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Cognitive conflict adaptation in generalized anxiety disorder

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A R T I C L E   I N F O

Article history:
Received 7 May 2013
Accepted 26 August 2013
Available online 1 September 2013

Keywords:
Anxiety
Generalized anxiety disorder
Cognitive control
Conflict adaptation
Event-related potential
N2
Anterior cingulate (ACC)

A B S T R A C T

Individuals with generalized anxiety disorder (GAD) display poor emotional conflict adaptation, a cognitive control process requiring the adjustment of performance based on previous-trial conflict. It is unclear whether GAD-related conflict adaptation difficulties are present during tasks without emotionally-salient stimuli. We examined conflict adaptation using the N2 component of the event-related potential (ERP) and behavioral responses on a Flanker task from 35 individuals with GAD and 35 controls. Groups did not differ on conflict adaptation accuracy: individuals with GAD also displayed intact RT conflict adaptation. In contrast, individuals with GAD showed decreased amplitude N2 principal component for conflict adaptation. Correlations showed increased anxiety and depressive symptoms were associated with longer RT conflict adaptation effects and lower ERP amplitudes, but not when separated by group. We conclude that individuals with GAD show reduced conflict-related component processes that may be influenced by compensatory activity, even in the absence of emotionally-salient stimuli.

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1. Introduction

There is an increasing focus on the role of cognitive and emotional control regulation processes on the mechanisms underlying psychiatric disorders. Understanding the nature of these processes may be useful in differentiating between disorders with similar pathophysiology and in understanding the mechanisms that contribute to psychopathology. Specifically, in generalized anxiety disorder (GAD) studies suggest that poor ability to detect emotional conflict and subsequently alter behavior may underlie dysfunctional emotion regulation behaviors and may be tied to altered attention and inhibitory control mechanisms (Etkin, Prater, Hoef, Menon, & Schatzberg, 2010). However, the preponderance of research to date has focused on the influence of emotional conflict on cognitive processing (i.e., when there are conflicting emotional stimuli). Due to the absence of research on cognitive control functioning in anxiety without emotional stimuli, it is unclear whether findings are due to generalized decrements in cognitive control or whether dysregulation is specific to the processing of emotional stimuli (Ernst, 2010). Thus, exploring conflict processing using non-emotional stimuli may help to elucidate the nature of deficits in cognitive processing in individuals with GAD.

A potential way to understand putative deficits in conflict processing in anxiety is through studies of emotional and cognitive conflict adaptation (also referred to as sequential-trial or Gratton effects; Gratton, Coles, & Donchin, 1992). Conflict adaptation requires both the accurate detection of conflict and the subsequent signaling for increased cognitive resources to adjust performance (Botvinick, Carter, Braver, Barch, & Cohen, 2001; Gratton et al., 1992). Conflict adaptation is typically seen during conflict-laden tasks, such as the Stroop or flanker, where conflict is created by similar (i.e., congruent) or differing (i.e., incongruent) target-stimulus properties and task-irrelevant information. Tasks that utilize cognitive or emotional target stimuli facilitate the examination of either cognitive or emotional processes (respectively) on conflict detection and resolution. Tasks that utilize task-irrelevant emotional distractors facilitate the examination of the impact of distracting emotional information on cognitive processes operating outside of the emotional system (Egner, Etkin, Gale, & Hirsch, 2008). Studies of emotional conflict adaptation in GAD suggest that poor abilities to detect emotional or cognitive conflict and subsequently adjust performance may play a role in clinical anxiety, as clinical levels of perseverative worry associated with GAD may place additional demands on cognitive systems in part by taxing attentional control systems (Etkin & Schatzberg, 2011). Differences in the processing of emotional information relative to “purely” cognitive information may elucidate cognitive processes that contribute to pathological levels of anxiety, including whether it is the cognitive processes...
that are impaired in clinical anxiety, or whether it is the processing of irrelevant emotional information that interferes with cognitive processing.

