The latent factors were allowed to covary freely, since there is empirical support for moderate correlations among these EF processes (e.g., Miyake et al. 2000).

The models that were examined included Miyake and colleagues’ (2000) original three-correlated-factor model involving separable shifting, updating, and inhibition factors, as well as their more recent hierarchical model in which the inhibition factor is subsumed by a common EF factor thought to reflect maintenance of task goals (Miyake & Friedman, 2012). In addition, other models examined included three, two-factor models in which two of the three EFs were assumed to be the same, as well as a one-factor model that collapsed all three EFs into a single factor.

**Regression analyses**

EF factor scores were extracted from the factor analysis with the best fit and used to explore the relationships between specific EF domains, trait NA, and measures of anxiety and depression. One person was excluded from these analyses due to missing questionnaire data, leaving $N = 95$. Hierarchical multiple regression analyses were conducted to examine whether trait NA, EF factor scores, and their interactions would significantly predict symptoms of anxiety and depression. Trait NA and EF factor scores were entered in the first step, each of the two-way interactions were entered in the second step, and the 3-way interaction was entered in the third step. Regression analyses were repeated with anxious apprehension (MASQ), anxious arousal (MASQ-AA), and anhedonic depression (MASQ-AD8) each as dependent variables (DVs). Analyses were repeated such that each 2-way interaction was entered in a separate model to
examine whether results were consistent when shared variance with the other 2-way interactions was not removed.

**Results**

**Confirmatory Factor Analyses**

Table 4 provides values for fit indices for each of the confirmatory factor analysis (CFA) models. The hierarchical factor model in which the inhibition factor is subsumed by a common EF factor with nested updating and shifting factors did not converge, indicating that this particular model is not a good fit for the data. The three-factor model with separate shifting, updating, and inhibition factors converged, although the shifting and updating factors were highly correlated \( r = .85, p < .001 \), suggesting that these factors were redundant. Additionally, both CFI and TLI fit indices equaled 1, indicating significant over-fitting of the model.

Model fit statistics indicated that a two-factor model with the updating and shifting factors combined into one factor with a separate inhibition factor provided excellent fit to the data \( (\chi^2 = 23.30, p = 0.39; \text{CFI} = .99; \text{TLI} = .98; \text{SRMR} = .05) \). All measurement weights were significant at \( p < .05 \) (see Table 5 for standardized estimates). Model fit statistics for the two alternative two-factor models tested (updating and inhibition factors combined, with a separate shifting factor; shifting and inhibition factors combined, with a separate updating factor) revealed poor model fit (significant \( \chi^2 ps < 0.01 \); both CFI < .72; TLI < .60; SRMRs = .09). Finally, a one-factor model did not fit the data well \( (\chi^2 = 51.93, p < 0.01; \text{CFI} = .71; \text{TLI} = .61; \text{SRMR} = .09) \).

**Relationships between EF, Trait NA, and Symptoms of Anxiety and Depression**

Table 6 shows the zero-order correlations between measures of EF, trait NA, and symptoms of anxiety and depression. The updating/shifting and inhibition factor scores did not
correlate with trait NA or symptoms of anxiety and depression (anxious apprehension, anxious arousal, and anhedonic depression). Regression analyses predicting each EF factor score with anxious apprehension, anxious arousal, and anhedonic depression entered simultaneously as the IVs in order to control for shared variance also revealed non-significant relationships ($p_s > .18$). Relationships remained non-significant when trait NA was added as an IV to the regression analyses ($p_s > .27$).

Table 7 summarizes the results of hierarchical multiple regression analyses in which trait NA, updating/shifting factor scores, and inhibition factor scores were entered in the first step, each of the two-way interactions were entered in the second step, and the 3-way interaction was entered in the third step to predict anxious apprehension, anxious arousal, and anhedonic depression. Table 8 summarizes the results of hierarchical multiple regression analyses in which each 2-way interaction was entered in a separate model to examine whether results were consistent when shared variance with the other 2-way interactions was not removed. Results were consistent across the two hierarchical multiple regression approaches.

As reported in Tables 7 and 8, trait NA significantly predicted symptoms of anxious apprehension, anxious arousal, anhedonic depression, but updating/shifting and inhibition factor scores did not. The interaction between trait NA and updating/shifting factor scores predicted anhedonic depression (Figure 3). Graphing this interaction showed that increased trait NA was associated with increased depression at better (indicated by -1 SD below the mean) updating/shifting ability, but more so when updating/shifting ability was worse (indicated by +1 SD above the mean). In addition, the interaction between updating/shifting factor scores and inhibition factor scores predicted anhedonic depression (Figure 4). Graphing this interaction showed that decreased updating/shifting ability (reflected in higher scores) was associated with
increased depression when inhibition ability was worse (+1 SD). Tests of simple slopes for both interactions indicated that all slopes were significant. No other interactions were significant.

**Discussion**

The present study examined relationships among specific domains of EF and dimensions of anxiety and depression, as well as trait NA, in order to test the hypothesis that EF deficits contribute to the cognitive and emotional dysfunction observed in anxiety and depression (e.g., cognitive biases, emotion dysregulation). Further, in order to better understand the mechanisms through which emotion-cognition interactions contribute to development and maintenance of psychopathology, the hypothesis that interactions between emotional and cognitive risk factors (trait NA and EF deficits) would be associated with anxiety and depression was tested. In the service of these goals, the present study addressed limitations of previous research by utilizing Miyake and colleagues’ factor-analytic approach to EF tasks in order to isolate specific EF domains of interest (inhibition, shifting, updating) from other task-relevant processes. Furthermore, the dimensions of anxious apprehension, anxious arousal, and anhedonic depression were considered, given that these dimensions cut across various DSM disorders and have distinct correlates. The present study also aimed to determine whether the pattern of EF deficits (as measured by neuropsychological tasks) would replicate those observed by Warren and colleagues, who assessed EF via self-report.

Attempts to replicate Miyake and colleagues’ initial 3-component model of inhibition, shifting, and updating or their more recent 3-factor hierarchical model involving a common EF and nested shifting and updating functions were unsuccessful. Instead, a 2-factor model with an inhibition-specific factor and a factor subsuming the updating and shifting tasks best fit the present data. There are likely numerous reasons that neither of their 3-factor models could be
replicated. Sample size may have been one factor that contributed to difficulty replicating either 3-factor model, as the present study involved 96 participants, whereas Miyake and colleagues previous work involved sample sizes ranging from 137 to 945 individuals (Friedman et al., 2008; Friedman, Miyake, Robinson, & Hewitt, 2011; Miyake et al., 2000).

Another contributing factor may be related to some of the specific tasks that were selected for the present study. Although several of the present tasks were either the same as or similar to those used by Miyake and colleagues, some tasks differed (e.g., DKEFS trail-making, DKEFS verbal fluency). These tasks were conceptualized as primarily indexing shifting, but they may involve updating and as well. For example, in order to shift back and forth between numbers and letters effectively, the trail-making test involves the maintenance of task goals in working memory while updating its contents to make sure individuals are correctly sequencing. Similarly, the verbal fluency test involves monitoring and updating working memory as individuals shift between two categories (fruits and furniture) in order to track the words they have already said to avoid repeating words (for a review, see Snyder, 2013).

Although neither of their 3-factor models was able to be replicated, a 2-factor model with inhibition and updating/shifting factors was an excellent fit to present data. Several researchers have proposed that effective goal pursuit in changing environments involves a balance between two key aspects of EF/top-down control – stability versus flexibility (e.g., Dosenbach, Fair, Cohen, Schlaggar, & Peterson, 2008; Dreisbach, 2006). More specifically, it involves the maintenance of task sets and goals in the face of distraction, while also being adaptable such that one can flexibility switch between goals in response to changing environmental demands. Dysfunction in stability can result in rigidity or perseveration, whereas dysfunction in flexibility can result in distractibility (Dreisbach, 2006). In the present study, it may be the case that the
inhibition factor represents the function that enables stability, whereas the updating/shifting factor represents the function that enables flexibility.

Contrary to hypotheses and previous research in our laboratory (Warren et al., in preparation) that utilized self-report, results indicated that inhibition and updating/shifting factor scores were not correlated with trait NA nor dimensions of anxiety and depression. These results are not consistent with a recent meta-analysis of 113 EF studies that examined individuals with major depressive disorder (MDD), which found that MDD was associated with a range of EF impairments, including deficits in inhibition, shifting, updating of working memory, planning, and verbal fluency (Snyder, 2013). Further, more severe depressive symptoms were associated with greater EF deficits, specifically in the domains of inhibition, shifting, verbal working memory, and verbal fluency, as well as on the backward digit span test and WCST. The findings have been mixed in terms of whether individuals with subclinical dysphoria exhibit EF impairments (for a review, see Snyder, 2013).

The present study examined individuals with a range of depressive symptoms who may not have had any behavioral or functional impairments associated with their symptoms. Thus, symptom levels in the present sample may not have been severe enough to be associated with deficits on neuropsychological tests. The study may have also been limited in statistical power to detect small effects, given the distribution of depressive symptoms.

In terms of anxiety and EF, researchers have attempted to draw conclusions about patterns of EF deficits in specific anxiety disorders, despite numerous inconsistent findings in the literature. For example, a meta-analysis found that obsessive-compulsive disorder was consistently associated with deficits in several EFs (e.g., inhibition, shifting, updating, working memory; Snyder, Kaiser, Warren, & Heller, in press), whereas unpublished data from the same
authors indicated that social anxiety disorder was linked only to verbal working memory impairments. Conclusions could not be drawn for other anxiety disorders (e.g., generalized anxiety disorder [GAD], specific phobia) due to an inadequate number of studies examining them. A review of the EF and posttraumatic stress disorder (PTSD) literature reported consistent “subtle” impairments in response inhibition and regulation of attention in individuals with PTSD but mixed findings for working memory, shifting, and planning deficits (Aupperle, Melrose, Stein, & Paulus, 2011). Bredemeier and Berenbaum (2013) found that worry and symptoms of GAD were associated with working memory deficits during an n-back task but not during an OSPAN task.