The neural time course of these conflict adaptation processes can be measured using the conflict N2 component of the scalp-recorded event-related potential (ERP). The conflict N2 is a negative deflection in the ERP with a fronto-central scalp distribution that peaks approximately 250–350 ms after stimulus presentation (Nieuwenhuis, Yeung, Van Den Wildenberg, & Ridderinkhof, 2003; Yeung, Botvinick, & Cohen, 2004). The conflict N2 appears to be generated in the anterior cingulate cortex (ACC), and is more negative on incongruent than congruent trials, suggesting that it may reflect the allocation of top-down cognitive control to reduce conflict (van Veen & Carter, 2002a,b; Yeung et al., 2004). Conflict N2 amplitudes are less negative on incongruent trials preceded by incongruent trials (iC) relative to incongruent trials following congruent trials (cC; Clayson & Larson, 2011a; Clayson & Larson, 2011b). This top-down bias decreases in levels of conflict on the following trial, resulting behaviorally in faster response times (RTs) and decreased error rates on iC trials relative to cC trials (e.g., Clayson & Larson, 2011a; Clayson & Larson, 2011b; Forster, Cameron, Cohen, & Cho, 2011; Gratton et al., 1992; Ullsperger, Blyisma, & Botvinick, 2005). Alternatively, faster RTs and lower error rates on iC relative to cC trials may be the result of the facilitative effects of repetition priming (Mayr, Awh, & Laurey, 2003), although this possibility remains controversial and studies using the precise task employed in the current study show conflict adaptation effects when repetition priming is controlled (Clayson & Larson, 2011a; Clayson & Larson, 2011b; Forster et al., 2011; Ullsperger, Blyisma, & Botvinick, 2005). Conversely, RTs and error rates are increased on iC trials relative to cC trials due to switching between congruencies (see Egner, 2007, for review). These neural and behavioral indices of conflict adaptation may be sensitive to subtle differences in cognitive processing, ideal for identifying the specific nature of cognitive processing deficits in anxiety disorders.

Research suggests that the neural processes implicated in conflict adaptation are altered in GAD. During conflict adaptation, the ACC detects conflict and subsequently signals the dorsolateral prefrontal cortex (PFC) and right ventromedial PFC to increase cognitive control (Egner, 2011; Egner & Hirsch, 2005; Korns et al., 2004). In emotional conflict adaptation, activity increases within the rostral ACC, inhibiting activity within the amygdala in order to decrease emotional responsiveness to distracting affective stimuli (Egner, Etkin, Gale, & Hirsch, 2008). In a recent study conducted by Etkin, Prater, Hoef, Menon, & Schatzberg (2010), individuals with GAD displayed decreased activation of the ACC that subsequently did not dampen amygdala response on an emotional conflict task in which emotionally salient words were overlaid on emotional faces (e.g., the word HAPPY overlaid on a fearful face). These results may suggest that GAD is associated with an attenuated response to conflict resulting in impaired top-down control and emotional dysregulation (Etkin et al., 2010). Similarly, individuals with panic disorder showed decreased conflict adaptation effects relative to psychiatrically-healthy controls during a similar emotional conflict task, including reduced dorsal ACC recruitment and increased amygdala activation during trials following incongruent trials (Chechko et al., 2009). Taken together, these findings suggest that abnormal patterns of activation observed within the ACC and amygdala during emotional conflict adaptation may be related to emotional dysregulation associated with anxiety.

Behavioral studies of individuals with clinical levels of anxiety corroborate neuroimaging findings by demonstrating decreased control following conflict, highlighting important differences in top-down regulation. Across multiple studies using an emotional conflict task, individuals with GAD did not display increased RTs relative to controls on iC trials relative to cC trials (Etkin et al., 2010; Etkin & Schatzberg, 2011), evidencing deficits specific to emotional conflict adaptation. Further, the degree of impairment in emotional conflict adaptation was correlated with levels of anxiety among patients with GAD, adding support to a relationship between conflict processing deficits and symptoms of clinical anxiety (Etkin et al., 2010). Together, these findings suggest that pathological anxiety may differentially alter cognitive control mechanisms during emotional processing, resulting in decreased cognitive flexibility that may contribute to the pervasive maintenance of worry characteristic of clinical anxiety.

Though it is clear that both neural and behavioral indices of conflict adaptation are altered in anxiety disorders, it is uncertain whether conflict processing deficits are primary, secondary, or independent of deficits in emotional processing. In one behavioral study, adults with obsessive compulsive disorder (OCD) and unipolar depression displayed response repetition slowing during a non-emotional Stroop task, possibly due to increased levels of rumination in these individuals (Merian, Diamond, Toder, & Nemets, 2010). These findings lend support to possible conflict adaptation deficits in the absence of emotional stimuli in anxiety disorders. However, no studies to date have examined neural and behavioral indices of conflict adaptation in GAD without emotional stimuli. If differences are present on purely cognitive tasks, it may be that anxiety disorders are associated with deficits in conflict adaptation independent of emotional processing.

Of note, conflict adaptation processes may differ among anxiety disorders and other comorbid conditions. Whereas GAD shares many characteristics with other anxiety disorders, the nature of the pervasive worry in GAD may uniquely affect cognitive systems involved in conflict adaptation by reducing the available resources needed to complete the task (Etkin & Schatzberg, 2011). It may also be that differences in compensatory processes associated with anxiety are related to distinct cognitive processes that distinguish anxiety disorders (Armstrong, Zald, & Olatunji, 2011). While some similarities in behavioral performance and neural activation have been observed among anxiety disorders and other comorbid conditions (e.g., depression), distinct patterns of activation and behavior have also been observed, again pointing to important differences in cognitive processing and neural activation (Etkin & Schatzberg, 2011). Thus, our primary focus was to determine the nature of cognitive control processing in individuals with GAD.

Based on the absence of neural and behavioral research in anxiety disorders, we aimed to compare electrophysiological (conflict N2) and behavioral (RTs, error rates) indices of conflict adaptation between individuals with GAD and controls using a non-emotional modified flanker task (Eriksen & Eriksen, 1974). Based on previous research, we predicted that participants with clinical levels of anxiety would display reduced behavioral modification and electrophysiological activation based on previous trial conflict, suggestive of deficits in basic cognitive processing. Specifically, we hypothesized that individuals with GAD would display attenuated N2 amplitudes relative to controls and would not display modulations in N2 amplitude based on previous-trial conflict. Similarly, we predicted that individuals with GAD would not display increased RTs on iC trials relative to cC trials, again indicating deficits in cognitive control following conflict.

2. Method

2.1. Participants

All participants provided written informed consent as approved by the Brigham Young University Institutional Review Board. Individuals with GAD were recruited via referral from university and
of depression, state anxiety, and trait anxiety relative to control participants (|t| > 5.8, \( p < 0.001 \); see Table 1).

2.3. Experimental task

Participants completed a modified version of the Eriksen Flanker Task (Eriksen & Eriksen, 1974). Each trial consisted of either congruent (««, »») or incongruent («>, »<) arrow stimuli presented in white on a black background of a 17-inch computer monitor approximately 20 inches from the participant’s head. Participants were instructed to respond as quickly and accurately as possible with a right-hand key press. An index-finger button press was used if the target stimulus (i.e., middle arrow) pointed to the left and a middle-finger button press was used if the target stimulus pointed to the right. No feedback about performance was provided during the task. Flanker stimuli were presented 100 ms prior to the onset of the target stimulus, which remained on the screen for 600 ms. If the participant responded after 1600 ms, the trial was counted as an error of omission. The ITI varied randomly between 800 ms, 1000 ms, and 1200 ms, with a mean of 1000 ms. Three blocks of 266 trials (798 total trials) were presented, with 354 congruent trials (45%) and 444 incongruent trials (55%). Given that participants tend to make more errors on incongruent trials than congruent trials, we included more incongruent trials in an effort to keep the number of trials similar between conditions. Participants completed 24 practice trials to ensure understanding prior to beginning the experimental task.