Mixed findings and inconsistencies in the anxiety literature may be due in part to high rates of comorbidity among anxiety disorders themselves and also with depressive disorders, an issue that is typically not considered in individual studies. In addition, the dimensions of anxious apprehension and anxious arousal are rarely distinguished, even though evidence shows that they have distinct cognitive, emotional, and neural correlates and have different contributions to various anxiety disorders (e.g., Engels et al., 2007). Although the present study did distinguish these dimensional aspects of anxiety, neither showed specific relationships with inhibition or updating/shifting abilities. As with depression, the lack of findings regarding relationships between EFs and dimensions of anxiety may be due in part to levels of symptom severity and sample size.

In addition, task difficulty may have played a role specifically for anxiety. The attentional control theory asserts that small or nonexistent effects of anxiety on task performance are due to anxiety impairing task efficiency more so than effectiveness because of the recruitment of compensatory strategies (e.g., increased effort and/or resource use) by anxious individuals.
Anxiety may lead to impaired performance when task demands/difficulty increase and compensatory strategies break down and are no longer adequate (see Eysenck et al., 2007). Thus, it may be the case that the tasks used in the present study were not demanding enough to disrupt compensatory strategies and lead to impaired performance. Inducing a negative state in those prone to anxious apprehension or anxious arousal may be necessary in order to observe executive dysfunction, given research showing that only the interaction of state and trait NA and not either alone was associated with impaired performance on an EF task (Hur et al., under review).

Although there were no significant relationships among aspects of EF and anxiety, depression, and trait NA, present results highlight the importance of considering interactions between constructs in order to shed light on how facets of emotion and cognition can contribute to psychopathology. Specifically, trait NA interacted with updating/shifting factor scores to predict symptoms of anhedonic depression. Increased trait NA was associated with increased depression at worse updating/shifting abilities (see Figure 3). As mentioned above, individuals high in trait NA tend to experience negative moods, demonstrate biases for attending to and recalling negative information, and make negative appraisals and judgments. Deficits in shifting and updating of working memory likely exacerbate these predispositions, given evidence that effective emotion-regulation strategies (e.g., modifying attention to and interpretation of emotional information) rely on intact EFs. For example, studies have shown that the same neural mechanisms that implement executive processes (e.g., DLPFC, ACC) are recruited when adaptive emotion regulation techniques are employed (for a review, see Ochsner & Gross, 2005). In addition, better working memory abilities have been linked to enhanced self-regulatory behavior (Hofmann, Gschwendner, Friese, Wiers, & Schmitt, 2008) and reductions in the experience and expression of emotion after reappraisal of emotional material (Schmeichel,
Volokhov, & Deamaree, 2008). Thus, current results suggest that problems updating working memory and flexibly shifting from ineffective regulation strategies to more adaptive ones in individuals high in trait NA contribute to the development of more severe depressive symptoms.

Further, the present study lends some empirical support to the hypothesis that difficulties shifting attention away from negative thoughts and material and updating working memory to remove task-irrelevant emotional information in those with a tendency to be in negative moods leads to persistent rumination and prolonged NA, key characteristics of depression. It is also likely that initial deficits in updating and shifting contribute to problems ignoring distracting information (both emotional and non-emotional in nature) and persisting in goal achievement. Over time, this may result in frustration, general negativity, and pessimism regarding one’s abilities and could facilitate the onset of depressive symptoms.

The interaction between updating/shifting factor scores and inhibition factor scores also predicted symptoms of depression. Specifically, decreased updating/shifting ability was associated with increased depression when inhibition ability was worse (see Figure 4). Although several researchers have implicated dysfunction in specific EFs (e.g., inhibition, updating of working memory, shifting) in the development and maintenance of depression (e.g., Joormann & Gotlib, 2010), the potential interactive effects of these deficits does not appear to have been considered previously. Results suggest that difficulty inhibiting task-irrelevant thoughts and distractions in conjunction with problems removing them from working memory once they have entered in order to shift back to current tasks and goals is associated with greater symptoms of depression. Conversely, being better at inhibiting task-irrelevant thoughts and distracters appears to buffer against depression in individuals with deficits in updating/shifting. Better inhibition likely means that these individual do not need to rely as much on updating working memory to
remove irrelevant information or frequently shifting back to the task at hand in order to persevere in goal achievement.

The present study offers insight into potential mechanisms through which certain risk factors, specifically trait NA and EF deficits, contribute to psychopathology. Further, it supports the importance of considering interactions between facets of emotion and cognition when examining how various risk factors may lead to the development and maintenance of depression. Finally, it provides additional evidence that EF is not a unitary construct and that considering the interactive effects of distinct aspects of EF is likely an important avenue for further research. Present results have implications for the prevention and treatment of psychopathology, suggesting that exploring ways to improve EFs (e.g., EF training) is likely to be fruitful, particularly in those who are at risk for depression due to high levels of trait NA.
CHAPTER 4

THE EFFECTS OF MOTIVATIONAL CONTEXT ON NEURAL CORRELATES OF TRAIT NEGATIVE AFFECT DURING AN EMOTIONAL TASK

Research has demonstrated that trait negative affect (NA) and motivational dysfunction are key risk factors associated with increased likelihood of developing anxiety and depression, as well as vulnerability to comorbidity and relapse (Clark, 2005; Gotlib & Joorman, 2010; Krueger, Caspi, Moffitt, Silva, & McGee, 1996). However, little is known about the mechanisms by which they confer vulnerability. The present study investigated the neural mechanisms associated with trait NA in a context involving motivational and emotional processes.

In addition to sharing a core feature of trait NA, anxiety and depression are both characterized by motivational dysfunction, which includes enhanced avoidance behavior and heightened sensitivity and responsivity to negative stimuli and cues signaling potential punishment (Davidson, 2002; Pizzagalli, Dillon, Bogdan, & Holmes, 2011). Individuals with anxiety and depression also exhibit dysfunction responding to rewarding stimuli, though in distinct ways. Depression is associated with hyporesponsivity, whereas anxiety is associated with hypersensitivity to rewarding stimuli (Bar Haim et al., 2009; Guyer et al., 2006; 2012; Pizzagalli, Dillon, Bogdan, & Holmes, 2011). Anxiety and depression are also characterized by dysfunction in brain areas that implement motivation-related processes (Crocker et al., 2013), including dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex (ACC), striatum, nucleus accumbens (NAcc), and orbitofrontal cortex (OFC).

Like anxiety and depression, trait NA has been associated with increased response to negative information. For example, trait NA predicted self-reported distress after negative emotional imagery, negative emotional slides, and negative film clips (Gross, Sutton, &
Ketelaar, 1998; Larsen & Ketelaar, 1991; Zelenski & Larsen, 1999). Furthermore, trait NA has been linked to increased anxiety in anticipation of punishment (Carver & White, 1994), enhanced avoidance behavior (Larsen & Ketelaar, 1989; Watson, Clark, & Harkness, 1994), and abnormal behavioral and physiological responses to negative feedback (Derryberry & Reed, 1994; Hajcak, McDonald, & Simons, 2004; Luu, Collins, & Tucker, 2000). Robinson and colleagues (2010) found that post-error slowing of responses after receiving feedback about mistakes was associated with reduced accuracy in high trait NA individuals, suggesting that trait NA is linked to deficits in appropriately regulating behavior after negative feedback. There is some evidence that high trait NA is related to enhanced sensitivity to positive incentives in addition to negative incentives. Ball and Zuckerman (1990) found that trait NA was associated with higher self-reported reward and punishment expectancy. However, little research has explored the relationship between trait NA and reward processes, and apparently no work has focused on neural mechanisms associated with motivational processing in individuals high in trait NA.

Trait NA has also been associated with attentional control problems, such that individuals high in trait NA had difficulties attending to and maintaining task goals when distracting, emotionally-arousing information was present (Crocker et al., 2012). This work suggests that trait NA is associated with maladaptive emotion-cognition interactions. However, the literature has yet to address the role of motivation in these interactions in individuals high in trait NA. Deficits in executive function (EF) including attentional control may contribute to maladaptive motivational processing, such that goals are not appropriately selected based on their predicted value, behaviors are not initiated to achieve selected goals, and goal-directed action is not maintained across time, particularly in the face of emotional distraction.
Studies examining motivation-cognition interactions in healthy individuals have found that manipulating the motivational context via reward and punishment incentives enhances cognitive processes and performance on a range of tasks involving EF, including attention tasks (Engelmann, Damaraju, Padmala, & Pessoa, 2009; Engelmann & Pessoa, 2007), response-conflict tasks (Padmala & Pessoa; 2011), set-shifting tasks (Savine, Beck, Edwards, Chiew, & Braver, 2010), and working memory tasks (Jimura, Locke, & Braver; 2010; Pochon et al., 2002; Taylor et al., 2004). These behavioral results were accompanied by increased activity in brain regions involved in task-relevant and reward-related processing (e.g., DLFPC, OFC, striatum). Small and colleagues (2005) found that, although reward and punishment trials both led to faster target detection than neutral trials, they were associated with dissociable neural mechanisms. Reward trials were associated with increased activity in OFC, whereas punishment trials were associated with increased activity in dorsal ACC (dACC) and insula. Both incentive types were associated with enhanced activity in visual cortex and posterior cingulate cortex (PCC).

The effects of manipulating reward and punishment incentives have also been examined in individuals with depression and anxiety during cognitive tasks. In a study utilizing a verbal memory task, individuals with depression failed to adaptively alter their performance in either rewarding or punishing contexts in order to optimize their chances of winning money, whereas individuals without depression successfully improved their performance (Henriques & Davidson, 2000). This effect was also observed in depressed adolescents; they did not exhibit the incentive-related performance enhancement healthy adolescents showed during an inhibition task (Jazbec, McClure, Hardin, Pine, & Ernst, 2005). Similarly, high trait anxious individuals failed to improve their performance during a demanding EF task when monetary incentives were offered,
whereas low trait anxious individuals demonstrated the expected enhanced performance for the reward condition over the no-reward condition (Eysenck, 1985).