2.4. Electrophysiological data recording and reduction

Electroencephalogram (EEG) was recorded from 128 scalp sites using a geodesic sensor net and Electrical Geodesics, Inc. (EGI; Eugene, OR) amplifier system (20K nominal gain, band-pass = 0.10–100 Hz). During recording, EEG was referenced to the vertex electrode and digitized continuously at 250 Hz with a 24-bit analog-to-digital converter. Impedances were maintained below 50 kΩ. Data were digitally low-pass filtered at 30 Hz.

Individual-subject stimulus-locked averages were calculated using a window from −250 ms prior to stimulus presentation to 1000 ms following stimulus presentation for C, C, IC, and IC trials. Eye blinks were removed from the segmented waveforms using independent components analysis (ICA) implemented in the ERP PCA Toolkit (Dien, 2010). The ICA components that correlated at .9 with the scalp topography of two blink templates, one generated based on the current data and another provided by the ERP PCA Toolkit author, were removed from the data (Dien, Michelson, & Franklin, 2010). Trials were considered bad if more than 15% of channels were marked bad. Channels were marked bad if the fast average amplitude exceeded 100 μV or if the differential average amplitude exceeded 50 μV. Data were average referenced including the polar average reference effect (PARE) correction (Junghäner, Elbert, Tucker, & Braun, 1999). Waveforms were baseline corrected using a 200 ms window from −250 ms to −50 ms prior to stimulus presentation.

Single-subject average N2 amplitude was first analyzed then individual-subject ERPs were analyzed using a temporospatial principal components analysis (PCA) to ensure that functionally equivalent ERP activity were compared between groups. N2 amplitude was first extracted using an adaptive mean approach to avoid biasing effects of background EEG noise (Clayson, Baldwin, & Larson, 2013). N2 amplitude data were quantified as the average ERP activity from 16 ms (four samples) pre-peak to 16 ms post-peak negative amplitude between 270 ms and 380 ms at channel FCz.

To extract ERP components related to conflict monitoring and conflict adaptation, temporospatial PCA was conducted using the ERP PCA Toolkit (Dien, 2010; Foti, Weinberg, Dien, & Hajcak, 2011).
We followed previously published guidelines to extract ERP components (Dien, Beal, & Berg, 2005; Dien, Khoe, & Mangun, 2007; Foti et al., 2011). All single subject averages were included in the PCA; factors were chosen based on scree plots (Catell, 1966) using the parallel test (Horn, 1965). A temporal PCA with promax rotation using all time points from single subject averages as variables with participants, trials, and electrodes as observations was first conducted and yielded 16 temporal factors (TFs). A subsequent spatial PCA with infomax rotation using electrode sites as the variables and participants, trials, and temporal factors as observations yielded 7 spatial factors (SFs; Dalbert, 1992; Dien et al., 2007).

Similar to previous work using temporospatial PCA to extract N2 activity (Clawson, Clayson, & Larson, 2013), the TFSF (temporospatial factor) that most closely matched the expected scalp topography and latency for the N2 was extracted based on visual inspection of the grand average waveforms, the TFSFs, and prior research on the N2 (Danielmeier, Wessel, Steinhauser, & Ullsperger, 2009; Nieuwenhuis et al., 2003). First, the TFs that contributed less than 1% to the total variance or showed peak activation in the baseline time window were excluded from further examination in order to remove TFSFs that were not likely meaningfully contributing to the activity of interest in the current examination (for a similar approach see Foti et al., 2011; Kujawa, Weinberg, Hajcak, & Klein, 2013). Of the remaining 22 components, three TFSFs showed peak activation between 250 ms and 350 ms following stimulus presentation, the time window frequently used to extract N2 activity (Nieuwenhuis et al., 2003; Yeung et al., 2004). Of those three components only TFSF2 showed fronto-medial peak activation. Thus, TFSF2 best reflected the N2 and showed peak activation at FCz and peak latency at 318 ms (see Larson, Clayson, & Baldwin, 2012b for sensor layout). TFSF2 showed a similar scalp topography and peak latency compared to other work using temporospatial PCA to extract the N2 (Clawson et al., 2013) suggesting that TFSF2 accurately reflects N2 activity. Amplitude data was extracted as the peak-latency instantaneous amplitude of the N2 TFSF.

### 2.5. Data analysis

In order to overcome the biasing effects of nonnormality, (co)variance heterogeneity between groups, non-orthogonal groups, and to reduce Type I error (Dien & Santuzzi, 2005), robust analyses of variance (ANOVA) were conducted using the ERP PCA Toolkit (Dien, 2010; Keselman, Wilcox, & Lux, 2003). Robust ANOVA statistics are interpreted in a similar manner as traditional ANOVAs, but are not susceptible to assumption violations in the same way as traditional ANOVAs. To decompose significant interactions, Fisher's least significant difference approach was used to control for family-wise Type I error. The seed for the number generation was set at 1000, and the number of iterations used for bootstrapping was 50,000 (Clayson & Larson, 2012; Dien, Franklin, & May, 2006; Dien et al., 2010; Larson, Clayson, Clayson, & South, 2012a). Response time data were calculated excluding omitted-response trials. For RTs and ERPs, error trials and post-error trials were also excluded due to previous research showing faster RTs on error trials and slower RTs on post-error trials (Clayson & Larson, 2011a; Larson, Kaufman, & Perlstein, 2009b).

Separate 2-Group (GAD, controls) × 2-Previous-trial Congruency (congruent, incongruent) × 2-Current-trial Congruency (congruent, incongruent) robust ANOVAs were first conducted for RTs, error rates, N2 single-subject average amplitude, and N2 TFSF amplitudes to verify that conflict adaptation effects were present in the data. Conflict adaptation was defined as a significant Previous-trial Congruency × Current-trial Congruency interaction and a significant subsequent cl/il difference on decomposition (Clayson & Larson, 2012). We did not examine repetition priming in this study to reduce the possibility of multiple comparisons as we have previously shown that repetition priming does not significantly alter ERP or behavioral conflict adaptation using an identical task (Clayson & Larson, 2011b).

Next, we wanted to examine the dimensional role of trait anxiety symptoms. Thus, in order to examine the relationship between
N2 conflict adaptation effect amplitudes and trait anxiety and depression levels zero-order correlations were conducted including all participants as well as separately for controls and individuals with GAD. Mean conflict adaptation effects were calculated using the formula \([cI - cC - iI - cI]\) (see Clasen & Larson, 2012). For ease of interpretation, the inverse of N2 amplitude data was used in order to make higher mean conflict adaptation scores evidence of improved control implementation similar to RT and error rate mean conflict adaptation scores (i.e., increased N2, RTs and error rate mean conflict adaptation scores evidencing greater implementation of control). The correlations between mean RT and mean scalp-channel N2 and principal-component N2 conflict adaptation scores were also examined.

3. Results

3.1. Response times

Response time data are presented in Table 1. A Group × Previous-trial Congruency × Current-trial Congruency robust ANOVA on RTs indicated a nonsignificant main effect of group, \(T_{WJ}(c_{1.0.66.8}) = 0.02, p = 0.90.\) Incongruent-trial RTs were longer than congruent trial RTs as indicated by a main effect of current-trial congruency, \(T_{WJ}(c_{1.0.66.2}) = 1.112.09, p < 0.0001.\) The Group × Current-trial Congruency interaction was not significant, \(T_{WJ}(c_{1.0.66.2}) = 3.48, p = 0.07.\) The Previous-trial Congruency × Current-trial Congruency interaction was significant, \(T_{WJ}(c_{1.0.65.5}) = 85.50, p < 0.0001.\) Longer RTs were shown for cl trials compared to il trials, \(T_{WJ}(c_{1.0.58.6}) = 11.07, p = 0.002,\) and for ic trials relative to cc trials, \(T_{WJ}(c_{1.0.65.4}) = 108.14, p < 0.0001.\) Thus, overall RT data showed reliable conflict adaptation effects. Notably, the Group × Previous-trial × Current-trial Congruency was also significant, \(T_{WJ}(c_{1.0.67.6}) = 21.35, p < 0.0001.\)