The failure of motivational contexts to appropriately modulate EFs in individuals with anxiety and depression is likely related to dysfunction in brain networks associated with incentive processing and task-relevant processing. Further, it is likely that networks involved in implementing motivation-related processes and EFs fail to communicate appropriately in order to integrate various functions and successfully execute goal-driven behavior. Studies of healthy individuals have implicated several “hub” regions that link the two networks and integrate incentive-related processes and EFs: DLPFC, ACC, and PCC (Jimura, et al., 2010; Locke & Braver, 2008; Pessoa, 2009; Pessoa & Engelmann, 2010; Pochon et al., 2002; Taylor et al., 2004), all three of which have been associated with dysfunction in anxiety and depression (Bench, Friston, Brown, Frackowiak, & Dolan, 1993; Bishop, 2008; Engels et al., 2007, 2010; Herrington et al., 2010; Mayberg, 1997; Mayberg et al., 1999).

Despite accumulating research examining motivation in anxiety and depression, it appears that studies have not yet addressed the neural mechanisms associated with motivational processing in individuals high in trait NA. This research is necessary in order to understand the mechanisms through which trait NA and motivational dysfunction contribute to the development and maintenance of anxiety and depression. Thus, one goal of the present study was to determine how trait NA modulates brain activation in response to cues indicating the potential for reward and punishment. Given some evidence that trait NA is associated with increased sensitivity to both positive and negative incentives (Ball & Zuckerman, 1990), it was hypothesized that reward and punishment cues would be associated with hyperactivity in regions involved in implementing motivation-related processes (e.g., OFC, dACC, striatum). Further, it was
hypothesized that reward and punishment cues would be associated with distinct patterns of brain activity. Specifically, it was predicted that reward cues would be associated with increased activity in OFC, striatum, and NAcc. Anxiety and depression have been associated with opposite patterns of striatal and NAcc activation in anticipation of reward (increased activity for anxiety, decreased activity for depression). Hypotheses regarding trait NA and reward anticipation were more in line with anxiety findings, given that depression findings were thought to reflect anhedonia specifically, a facet of depression distinct from trait NA. In terms of punishment cues, it was predicted that trait NA would be associated with increased activity in striatum as well regions that have been implicated in threat-related processing, including PFC, dACC, and parietal cortex.

A second goal of the present study was to examine how motivational contexts may modulate EFs/cognitive processes in individuals high in trait NA when distracting emotional information is present. Previous research indicates that trait NA is associated with problematic emotion-cognition interactions in the context of highly arousing, emotional information (Crocker et al., 2012) but has not examined how motivation may modulate this interaction. A consideration of interactions between various psychological processes in trait NA will enhance our understanding of how trait NA contributes to the emotional, motivational, and cognitive symptoms observed in anxiety and depressive disorders. It was hypothesized that trait NA would be associated with dysfunction in networks/regions that implement emotion, cognition, and motivational processes. Based on previous work, it was hypothesized that trait NA will be associated with dysfunction in brain areas involved in top-down attentional control, including DLPFC, ACC, and parietal cortex (Crocker et al., 2013), as well as regions that integrate incentive-related processes with EFs, (e.g., PCC). Further, it was expected that rewarding and punishing contexts would differentially
modulate activity in these regions, though neither context would be associated with facilitated reaction time (RT) for individuals high in trait NA. Specifically, it was hypothesized that trait NA would be associated with hypoactivation in regions involved in top-down control and incentive processing during rewarding contexts, reflecting difficulty effectively integrating these processes to achieve rewarding outcomes. In contrast, it was expected that trait NA would be associated with hyperactivation in similar areas during punishing contexts, reflecting attempts to overcome anxiety about potential punishment in order to appropriately perform the task.

The present study utilized a locally modified version of the monetary incentive delay (MID) task (modified from Dillon et al., 2008; Knutson, Westdorp, Kaiser & Hommer, 2000; Knutson, Fong, Adams, Varner & Hommer, 2001; Knutson, Fong, Bennett, Adams, & Hommer, 2003) that included both reward and punishment cues as well as distracting emotional content during the subsequent response period. Because the task required attentional control in order to ignore the task-irrelevant, emotional information, it permitted the examination of how NA modulates brain networks involved in integrating attentional control with emotion and incentive-related processes. Crocker et al. (2012) demonstrated that trait and state NA are associated with distinct neural mechanisms. Thus, state NA was included in present analyses in order to identify the unique contributions of trait NA.

**Method**

**Participants**

Participants were recruited from a large pool of undergraduates who were enrolled in a psychology course. During group screening sessions, potential laboratory participants completed a series of questionnaires, including the Negative Affect (NA) and Positive Affect (PA) subscales of the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen,
Participants received course credit for completing questionnaires and were selected to have a range of NA and PA scores to allow both categorical and dimensional analytic strategies. Specifically, participants were contacted to participate in the present study (1) if they scored at or above the 80th percentile (≥ 29) on the NA subscale of the PANAS and at or below the 50th percentile (≤ 34) on the PA subscale; (2) if they scored at or above the 80th percentile (≥ 41) on the PA subscale and at or below the 50th percentile (≤ 22) on the NA subscale; or (3) if they scored at or below the 50th percentile (≤ 22 on the NA subscale and ≤ 34 on the PA subscale) on the NA and PA subscales. Percentile cutoff scores were determined using a large sample of college students (N = 600). The present investigation utilized a dimensional analytic approach.

Individuals who agreed to participate were given a laboratory tour, during which they completed various questionnaires and were screened for a history of serious brain injury, abnormal hearing or vision, claustrophobia, left-handedness, metal in their body, pregnancy, and nonnative English-speaking. A total of 98 participants completed the fMRI protocol. Data were not retained for participants who did not have two usable blocks of functional data. Blocks of data were deemed unusable if participants: (1) moved more than one voxel (2.13 mm) between adjacent fMRI volumes, (2) committed errors on 13% or more of the trials, or (3) had poor registration. These exclusions left a total of 85 participants included in present analyses (49% female, M age = 19.27, SD = 1.04), 81 of which overlapped with participants in study 2 (which examined performance on neuropsychological measures and did not address fMRI).

Questionnaires

During a laboratory tour, participants completed the 28-item Negative Temperament scale of the General Temperament Survey (GTS-NT) to assess trait negative affect (Watson & Clark, 1993). Participants were instructed to decide whether each statement mostly described
them and to rate each item as 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.” Past research suggests that the GTS-NT has excellent test-retest reliability and good convergent and discriminant validity (Watson & Clark, 1993). State NA was measured using the Negative Affect scale from the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988), which was administered immediately before participants performed the task during fMRI. Participants indicated the extent to which they were feeling each of 10 negative emotions (e.g., afraid, nervous, irritable, upset) right then on a scale from 1 (“very slightly or not at all”) to 5 (“extremely”). The PANAS also has been found to have good psychometric properties (Watson & Clark, 1999; Watson et al., 1988). Internal consistencies (measured using Cronbach’s alpha) for the GTS-NT and PANAS NA scales in the present sample were .90 and .83, respectively.

**Stimuli and Experimental Design**

Participants completed a modified version of the MID task during separate fMRI and EEG neuroimaging sessions. A session consisting of a battery of neuropsychological measures was always completed between fMRI and EEG sessions, but the order of neuroimaging sessions was counterbalanced across participants. Participants were paid for their participation in each part of the study. Only fMRI data from the modified MID task are discussed here.

The modified MID task (Figure 5) consisted of a practice block containing 24 trials followed by 3 blocks of 48 trials, yielding a total of 144 task trials. Task timing was determined using a custom genetic algorithm (based in part on Wager & Nichols, 2003). Trials consist of three phases: anticipation, action, and feedback. During the anticipation phase at the beginning of each trial, a cue appeared on the screen for 1.5 s signaling one of four potential monetary
Outcomes: (1) potential reward or punishment, (2) potential reward only, (3) potential punishment only, or (4) neither reward nor punishment possible. After cue offset, a fixation dot appeared for a variable interstimulus interval (ISI; 3, 4.5, 6, 7.5 s) before the action phase. During this phase, a target emotion word (positive, neutral, or negative) appeared on the screen and changed color after a variable amount of time (see below). The emotion word remained on the screen for a total of 1.5 s and was followed by a variable ISI (3, 4.5, 6, 7.5 s), after which the feedback period (1.5 s) indicated to participants if they had won or lost money, if there was no money change, or if they had made an error. Errors were defined as pressing a button before the target word appeared, pressing a button other than the designated button (which was under the right index finger during the target period), or failing to press a button in response to the target. Trials were separated by variable offset-to-onset intertrial intervals (ITI; 3, 4.5, 6, and 7.5 s).

Participants were instructed that the monetary outcome of each trial was based on how fast they pressed the button after the emotion word appeared on the screen. Success was defined as pressing the button before the word changed color. The time before the word changed color varied in a way that facilitated obtaining an equal number of successful and failed trails. To accomplish this, a distribution of the participant’s reaction times (RTs) from the previous block (the practice block in the case of the first task block) was used to identify RTs corresponding to the 15th and 85th percentiles. On trials biased by the software to facilitate successful performance, the word changed color after the amount of time corresponding approximately to the 85th percentile of the RT distribution. On trials biased toward failure, the word changed color after the amount of time corresponding approximately to the 15th percentile. Word color change times varied around those two set points in order to mask the predetermined nature of the trials.
Performance on reward and punishment trials was associated with a monetary reward or loss ranging from $1.80 to $2.35 (mean: $2.08). Cues did not indicate reward/loss magnitudes, only the potential for reward or punishment. The specific reward or loss value was provided during the feedback period on each trial. Participants were informed that they could receive a bonus task block (in which they could win but not lose money) at the end of the three task blocks, contingent upon their overall task performance. The term “overall task performance” was left vague and was determined by the experimenter as generally performing the task as instructed. The possibility of the bonus block served to maintain motivation across all trials, including those where no money was at stake. All participants exhibited appropriate behavior and earned the bonus block. Participants did not receive feedback about cumulative earnings during either the main task or bonus blocks.

The 144 emotion words used as target stimuli in the task were selected from the Affective Norms for English Words (ANEW) set (see Table 9; Bradley & Lang, 1999). Forty-eight positive (e.g., joy, fun), 48 neutral (e.g., glass, statue), and 48 negative (e.g., war, cancer) words were selected on the basis of established norms for arousal, valence, word length, and frequency of use in the English language (Bradley & Lang, 1999). Positive and negative words were selected to be highly arousing, whereas neutral words were selected to be low in arousal value. Positive and negative words had equivalent arousal levels ($t (47) = .24, p = .81$), and each of these arousal levels was higher than the arousal level of neutral words ($t (47) = 23.32, p < .001$, and $t (47) = 24.73, p < .001$, respectively). All three word types were equated on word length and frequency of use.