For controls, the Previous-trial Congruency × Current-trial Congruency interaction was significant, \(T_{WJ}(c_{1.0.34.0}) = 11.64, p = 0.002.\) RTs were longer for ic trials compared to cc trials, \(T_{WJ}(c_{1.0.34.0}) = 14.84, p < 0.001;\) however, RTs were similar for cl and il trials, \(T_{WJ}(c_{1.0.34.0}) = 0.22, p = 0.64.\) These findings indicate that the Previous-trial Congruency × Current-trial Congruency interaction was primarily the result of slowing associated with switching congruencies on an ic trial compared to cc trial rather than conflict adaptation effects for the control participants (see Clasen & Larson, 2011b).

For individuals with GAD, the Previous-trial Congruency × Current-trial Congruency interaction was significant, \(T_{WJ}(c_{1.0.34.0}) = 88.95, p < 0.0001.\) RTs were longer for cl trials than for il trials indicating that RTs showed significant conflict adaptation effects, \(T_{WJ}(c_{1.0.34.0}) = 13.48, p = 0.002; iC-trial RTs were also longer than cc-trial RTs, \(T_{WJ}(c_{1.0.34.0}) = 137.25, p < 0.0001.\) In sum, significant RT conflict adaptation effects were observed for individuals with GAD.

3.2. Error rates

Error rate data are presented in Table 1. A robust ANOVA on error rates yielded a significant main effect of current-trial congruency with larger error rates for incongruent than for congruent trials, \(T_{WJ}(c_{1.0.67.5}) = 139.37, p < 0.0001.\) The Previous-trial Congruency × Current-trial Congruency interaction was also significant, \(T_{WJ}(c_{1.0.68.0}) = 52.39, p < 0.0001.\) Error rates were larger for cl trials than for il trials suggesting that significant conflict adaptation effects were exhibited in error rate data, \(T_{WJ}(c_{1.0.67.7}) = 53.35, p < 0.0001.\) Error rates were similar for ic and cc trials, \(T_{WJ}(c_{1.0.67.9}) = 2.20, p = 0.14.\) The main effect of group and interactions with group were not significant (Ts < 3.3, \(ps > 0.07).\) Thus, participants in both groups exhibited similar error rates regardless of condition.

3.3. N2 amplitude

N2 grand average waveforms and scalp voltage maps are presented in Fig. 1. Summary data for the N2 are presented in Table 1. Importantly, there were no significant group differences observed between individuals with GAD and controls for background noise.
estimates (see Clayson et al., 2013; Schimmel, 1967) or number of trials corrected for ocular artifact (Ts < 1.9, ps > 0.17). Single subject averages for controls had an average ± standard deviation of 145 ± 26 cC trials, 146 ± 26 cl trials, 152 ± 25 iC trials, and 163 ± 35 il trials. Averages for individuals with GAD included 117 ± 34 cC trials, 125 ± 37 cl trials, 129 ± 38 iC trials, and 145 ± 46 il trials.