Stimuli for the modified MID task were displayed using back projection, and presentation and RT measurement were controlled by locally written Matlab code (version 2009a, The
MathWorks, Natick, MA) using Psychophysics Toolbox extensions (version 2.54; Brainard, 1997; Pelli, 1997).

**fMRI Data Acquisition**

MR data were acquired using a Siemens Magnetom Trio 3T scanner. While participants performed the practice block, two MPRAGE structural sequences were acquired (192 axial slices with isotropic spatial resolution of 0.9 mm) for registering each participant’s functional data to standard space. Upon completion of structural scans and the practice block, gradient field maps were collected to correct for geometric distortions in the functional data caused by magnetic field inhomogeneities (Jezzard & Balaban, 1995). A set of 331 functional imaging volumes was collected during each of the three task blocks using a Siemens gradient echo-planar imaging sequence (repetition time [TR] 3000 ms, echo time [TE] 25 ms, flip angle 90°, field of view [FOV] 256 mm) for a total of 993 functional volumes. Each volume consisted of 50 oblique axial slices (slice thickness 2.40 mm, in-plane voxel size: 2.13 mm x 2.13 mm) acquired parallel to the plane containing the anterior and posterior commissures. Three volumes at the beginning of each task block were discarded to allow the scanner to reach steady state.

**fMRI Data Reduction and Analysis**

Functional neuroimaging data processing and statistical analysis were implemented primarily using the FMRI Expert Analysis Tool (FEAT), version 6.00, part of the FSL analysis package (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/). Functional data for each participant were motion-corrected using rigid-body registration implemented in FSL’s linear registration tool, MCFLIRT (Jenkinson, Bannister, Brady, & Smith, 2002). This process registers the functional volume at each time point to the volume corresponding to the middle time point. The data were then
temporally filtered with a 1/90 Hz high-pass filter, spatially smoothed using a 3-D Gaussian kernel (FWHM = 5 mm), slice-time-corrected, and fieldmap-corrected.

Level 1 regression analyses were then performed for each block of each participant’s preprocessed functional time series data using FMRIB’s Improved Linear Model with autocorrelation correction (FILM; Woolrich et al., 2001). Statistical maps were generated via multiple regression computed for each intracerebral voxel. A separate predictor was entered for each experimental condition and convolved with a gamma function to approximate the temporal course of the blood-oxygen-level-dependent (BOLD) hemodynamic response function. The task consisted of four cue types (reward/no reward, punishment/no punishment, reward/punishment, and no reward/no punishment), three word types (positive, negative, neutral), and two feedback types (success and failure). Predictors relevant to present hypotheses include the four cue conditions (modeling the cue period) and the twelve word conditions (combining each of the three word types with each of the four cue types to model the word period). The feedback period was modeled but will not be discussed further. Three additional predictors of no interest were included to account for performance errors, one modeling each period of the task (cue, emotion word, feedback). Each predictor yielded a per-voxel effect-size parameter estimate (β) map representing the magnitude of activation.

To create comparisons of interest, β values were contrasted for the relevant parameters. For the cue period, two orthogonal contrasts were created: (1) a reward comparison was created by contrasting cues signaling the potential to win money with cues signaling no potential to win money and (2) a punishment comparison was created by contrasting cues signaling the potential to lose money with cues signaling no potential to lose money. Three orthogonal contrasts were created for the word period: (1) an arousal comparison (average of positive and negative words
vs. neutral words), (2) an arousal by reward cue interaction, and (3) an arousal by punishment cue interaction. The two interaction contrasts tested whether the effect of arousing words was modulated by motivational context.

Functional activation maps for each participant were then warped into a common stereotaxic space (the 2009 Montreal Neurological Institute [MNI] 152 symmetrical 1 mm x 1 mm x 1 mm template, resampled to 2 mm x 2 mm x 2 mm; Fonov et al., 2009) using FMRIB’s Non-Linear Image Registration Tool (FNIRT; Andersson et al., 2007). Level 2 analyses were then performed to combine the three task blocks within each participant. An average of each contrast across the three task blocks for each participant was computed using a fixed-effects model.

Group inferential statistical analyses of brain activation were carried out using FLAME (FMRIB’s Local Analysis of Mixed Effects). To identify brain regions that were uniquely moderated by trait NA, scores for trait and state NA were simultaneously entered as independent variables (IVs) into third-level regression analyses that were used to predict contrasts of interest. Each third-level regression analysis produced a $\beta$ map of interest reflecting the unique variance associated with trait NA.

Two-tailed $t$ tests were conducted on the $\beta$ maps for trait NA and then converted to $z$ scores to determine the significance of the $\beta$s. On the basis of a priori hypotheses, several masks based on the Harvard-Oxford probabilistic atlas available in FSL were used to limit the number of voxels under consideration in order to help control family-wise error rate. These masks were of (1) bilateral frontal and cingulate cortices, (2) bilateral parietal cortex, (3) bilateral NAcc, (4) bilateral caudate, (5) bilateral putamen, and (6) bilateral amygdala. To correct for multiple comparisons, Monte Carlo simulations were carried out via AFNI’s AlphaSim (Ward, 2000)
program to estimate the appropriate cluster size for each mask at an overall family-wise error rate of $p \leq .05$ with a minimum individual voxel $z$ threshold of 2.05.

**Behavioral Performance**

Average RTs were calculated for high-arousing and neutral words as a function of preceding cue type for each participant. A motivational context (reward, punishment) $\times$ word type (high-arousing, neutral) repeated measures analysis of variance (ANOVA) was conducted with trait NA entered as a covariate of interest, along with state NA as a covariate not of interest. ANOVAs were conducted using IBM SPSS Statistics version 22.

**Results**

**Behavioral Performance**

The analysis of RT revealed an interaction between word type and trait NA, $F(1,82) = 3.91, p = .05$. To examine the nature of this interaction, participants were divided into those above and below the median for trait NA. As seen in Figure 6, individuals low in trait NA exhibited longer RTs for high-arousing than neutral words ($t(40) = 2.21, p < .05$), whereas individuals high in trait NA exhibited no difference in RT for high-arousing and neutral words ($t(40) = -1.30, p = .20$). No other interactions with trait NA were significant.

**Activation for Reward Cue Contrast Associated with Trait NA**

Table 10 lists the three brain regions in which activation related to the reward cue contrast was correlated with trait NA (2 regions positively correlated, 1 region negatively correlated). Higher levels of trait NA were associated with more activation in left posterior DFPFC (middle frontal gyrus [MFG]/precentral gyrus) and left parietal operculum cortex/supramarginal gyrus (see Figure 7). Higher trait NA was associated with less brain activation in left anterior-middle OFC.
Activation for Punishment Cue Contrast Associated with Trait NA

Table 10 lists the eight brain regions in which activation related to the punishment cue contrast was correlated negatively with trait NA. Higher trait NA was associated with less brain activation in right MFG, medial frontal cortex, bilateral frontal pole, right anterior-middle OFC, PCC, precuneus, precuneus/intracalcarine cortex, and left NAcc (see Figure 7).

Activation for Arousal Word Contrast Associated with Trait NA

Table 11 lists the six brain regions in which activation related to the arousal word contrast was correlated positively with trait NA. Higher trait NA was associated with more brain activation in left MFG/frontal pole/superior frontal gyrus (SFG), right MFG/frontal pole, PCC, left superior parietal lobule/postcentral gyrus/supramarginal gyrus, precuneus, and left caudate (see Figure 8).

Activation for Arousal x Reward Word Contrast Associated with Trait NA

Table 11 lists the five brain regions in which activation related to the interaction of word arousal level and rewarding context was correlated positively with trait NA. Higher trait NA was associated with increased activation in left MFG/frontal pole/SFG, right MFG/frontal pole/SFG, PCC/posterior dACC, left supramarginal gyrus/angular gyrus/parietal operculum cortex, and precuneus (see Figure 8). Importantly, the left and right MFG regions overlapped with the regions showing a main effect for the arousal contrast. To examine the nature of the interaction in left and right MFG, participants were divided into those above and below the median on trait NA, and brain activation was plotted for high-arousing and neutral words in rewarding and non-rewarding contexts (see Figure 9). For both left and right MFG, individuals high in trait NA exhibited greater activation for high-arousing than neutral words in rewarding contexts but no difference was observed across word types in non-rewarding contexts. For individuals low in
trait NA, greater activation was observed for high-arousing versus neutral words in non-rewarding contexts in left MFG, whereas greater activation for neutral than high-arousing words was observed in rewarding contexts in right MFG.

**Activation for Arousal x Punishment Word Contrast Associated with Trait NA**

There were no regions in which activation significantly correlated with trait NA for the interaction between word arousal level and punishing contexts.

**Discussion**

The present study examined how trait NA modulates brain regions involved in integrating emotional, motivational, and cognitive processes in order to identify mechanisms through which trait NA may contribute to symptoms of anxiety and depression. Specifically, the anticipation of potential reward and punishment was examined, as well as the influence of these incentivizing contexts on brain activation during an action phase involving distracting emotional words. As hypothesized, reward and punishment cues were not associated with facilitated behavioral performance in individuals high in trait NA, though they were associated with distinct patterns of brain activation. Hypotheses that reward anticipation would be associated with increased activation in OFC, striatum, and NAcc, whereas punishment anticipation would be associated with increased activation in striatum, PFC, dACC, and parietal cortex were not supported.

Instead, trait NA was associated with increased activation during the anticipation of potential reward in posterior DLPFC and parietal cortex, as well as decreased activation in OFC. The cascade-of-control model asserts that posterior DLPFC imposes a top-down attentional set to maintain task goals and ignore distracting information and biases processing of task-relevant information via signals to parietal regions (Banich, 2009). Similarly, Corbetta and colleagues (2008) proposed that posterior DLPFC is part of a top-down attention network that uses previous
experiences and information about current goals and expectations to select the most behaviorally relevant stimuli. Crocker et al. (2012; in preparation) found that trait NA was associated with decreased activation in posterior DLPFC during attentional control tasks involving both task-irrelevant emotional and non-emotional information. Those results suggested that individuals high in trait NA have difficulty engaging top-down attentional control to maintain task goals in the presence of distracting information.

In the present study, emotional information was not pertinent to the task at hand. Increased activation in posterior DLPFC during the anticipation phase may reflect attempts by individuals high in trait NA to exert proactive control in preparation for responding to the distracting emotional nature of the upcoming word in order to perform the task successfully and obtain rewarding outcomes. They may have learned to implement this compensatory strategy after previous experiences with distracting emotional information that was challenging for them to ignore, especially in contexts where incentives were high enough for them to do so.

Braver (2012, pg. 106) described proactive control as “the sustained and anticipatory maintenance of goal-relevant information within lateral PFC to enable optimal cognitive performance.” Braver et al. (2007) proposed that cues signaling the potential for reward enhance activity in this region prior to imperative stimuli in order to prevent task interference. Thus, individuals high in trait NA may be ramping up more proactive control than those low in trait NA when incentives are present in order to achieve equivalent behavioral outcomes, suggesting they are less cognitively efficient. This interpretation is supported by the fact that trait NA was not associated with facilitated RT for reward versus no reward trials.

Increased activation in posterior DLPFC was found only for reward anticipation, not for punishment anticipation. Individuals high in trait NA are generally pessimistic, and reward cues
may activate expectations that achieving positive outcomes is difficult (though possible) for them. Thus, in contexts with the potential for reward/positive outcomes, these individuals may have developed a strategy to overcome their difficulties ignoring irrelevant information in order to persist in goal achievement. However, in contexts where punishment/negative outcomes are possible, they may believe that failure is very likely and therefore do not attempt to exert effortful control to avoid it.

Trait NA was also associated with increased activation in left parietal operculum cortex/supramarginal gyrus during the anticipation of potential reward. Rushworth and colleagues (2001a; 2001b; 2003) asserted that left supramarginal gyrus plays a key role in “motor attention” and may update representations of the relative positions of body parts in preparation for making motor movements, particularly hand movements. Increased activation in this region in individuals high in trait NA may reflect enhanced preparation for making fast motor responses to the upcoming target words in order to try to obtain rewarding outcomes. Although inconclusive without formal connectivity analyses, posterior DLPFC may be providing input to this parietal region to enhance its preparatory activity as part of a proactive attentional strategy, a possibility supported by a positive correlation between the two regions ($r = .51, p \leq .001$).

Trait NA was associated with decreased activation in left anterior-middle OFC during the anticipation of potential reward, contrary to expectations that it would be associated with increased activation, thought to reflect enhanced sensitivity to reward. OFC is involved in determining and maintaining the motivational value of stimuli and communicating this information to DLPFC to use in planning and implementing goal-directed behavior (for a review, see Spielberg et al., 2012a). Less OFC activation in individuals high in trait NA may reflect
difficulty assessing and/or maintaining the hedonic value of stimuli. Further, OFC may not be effectively interacting with DLPFC in order for motivational information to be integrated with executive processes important for goal achievement. In fact, activation in posterior DLPFC was uncorrelated with OFC activation ($r = .02, p = .88$). Future research should examine whether trait NA disrupts connectivity between DLPFC and OFC and whether this contributes to the decreased approach-related behavior that is observed in depression.

In contrast to the anticipation of potential reward, trait NA was associated with decreased activation in several regions during the anticipation of potential punishment, including right MFG, medial frontal cortex, bilateral frontal pole, right anterior-middle OFC, PCC, precuneus, and left NAcc. These results are contrary to the hypothesis that trait NA would be associated with hyperactivation in regions involved in incentive and threat processing (striatum, PFC, dACC, parietal cortex) in response to punishment cues. It is possible that enhanced sensitivity to both reward and punishment is reflected by increased activation in regions involved in incentive processing during the actual receipt of rewards and punishments, rather than during their anticipation.

Several of the areas associated with punishment anticipation overlap with nodes of a network that implements avoidance-related goals (Spielberg et al., 2012a). The right MFG region found in the present study overlaps with a region that has been associated with avoidance temperament, or the tendency to be sensitive to and attempt to avoid negative outcomes (Spielberg et al., 2011). This region is active during cues signaling the potential for negative outcomes and appears to integrate this motivation-related information with EF in order to plan goal-directed behavior (Spielberg, Heller, & Miller, 2013). Spielberg et al. (2011) proposed that this region biases activity in other regions to impose a “motivational set” in order to avoid
punishment. Further, this region showed enhanced connectivity to various regions, including OFC, PCC/precuneus, and NAcc, during the maintenance of goal pursuit in the face of distracting information (Spielberg et al., 2012a). In the present study, decreased activation in a network that implements avoidance-related goal pursuit during the anticipation of potential punishment in individuals high in trait NA suggests that they have difficulty engaging adaptive avoidance strategies when faced with potentially negative outcomes. DLPFC may not be receiving information from other areas in order to appropriately integrate motivational and executive processes and/or is not effectively biasing them for upcoming action.

As mentioned previously, trait NA is associated with pessimism and a generally negative outlook on life. When faced with potential punishment, individuals high in trait NA may feel that, no matter what they do, bad outcomes are very likely, so developing plans and increasing preparatory action to try to avoid them is futile. Over time, a failure to implement adaptive avoidance strategies may lead to an increase in either perceived or actual punishment, which could contribute to the development of an enhanced sensitivity to punishment/negative stimuli and/or hopelessness, both of which are associated with psychopathology.

In addition to the regions overlapping with an avoidance network, trait NA was associated with less activation in bilateral frontal pole and medial frontal cortex. Frontal pole has been associated with shifting focus from internal (e.g., self-generate thoughts) to external stimuli, (Badre & D’Esposito, 2009; Burgess et al., 2007). Thus, trait NA appears to be associated with difficulty switching from internal processing (potentially dwelling on past mistakes and failures) to coordinating a rapid motor response in order to avoid punishment. Medial frontal cortex has been associated with the valence and intensity of emotional outcomes, particularly positive ones, implicating it in reward-guided decision-making (Grabenhorst & Rolls, 2011). Less activation
for individuals high in trait NA in this region may reflect less expectation of positive outcomes (successfully avoiding punishment).

During the action phase, individuals high in trait NA appeared to be engaged in processing the meaning of the high-arousing, emotional words, as evidenced by increased activation in bilateral MFG, PCC, left superior parietal lobule, precuneus, and left caudate for the arousal contrast. This is consistent with previous work showing that individuals high in trait NA have difficulty ignoring emotional information (Crocker et al., 2012). Notably, activation in left and right MFG was qualified by an interaction between arousal and rewarding contexts (see below). Individuals low in trait NA exhibited longer RTs for high-arousing words relative to neutral words, whereas individuals high in trait NA did not show a difference in RT as a function of word type. Thus, increased activation in these regions for high-arousing words in conjunction with equivalent behavioral performance across word types suggests that individual high in trait NA engaged a compensatory strategy in order to perform the task successfully.

Importantly, the present study examined how emotional processing was modulated by the motivational context. It was expected that rewarding and punishing contexts would differentially modulate activity in regions that integrate incentive-related processes with EFs (e.g., DLPFC, PCC). However, the interaction of word arousal level and punishing context was not associated with activation in any region. In contrast, rewarding contexts did modulate activation in various regions involved in top-down control and integrating EFs and motivation-related processes for high-arousing versus neutral words, including bilateral MFG, PCC/posterior dACC, left supramarginal gyrus, and precuneus. Of particular interest are areas that also showed a main effect of arousal (left and right MFG), given that one aim of the study was to examine whether the degree to which individuals high in trait NA attend to and are distracted by high-arousing
stimuli depends on the motivational context. Previous studies have found that lateral PFC (MFG) is sensitive to manipulations of motivational value and cognitive control, suggesting that it integrates motivational and executive functions (for a review, see Chiew & Braver, 2011). Supporting this assertion, regions in left and right MFG (overlapping with those in the present study) correlated with trait approach and avoidance motivation during tasks requiring EF to ignore non-emotional and emotionally arousing distracters (Spielberg et al., 2011; 2012b). Spielberg and colleagues (2011) suggested that these regions implement a motivational set that biases processing to be congruent with goals.

Examining the pattern of the interaction between word arousal level and rewarding context in left and right MFG for individuals high in trait NA indicated that high-arousing words were associated with increased activation in rewarding contexts; this difference was not observed in non-rewarding contexts (see Figure 9). For individuals low in trait NA, left MFG was associated with increased activation for high-arousing words in non-rewarding contexts only. For right MFG, increased activation was observed for neutral words in rewarding contexts only. This pattern of activation in bilateral MFG indicates individuals high in trait NA were engaging more top-down control in rewarding contexts to ignore the distracting nature of the arousing words in order to maintain task goals and minimize its impact on performance. This was not the case when incentives were not present. Thus, rewarding contexts appeared to enhance cognitive control in these individuals.

Considering these results for the action phase of the task together with those from the anticipation phase, it appears that individuals high in trait NA recruit compensatory mechanisms both proactively and reactively in order to maintain task goals in the face of distraction and approach potentially rewarding outcomes. Proactive control strategies alone may not suffice,
leading to the need to recruit bilateral MFG during the action phase. Future research would benefit from investigating whether these compensatory strategies break down during more difficult or cognitively demanding tasks. It may be the case that, for individuals who experience repeated difficulty implementing them in challenging environments, approach motivation decreases and leads to the development of depression. In contrast, it appears that during the anticipation of punishment, individuals high in trait NA have difficulty engaging adaptive avoidance strategies. Future research should examine whether decreased activation in a network that implements avoidance-related goal pursuit when facing potential punishment is associated with the failure to effectively use negative feedback to improve subsequent performance that is observed in depression. Finally, future research should determine whether any of the patterns of brain activation observed in the present study are markers of risk for anxiety and depression.
CHAPTER 5
INTEGRATIVE DISCUSSION

The primary goal of the present series of studies was to clarify psychological and biological mechanisms through which trait NA may lead to the development and maintenance of anxiety and depressive disorders. It is well established that trait NA is a risk factor for these disorders but little is known about how it fosters them. The present research tested the overarching hypothesis that one possible route is through triggering maladaptive cognitive and motivational processing that ultimately leads to some of the deficits that are characteristic of these mood disorders. Maladaptive processing associated with trait NA may not yet manifest in alterations in behavior because individuals high in trait NA have likely developed compensatory strategies that are effective, at least in the short term. Thus, neuroimaging methods were used to reveal the nature of possible dysfunction and associated neural mechanisms, given that this information would likely not be attainable via behavioral measures or self-report.