For the scalp-channel N2 amplitude data extracted from the traditional ERP averages, a main effect of current-trial congruency was shown such that N2 amplitudes were more negative for incongruent than for congruent trials, \( T_{\text{WJt/c}}(1.0,56.5) = 37.15, p < 0.0001 \). The Previous-trial Congruency \times Current-trial Congruency interaction was also significant indicating that significant conflict adaptation effects were observed, \( T_{\text{WJt/c}}(1.0,67.9) = 4.54, p = 0.04 \). Notably, scalp-channel N2 amplitude was more negative for cl trials than for il trials corroborating that significant conflict adaptation effects were shown for the scalp-channel N2, \( T_{\text{WJt/c}}(1.0,67.9) = 21.01, p < 0.0001 \). N2 amplitudes were more negative for cC trials compared to iC trials, \( T_{\text{WJt/c}}(1.0,67.2) = 4.81, p = 0.03 \). The Group \times Current-trial Congruency interaction was significant, \( T_{\text{WJt/c}}(1.0,65.5) = 4.13, p = 0.046 \). Both controls and individuals with GAD showed more negative scalp-channel N2 amplitude to incongruent trials compared to congruent trials, \( T_{\text{WJt/c}}(1.0,34.0) = 22.74, p < 0.0001 \); \( T_{\text{WJt/c}}(1.0,34.0) = 15.07, p < 0.001 \), respectively. Similar scalp-channel N2 amplitude was observed between groups for congruent and incongruent trials, \( T_{\text{WJt/c}}(1.0,59.0) = 0.95; T_{\text{WJt/c}}(1.0,56.5) = 1.24, p = 0.27 \), respectively. The Group \times Previous-trial Congruency \times Current-trial Congruency interaction was not significant, \( T_{\text{WJt/c}}(1.0,67.9) = 2.45, p = 0.12 \).

The principal-component N2 TFSF waveforms and scalp voltage maps are presented in Fig. 2. For N2 TFSF amplitude data, principal-component N2 amplitudes were more negative for incongruent trials than for congruent trials, \( T_{\text{WJt/c}}(1.0,64.3) = 57.32, p < 0.0001 \). The Previous-trial Congruency \times Current-trial Congruency interaction was significant, \( T_{\text{WJt/c}}(1.0,67.9) = 8.26, p = 0.005 \). Principal-component N2 amplitudes were more negative for cl trials than for il trials indicating that reliable conflict adaptation effects were demonstrated, \( T_{\text{WJt/c}}(1.0,65.1) = 7.64, p = 0.008 \); cC-trial principal-component N2 amplitude and iC-trial principal-component N2 amplitude were similar, \( T_{\text{WJt/c}}(1.0,66.1) = 1.18, p = 0.28 \). The main effect of group was not significant, \( T_{\text{WJt/c}}(1.0,61.5) = 0.50, p = 0.49 \).

The Group \times Current-trial Congruency interaction was significant, \( T_{\text{WJt/c}}(1.0,64.3) = 15.45, p < 0.001 \). Both controls and individuals with GAD showed more negative principal-component N2 amplitude for incongruent trials compared to congruent trials, \( T_{\text{WJt/c}}(1.0,34.0) = 53.30, p < 0.0001; T_{\text{WJt/c}}(1.0,34.0) = 8.73, p = 0.008 \), respectively. More negative incongruent-trial principal-component N2 amplitude was exhibited in controls relative to individuals with GAD, \( T_{\text{WJt/c}}(1.0,60.3) = 6.22, p = 0.02 \); group differences were not observed for congruent-trial principal-component N2 amplitude, \( T_{\text{WJt/c}}(1.0,64.2) = 1.95, p = 0.17 \).

Most importantly, the Group \times Previous-trial Congruency \times Current-trial Congruency interaction was also significant, \( T_{\text{WJt/c}}(1.0,67.9) = 5.02, p = 0.03 \). For controls, the Previous-trial Congruency \times Current-trial Congruency interaction was significant, \( T_{\text{WJt/c}}(1.0,34.0) = 13.62, p = 0.001 \). More negative principal-component N2 amplitude was exhibited for cl trials than for il trials indicating reliable conflict adaptation effects, \( T_{\text{WJt/c}}(1.0,34.0) = 10.57, p = 0.003 \). Nonsignificant differences were observed for iC and cC trials, \( T_{\text{WJt/c}}(1.0,34.0) = 1.37, p = 0.25 \). The Previous-trial Congruency \times Current-trial Congruency interaction was not significant for individuals with GAD, \( T_{\text{WJt/c}}(1.0,34.0) = 0.19, p = 0.66 \).