Overall, the findings across the studies reported here revealed that trait NA is associated with dysfunction in networks that implement attentional control, particularly top-down control, as well as networks that integrate motivational processes with EF. Thus, individuals high in trait NA have broad attentional control problems across contexts involving distraction, and these problems appear to be even more pronounced and likely harder to overcome when these individuals are experiencing negative moods. They also appear to have difficulty implementing appropriate strategies in order to avoid punishment. However, trait NA is not associated with impairments in behavioral performance on tasks involving EF, suggesting that they are able to recruit compensatory strategies, particularly when given incentive to do so (e.g., when reward is possible). Specific findings and implications are reviewed in more detail below.
The first study examined the hypothesis that trait NA fosters risk through a deficit in attentional control that is present across attentionally demanding contexts, regardless of whether distracting information is emotional in nature or not. Present results in conjunction with those from Crocker and colleagues (2012) supported this hypothesis; trait NA was associated with dysfunction in a top-down attention network during tasks involving both emotional and non-emotional task-irrelevant information. Further, the top-down attentional system in these individuals fails to bias a separate attentional system involved in the detection of behaviorally-relevant stimuli, suggesting that they also have difficulty reorienting attention to goal-consistent information once they are distracted. Thus, individuals high in trait NA appear to have difficulty maintaining task goals and persisting in goal achievement when salient distracters are present in the environment. Such difficulties may contribute to the development of core features of trait NA, including negatively-biased attention, pessimism, and poor self-esteem.

This study also highlighted the importance of considering the interaction between trait and state NA. Co-occurring high levels of trait and state NA were associated with decreased activity in several regions distinct from those that were correlated with trait NA alone, including a separate region in left DLPFC. Thus, the interaction of trait and state NA is associated with additional difficulty recruiting regions involved in maintaining a top-down, goal-congruent task set while dealing with distractions and switching attention back to focus on pertinent stimuli. Importantly, neither trait NA nor its interaction with state NA were associated with behavioral interference. The combination of dysfunction in brain networks and intact behavioral performance suggests disrupted efficiency of processing but not effectiveness of performance. This is consistent with the assertion that high trait NA is associated with inefficient executive function (Robinson & Tamir, 2005).
The second study tested the hypothesis that trait NA, as well as anxiety and depression, would be associated with objective EF impairments, but results did not support this hypothesis. There being no relationship between trait NA and performance on EF tasks involving updating/shifting and inhibition functions is consistent with the lack of impaired behavioral performance associated with trait NA in the first study. However, study 2 did support the hypothesis that interactions between emotional and cognitive risk factors, specifically trait NA and EF deficits, would be associated with symptoms of psychopathology. Specifically, increased levels of trait NA and impairments in updating/shifting were associated with increased levels of depression. It appears that individuals who tend to experience negative moods and also have difficulty updating their working memory to remove irrelevant emotional information and shift attention away from negative thoughts and material will develop some key features of depression, including persistent rumination, maladaptive emotion regulation abilities, and cognitive biases and dysfunction.

Taking these results together with the results from study 1, it seems that individuals high in trait NA experience difficulty performing tasks involving EFs, but they can effectively compensate to persist in goal achievement, at least in some contexts. However, when these compensatory strategies break down, dysfunction in regions involved in attentional control may ultimately manifest in observable problems during tasks involving updating and shifting and put one at greater risk for depressive symptoms. Study 2 also showed that the interaction of deficits in updating/shifting and inhibition functions were associated with greater symptoms of depression, highlighting the importance of distinguishing EF domains and considering their interactive effects.
Studies 1 and 2 offered insight into the potential mechanisms through which cognitive and emotional risk factors contribute to anxiety and depression. Study 3 extended this research by examining how trait NA modulates brain regions involved in integrating motivational processes with emotional and cognitive processes, given that motivational dysfunction is present in both anxiety and depression and also likely contributes to their development and maintenance. Results again support the assertion that individuals high in trait NA are able to recruit compensatory mechanisms proactively and reactively in particular contexts (e.g., Braver, 2012), specifically when reward is possible, in order to maintain task goals when distraction is present. However, when punishment is possible, they appear to have problems proactively engaging adaptive avoidance strategies in order to avoid potentially aversive outcomes. Results from both study 1 and 3 indicate that trait NA is associated with problematic connectivity between DLPFC and OFC, suggesting that individuals high in trait NA have difficulty integrating motivational information and top-down control to execute goal-directed behavior. This is consistent with dysfunctional interactions between cognitive and motivational processes observed in disorders which share a core feature of trait NA (depression and anxiety).

Future research would benefit from formal connectivity analyses to test this hypothesis. The field is moving toward a network approach in order to better understand interactions among cognitive, emotional, and motivational processes, which involve a complex array of operations engaging distributed networks of brain regions. It is likely that trait NA is associated with dysfunction in various networks. The pattern of problematic connectivity in individuals high in trait NA may be a better and more reliable marker of risk than the level of activation in particular regions. Research would also benefit from examining connectivity among regions across a variety of tasks and contexts recruiting a range of cognitive, emotional, and motivational
processes, as it is likely that patterns of connectivity depend on the nature of tasks and their
difficulty. Such research may also clarify the circumstances in which behavioral problems
manifest. Finally, future work should include longitudinal studies in order to address the
direction of causality for cognitive and emotional risk factors for anxiety and depression. This
work would benefit from a lifespan approach, given evidence that EF declines with age (De Luca
et al., 2003; MacPherson, Phillips, & Sala, 2002) and trait NA increases in older adults
(Steunenberg, Twisk, Beekman, Deeg, & Kerkhof, 2005; Teachman, 2006).

This line of research has the potential to lead to the identification of early markers of risk
for anxiety and depression that may not necessarily be observable via behavior or accessible
through self-report. This may foster the development of prevention strategies aimed at
addressing dysfunctional processing in those individuals identified as being at risk in order to
reduce the occurrence of these disorders. Further, understanding the nature of cognitive and
motivational dysfunction associated with trait NA and the mechanisms through which they
contribute to the onset and maintenance of anxiety and depression may also aid in the refinement
of interventions that will target them more effectively, potentially interrupting a downward spiral
toward more severe symptoms and comorbid conditions or recurrence. Evidence is beginning to
accrue that specific EFs can improve with training (e.g., attentional control, switching, updating
working memory; Dahlin, Neely, Larsson, Backman, & Nyberg, 2008; Erickson et al., 2007;
Olesen, Westerberg, & Klingberg, 2004) and that interventions targeting EFs are associated with
improvements in psychological symptoms (Amir, Beard, Burns, & Bomyea, 2009; Chambers,
Lo, & Allen, 2008). In fact, training-related increases in working memory abilities have been
linked to improvements in a range of cognitive skills (Brehmer, Westerberg, & Backman, 2012;
Chein & Morrison, 2010; Jaeggi, Buschkuehl, Jonides, & Shah, 2011), enhanced structure and
function of key brain regions (Olesen et al., 2004; Takeuchi et al., 2010), and improvements in quality of life (Vogt et al., 2009).

Other psychological interventions have also been linked to improvements in EFs and concomitant decreases in psychological symptoms. Specifically, mindfulness-based stress reduction (MBSR) is an effective intervention for treating a range of psychological disorders, including anxiety and depression (Hofmann, Sawyer, Witt, & Oh, 2010). The improvement in symptoms associated with mindfulness has been attributed to the fact that this technique utilizes cognitive strategies that involve strengthening EFs, including sustaining attention, flexibly switching the focus of attention, and inhibiting elaborative processing (Bishop et al., 2004). Interventions targeting specific EFs, particularly updating and shifting, would likely be beneficial for individuals high in trait NA who have not yet developed severe psychopathology.

Even current treatments that have been established as effective would benefit from further research on addressing problematic relationships among cognition, emotion, and motivation, given that many individuals drop out of treatment prematurely, do not fully recover after receiving therapy, and/or relapse after therapy has completed (Kendall & Sugarman, 1997; DeRubeis et al., 1999). It may be advantageous for interventions to initially target and enhance EF and motivational processing, as the efficacy of most empirically-supported psychotherapies depends on adequate EF (Mohlman & Gorman, 2005) and sufficient motivation to engage in treatment. For example, cognitive behavioral therapy often involves reappraisal, hypothesis generation, and self-monitoring, which all require EF (Gotlib & Joorman, 2010; Mohlman & Gorman, 2005). Boosting EF initially can not only help with the engagement of challenging treatment techniques, but may help individuals overcome motivation-related problems, including evaluating and selecting goals based on their anticipated benefits, implementing appropriate
approach and avoidance strategies to achieve these goals, and engaging in adaptive coping behaviors.

Further, it appears that trait NA moderates the effectiveness of interventions. One review found that higher levels of trait NA predicted worse treatment outcomes, particularly when assessed long-term (Mulder, 2002). Quilty and colleagues (2008) found that patients with MDD who responded to both medication and psychotherapy had lower levels of trait NA than nonresponders. Thus, it may be important to target trait NA prior to implementing certain treatments aimed at improving other key factors that maintain anxiety and depression. There is some evidence that pharmacotherapy, specifically selective serotonin reuptake inhibitors, may be particularly useful in reducing trait NA (Quilty, Meusel, & Bagby, 2008; Tang et al., 2008). In addition, Jackson and colleagues (2012) found that cognitive training was associated with changes in personality. Although their study examined inductive reasoning training and the personality trait of openness to experience, it suggests that a promising line of future research will be to determine whether particular psychological interventions will lead to reductions in trait NA. Evidence suggest that personality traits can change over time, particularly when individuals are exposed to certain situations/environments consistently (Roberts, 2009). More research is clearly needed in order to effectively target trait NA in individuals at risk in order to reduce the occurrence, duration, and chance of relapse of anxiety and depression.
## Tables and Figures

Table 1

**Brain Areas Moderated by Trait and State Negative Affect and Their Interaction**

<table>
<thead>
<tr>
<th>Region</th>
<th>Cluster Size mm³</th>
<th>Mean z value</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trait Negative Affect</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L middle frontal gyrus/precentral gyrus (posterior DLPFC)</td>
<td>2,243</td>
<td>-2.59</td>
<td>-45 8 36</td>
</tr>
<tr>
<td>R middle frontal gyrus/precentral gyrus (posterior DLPFC)</td>
<td>782</td>
<td>-2.38</td>
<td>39 8 37</td>
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<td>-21 57 27</td>
</tr>
<tr>
<td>Anterior-medial orbitofrontal cortex</td>
<td>1,007</td>
<td>2.32</td>
<td>4 51 -21</td>
</tr>
<tr>
<td>L postcentral gyrus</td>
<td>1,070</td>
<td>2.50</td>
<td>-65 -12 22</td>
</tr>
<tr>
<td><strong>Trait x State Negative Affect</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L middle frontal gyrus</td>
<td>880</td>
<td>-2.30</td>
<td>-41 22 29</td>
</tr>
<tr>
<td>L lateral frontal pole</td>
<td>1,219</td>
<td>-2.42</td>
<td>-17 57 29</td>
</tr>
<tr>
<td>L supramarginal gyrus</td>
<td>1,230</td>
<td>-2.34</td>
<td>-61 -33 41</td>
</tr>
</tbody>
</table>

*Note. L = left. R = right. Location = Coordinates are for the center-of-mass in MNI152 2009a symmetrical space*
Table 2.

**Descriptive Statistics for the Nine Executive Function Tasks**

<table>
<thead>
<tr>
<th>Task</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Skewness</th>
<th>Kurtosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keep track</td>
<td>96</td>
<td>.92</td>
<td>.13</td>
<td>.11</td>
<td>.13</td>
</tr>
<tr>
<td>Letter memory</td>
<td>96</td>
<td>.83</td>
<td>.28</td>
<td>.14</td>
<td>-.03</td>
</tr>
<tr>
<td>Spatial updating</td>
<td>96</td>
<td>.83</td>
<td>.26</td>
<td>-.09</td>
<td>-.75</td>
</tr>
<tr>
<td>Trail-making</td>
<td>96</td>
<td>28.97 s</td>
<td>14.39</td>
<td>-1.31</td>
<td>2.22</td>
</tr>
<tr>
<td>Plus-minus</td>
<td>96</td>
<td>14.03 s</td>
<td>10.44</td>
<td>-0.91</td>
<td>0.37</td>
</tr>
<tr>
<td>Verbal Fluency</td>
<td>96</td>
<td>79.26</td>
<td>16.87</td>
<td>0.43</td>
<td>0.13</td>
</tr>
<tr>
<td>Stop-signal</td>
<td>96</td>
<td>218.63 ms</td>
<td>30.89</td>
<td>-0.11</td>
<td>0.17</td>
</tr>
<tr>
<td>Tower of London</td>
<td>93</td>
<td>86.53 s</td>
<td>50.78</td>
<td>1.5</td>
<td>1.92</td>
</tr>
<tr>
<td>Color-word interference</td>
<td>95</td>
<td>21.94 s</td>
<td>7.77</td>
<td>0.12</td>
<td>0.43</td>
</tr>
</tbody>
</table>
Table 3.

*Correlations for the Executive Function Tasks*

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Keep track</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Letter memory</td>
<td>.35*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Spatial updating</td>
<td>.39*</td>
<td>.40*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Trail-making</td>
<td>.16</td>
<td>.23*</td>
<td>.17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Plus-minus</td>
<td>.12</td>
<td>.36*</td>
<td>.36*</td>
<td>.20*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Verbal Fluency</td>
<td>.40*</td>
<td>.33*</td>
<td>.27*</td>
<td>.34*</td>
<td>.21*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Stop-signal</td>
<td>-.03</td>
<td>.11</td>
<td>-.16</td>
<td>-.00</td>
<td>-.16</td>
<td>-.17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Tower of London</td>
<td>.03</td>
<td>.20</td>
<td>-.05</td>
<td>.00</td>
<td>.02</td>
<td>.10</td>
<td>.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Color-word interference</td>
<td>.08</td>
<td>.04</td>
<td>.11</td>
<td>.11</td>
<td>-.26*</td>
<td>.16</td>
<td>.26*</td>
<td>.19</td>
<td></td>
</tr>
</tbody>
</table>

*p ≤ .05
Table 4.

*Fit Indices for Confirmatory Factor Analysis Models*

<table>
<thead>
<tr>
<th>Model</th>
<th>df</th>
<th>$\chi^2$</th>
<th>p</th>
<th>CFI</th>
<th>TLI</th>
<th>SRMR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Three-factor models</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Separate Inhibition, Updating, &amp; Shifting</td>
<td>19</td>
<td>18.93</td>
<td>0.46</td>
<td>1</td>
<td>1.00</td>
<td>0.04</td>
</tr>
<tr>
<td>2) Common EF with nested Updating &amp; Shifting</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Two-factor models</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) Updating-Shifting collapsed &amp; Inhibition</td>
<td>23</td>
<td>24.30</td>
<td>0.39</td>
<td>0.99</td>
<td>0.98</td>
<td>0.05</td>
</tr>
<tr>
<td>4) Updating-Inhibition collapsed &amp; Shifting</td>
<td>26</td>
<td>51.27</td>
<td>0.00</td>
<td>0.71</td>
<td>0.59</td>
<td>0.09</td>
</tr>
<tr>
<td>5) Shifting-Inhibition collapsed &amp; Updating</td>
<td>26</td>
<td>51.34</td>
<td>0.00</td>
<td>0.70</td>
<td>0.59</td>
<td>0.09</td>
</tr>
<tr>
<td>6) <strong>One-factor model</strong></td>
<td>27</td>
<td>51.93</td>
<td>0.00</td>
<td>0.71</td>
<td>0.61</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Note: $\chi^2$ that were not significant at the .05 level indicate models with reasonable fits. Values above .95 for comparative fit index (CFI) and Tucker-Lewis index (TLI) and below .08 for standardized root mean-squared residual (SRMR) indicate good fit.
Table 5.

*Standardized Regression Coefficients for Confirmatory Factor Analysis*

<table>
<thead>
<tr>
<th></th>
<th>Shifting/Updating</th>
<th>Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Keep track</td>
<td>.60</td>
<td>-</td>
</tr>
<tr>
<td>2. Letter memory</td>
<td>.62</td>
<td>-</td>
</tr>
<tr>
<td>3. Spatial updating</td>
<td>.59</td>
<td>-</td>
</tr>
<tr>
<td>4. Trail-making</td>
<td>.39</td>
<td>-</td>
</tr>
<tr>
<td>5. Plus-minus</td>
<td>.70</td>
<td>-</td>
</tr>
<tr>
<td>6. Verbal Fluency</td>
<td>.56</td>
<td>-</td>
</tr>
<tr>
<td>7. Stop-signal</td>
<td>-</td>
<td>.36</td>
</tr>
<tr>
<td>8. Tower of London</td>
<td>-</td>
<td>.32</td>
</tr>
<tr>
<td>9. Color-word interference</td>
<td>-</td>
<td>.60</td>
</tr>
</tbody>
</table>

Interfactor correlation:
- Inhibition .22

Note: N = 96. All measurement weights were significant at \( p < .05 \). For the correlation between inhibition and shifting/updating factors, \( p = .32 \).
Table 6.

Correlations Between Measures of Executive Function, Trait Negative Affect, and Psychopathology

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Updating/shifting factor score</td>
<td></td>
<td>-.02</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Inhibition factor score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Trait negative affect</td>
<td>.12</td>
<td>.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Anxious apprehension</td>
<td>.13</td>
<td>.03</td>
<td>.84*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Anxious arousal</td>
<td>.10</td>
<td>.10</td>
<td>.43*</td>
<td>.30*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Anhedonic depression</td>
<td>-.01</td>
<td>.14</td>
<td>.63*</td>
<td>.53*</td>
<td>.40*</td>
<td></td>
</tr>
</tbody>
</table>

*p ≤ .05
Table 7.

Summary of a Single Hierarchical Multiple Regression Analysis Predicting Symptoms of Anxiety and Depression

<table>
<thead>
<tr>
<th></th>
<th>Anxious Apprehension</th>
<th>Anxious Arousal</th>
<th>Anhedonic Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$</td>
<td>$\Delta R^2$</td>
<td>$\beta$</td>
</tr>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait negative affect (NA)</td>
<td>.84**</td>
<td>.70**</td>
<td>.41**</td>
</tr>
<tr>
<td>Updating/shifting factor score</td>
<td>.01</td>
<td>.06</td>
<td></td>
</tr>
<tr>
<td>Inhibition factor score</td>
<td>-0.02</td>
<td>.08</td>
<td></td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait NA x updating/shifting</td>
<td>-0.12</td>
<td>.00</td>
<td>-0.11</td>
</tr>
<tr>
<td>Trait NA x inhibition</td>
<td>-0.19</td>
<td>.17</td>
<td></td>
</tr>
<tr>
<td>Updating/shifting x inhibition</td>
<td>.07</td>
<td>.32</td>
<td></td>
</tr>
<tr>
<td><strong>Step 3</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait NA x updating/shifting x inhibition</td>
<td>-1.06</td>
<td>.00</td>
<td>1.17</td>
</tr>
</tbody>
</table>

*p ≤ .05, ** p ≤ .01
Table 8.

Summary of Separate Hierarchical Multiple Regression Analyses Predicting Symptoms of Anxiety and Depression

<table>
<thead>
<tr>
<th>Step</th>
<th>Anxious Apprehension</th>
<th>Anxious Arousal</th>
<th>Anhedonic Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$</td>
<td>$\Delta R^2$</td>
<td>$\beta$</td>
</tr>
<tr>
<td>Step 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait negative affect (NA)</td>
<td>.83**</td>
<td>.70**</td>
<td>.43**</td>
</tr>
<tr>
<td>Updating/shifting factor score</td>
<td>.03</td>
<td>.05</td>
<td>-.08</td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait NA x updating/shifting</td>
<td>-.14</td>
<td>.00</td>
<td>-.10</td>
</tr>
<tr>
<td>Step 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait negative affect (NA)</td>
<td>.84**</td>
<td>.70**</td>
<td>.42**</td>
</tr>
<tr>
<td>Inhibition factor score</td>
<td>-.02</td>
<td>.08</td>
<td>.10</td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait NA x inhibition</td>
<td>-.13</td>
<td>.00</td>
<td>.32</td>
</tr>
<tr>
<td>Step 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Updating/shifting factor score</td>
<td>.12</td>
<td>.02</td>
<td>.11</td>
</tr>
<tr>
<td>Inhibition factor score</td>
<td>.03</td>
<td>.10</td>
<td>.14</td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Updating/shifting X inhibition</td>
<td>.86</td>
<td>.03</td>
<td>.76</td>
</tr>
<tr>
<td>Step 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait NA x updating/shifting x inhibition</td>
<td>-1.06</td>
<td>.00</td>
<td>1.17</td>
</tr>
</tbody>
</table>

*p ≤ .05, ** p ≤ .01
<table>
<thead>
<tr>
<th></th>
<th>Positive words</th>
<th>Neutral words</th>
<th>Negative words</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average arousal</td>
<td>6.59</td>
<td>3.73</td>
<td>6.56</td>
</tr>
<tr>
<td>Average valence</td>
<td>7.80</td>
<td>5.23</td>
<td>2.49</td>
</tr>
<tr>
<td>Average frequency</td>
<td>51.50</td>
<td>51.81</td>
<td>51.98</td>
</tr>
<tr>
<td>Average word length</td>
<td>5.38</td>
<td>5.33</td>
<td>5.38</td>
</tr>
</tbody>
</table>

*Note:* Word stimuli were selected from the Affective Norms for English Words (ANEW) set (Bradley & Lang, 1999). Arousal and valence data from the ANEW set are measured on a scale ranging from 1 to 9, with 9 corresponding to the most arousing and pleasant ratings, respectively. Frequency information was obtained from Toglia and Battig (1978).
Table 10

*Brain Areas Moderated by Trait Negative Affect During the Cue Period*

<table>
<thead>
<tr>
<th>Region</th>
<th>Cluster Size mm$^3$</th>
<th>Mean z value</th>
<th>Location</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reward</strong></td>
<td></td>
<td></td>
<td>X</td>
<td>Y</td>
</tr>
<tr>
<td>L middle frontal gyrus/precentral gyrus (posterior DLPFC)$^a$</td>
<td>190</td>
<td>2.41</td>
<td>-47</td>
<td>8</td>
</tr>
<tr>
<td>L parietal operculum cortex/supramarginal gyrus$^b$</td>
<td>156</td>
<td>2.52</td>
<td>-54</td>
<td>-32</td>
</tr>
<tr>
<td>L anterior-middle orbitofrontal cortex$^a$</td>
<td>97</td>
<td>-2.70</td>
<td>-24</td>
<td>57</td>
</tr>
<tr>
<td><strong>Punishment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R middle frontal gyrus$^a$</td>
<td>272</td>
<td>-2.42</td>
<td>36</td>
<td>26</td>
</tr>
<tr>
<td>Medial frontal cortex$^a$</td>
<td>1,187</td>
<td>-2.67</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td>Bilateral frontal pole$^a$</td>
<td>285</td>
<td>-2.44</td>
<td>-5</td>
<td>59</td>
</tr>
<tr>
<td>R anterior-middle orbitofrontal cortex$^a$</td>
<td>323</td>
<td>-2.42</td>
<td>24</td>
<td>61</td>
</tr>
</tbody>
</table>
Table 10 (cont.)

<table>
<thead>
<tr>
<th>Structure</th>
<th>Z</th>
<th>Peak</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior cingulate cortex&lt;sup&gt;a&lt;/sup&gt;</td>
<td>566</td>
<td>-2.38</td>
<td>1</td>
<td>-40</td>
<td>29</td>
</tr>
<tr>
<td>Precuneus&lt;sup&gt;b&lt;/sup&gt;</td>
<td>575</td>
<td>-2.38</td>
<td>1</td>
<td>-65</td>
<td>43</td>
</tr>
<tr>
<td>Precuneus/intracalcarine cortex&lt;sup&gt;b&lt;/sup&gt;</td>
<td>464</td>
<td>-2.40</td>
<td>-3</td>
<td>-60</td>
<td>16</td>
</tr>
<tr>
<td>L nucleus accumbens&lt;sup&gt;c&lt;/sup&gt;</td>
<td>28</td>
<td>-2.32</td>
<td>-8</td>
<td>12</td>
<td>-5</td>
</tr>
</tbody>
</table>

Note. L = left. R = right. Location = Coordinates are for the center-of-mass in MNI152 2009a symmetrical space. <sup>a</sup> = Correction for only frontal/cingulate cortex voxels. <sup>b</sup> = Correction for only parietal cortex voxels. <sup>c</sup> = Correction for only nucleus accumbens.
Table 11

*Brain Areas Moderated by Trait Negative Affect During the Word Period*

<table>
<thead>
<tr>
<th>Region</th>
<th>Cluster Size mm³</th>
<th>Mean z value</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td><strong>Arousal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L middle frontal gyrus/frontal pole/superior</td>
<td>392</td>
<td>2.45</td>
<td>-27</td>
</tr>
<tr>
<td>frontal gyrus¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R middle frontal gyrus/frontal pole¹</td>
<td>272</td>
<td>2.43</td>
<td>34</td>
</tr>
<tr>
<td>Posterior cingulate cortex¹</td>
<td>181</td>
<td>2.34</td>
<td>1</td>
</tr>
<tr>
<td>L superior parietal lobule/postcentral gyrus/</td>
<td>272</td>
<td>2.32</td>
<td>-44</td>
</tr>
<tr>
<td>supramarginal gyrus¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precuneus²</td>
<td>214</td>
<td>2.40</td>
<td>-3</td>
</tr>
<tr>
<td>L caudate²</td>
<td>47</td>
<td>2.29</td>
<td>-14</td>
</tr>
<tr>
<td><strong>Arousal X Reward</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R middle frontal gyrus/frontal pole/superior</td>
<td>426</td>
<td>2.37</td>
<td>28</td>
</tr>
<tr>
<td>frontal gyrus¹</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 11 (cont.)

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>Z-score</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>MNI152 2009a Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>L middle frontal gyrus/frontal pole/superior frontal gyrus&lt;sup&gt;a&lt;/sup&gt;</td>
<td>142</td>
<td>2.55</td>
<td>-25</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>Posterior cingulate cortex/posterior dorsal anterior cingulate cortex&lt;sup&gt;a&lt;/sup&gt;</td>
<td>177</td>
<td>2.35</td>
<td>2</td>
<td>-18</td>
<td>42</td>
</tr>
<tr>
<td>L supramarginal gyrus/angular gyrus/parietal operculum cortex&lt;sup&gt;b&lt;/sup&gt;</td>
<td>254</td>
<td>2.42</td>
<td>-59</td>
<td>-41</td>
<td>24</td>
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<tr>
<td>Precuneus&lt;sup&gt;b&lt;/sup&gt;</td>
<td>681</td>
<td>2.51</td>
<td>-1</td>
<td>-61</td>
<td>20</td>
</tr>
</tbody>
</table>

*Note.* L = left. R = right. Location = Coordinates are for the center-of-mass in MNI152 2009a symmetrical space. <sup>a</sup> = Correction for only frontal/cingulate cortex voxels. <sup>b</sup> = Correction for only parietal cortex voxels. <sup>c</sup> = Correction for only caudate voxels.
Figure 1. Areas uniquely associated with either trait or state negative affect (NA) during attentional control task. Blue = decreased brain activation associated with trait NA (panels A-E). Red = increased brain activation associated with state NA (panels F-H). L = Left.
Figure 2. Brain areas associated with the interaction between trait and state negative affect (NA) during attentional control task. Blue = Less activation. L = Left. Graphing the two-way interaction for each region shows that trait NA’s relationship with these brain areas depends on the level of co-occurring state NA, such that increased trait NA is associated with decreased activation in all of these areas at high levels of state NA.
Figure 3. Graph of the interaction between trait negative affect and updating/shifting factor scores predicting depression. Note that for graphing purposes, higher updating/shifting factor scores indicate worse ability, main effects were not removed.
Figure 4. Graph of the interaction between updating/shifting factor scores and inhibition factor scores predicting depression. Note that for graphing purposes, higher factor scores indicate worse ability, main effects were not removed.
Figure 5. Sequence of the custom Monetary Incentive Delay. A cue appears first, indicating the potential for reward and/or punishment and is followed by a fixation dot. The target word then appears indicating that the participant should press the button. The target word changes color and is replaced by a box indicating that feedback will appear shortly. Feedback is then presented and followed by a box indicating that a new trial will start soon.
Figure 6. Reaction times for high-arousing and neutral words for individuals high and low in trait negative affect (NA). Error bars represent 1 standard error.
Figure 7. Panels A-C: Regions moderated by trait negative affect (NA) for reward vs. no reward cue contrast. Panels D-I: Regions moderated by trait NA for punishment vs. no punishment cue contrast. Orange = positive correlations with trait NA. Blue = negative correlations with trait NA. L = left. X and Z = coordinates in MNI 2009a space.
Figure 8. Panels A-D: Regions moderated by trait negative affect (NA) for high arousing vs. neutral word contrast. Panels E-G: Regions moderated by trait NA for reward x arousal word contrast. Orange = positive correlations with trait NA. L = left. X and Z = coordinates in MNI 2009a space.
Figure 9. fMRI interaction between arousal level and rewarding contexts for individuals high and low in trait negative affect (NA). A = left middle frontal gyrus. B = right middle frontal gyrus. Error bars represent 1 standard error.
REFERENCES


![](https://via.placeholder.com/150)