3.4. Zero-order correlations

To examine the relationship between endorsed anxiety and depression symptoms and indices of conflict adaptation across a range of symptom severity, we included all participants regardless of diagnosis in correlational analyses. Higher BDI-II, STAI-State, and STAI-Trait scores were associated with higher mean RT conflict adaptation effects, \( r(68) = 0.32, p = 0.007; r(68) = 0.40, p = 0.001; r(68) = 0.44, p = 0.0001 \), respectively (see Fig. 3). Higher STAI-State
scores were related to higher mean error rate conflict adaptation effects, $r(68) = 0.28$, $p = 0.02$ (see Fig. 3). Higher BDI-II and STAI-Trait scores were related to lower (less negative) mean principal-component N2 overall conflict adaptation effect amplitudes, $r(68) = -0.29$, $p = 0.02$; $r(68) = -0.28$, $p = 0.02$, respectively (see Fig. 4). Mean principal-component N2 and mean scalp-channel N2 conflict adaptation effects were inversely related to mean RT conflict adaptation effects, such that higher principal-component N2 and scalp-channel N2 conflict adaptation scores were related to lower mean RT conflict adaptation scores; $r(68) = -0.24$, $p = 0.047$; $r(68) = -0.24$, $p = 0.048$, respectively. None of the remaining correlations were significant ($|r| < 0.19, p > 0.12$; see Table 2).

When examining the correlations between mean CA effects and BDI-II, STAI-Trait, and STAI-State scores separately for controls and individuals with GAD, none of the correlations were significant ($|r| < 0.31, p > 0.08$; see Table 2). Furthermore, the relationship between mean principal-component N2 and mean scalp-channel N2 conflict adaptation scores and mean RT conflict adaptation scores were not significant for either group ($|r| < 0.27, p > 0.11$).

4. Discussion

We capitalized on the temporal resolution of ERPs to show decreased trial-by-trial conflict adaptation neural processes in

![Fig. 3. Scatterplots of the relationship between mean response time (RT) and error rate conflict adaptation effects and depression and anxiety measures. BDI-II = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory.](image)

| Table 2 | Zero-order correlations for measures of conflict adaptation (CA) and depression and anxiety scores. |
|----------|---------------------------------|---------------------------------|---------------------------------|
| Group    | Mean RT CA effects              | Mean error rate CA effects       | Mean N2 TFSF CA effects         |
|          | $0.32^*$                        | $0.09$                          | $-0.29^*$                       |
|          | Mean error rate CA effects       | Mean N2 CA effects              | Mean N2 CA effects              |
|          | $0.02$                          | $-0.12$                         | $-0.18$                         |
|          | Mean N2 TFSF CA effects         | Mean N2 CA effects              | Mean N2 CA effects              |
|          | $-0.23$                         | $-0.18$                         | $-0.07$                         |
|          | Mean N2 CA effects              | Mean N2 CA effects              | Mean N2 CA effects              |
|          | $-0.18$                         | $-0.07$                         | $-0.11$                         |
|          | Mean RT CA effects              | Mean error rate CA effects       | Mean N2 TFSF CA effects         |
|          | $-0.12$                         | $-0.12$                         | $-0.05$                         |
|          | Mean error rate CA effects       | Mean N2 CA effects              | Mean N2 CA effects              |
|          | $-0.14$                         | $-0.12$                         | $0.11$                          |

$p < 0.05$.

$^* p < 0.01$.

BDI-II = Beck depression inventory.

STAI = State-trait anxiety inventory.

RT = Response time.

TFSF = Temporospatial factor.

GAD = Generalized anxiety disorder.
individuals with GAD relative to demographically similar control participants using stimuli without emotional content or performance feedback. We observed no significant group differences for accuracy and intact RT-related conflict adaptation in individuals with GAD. Electrophysiological data revealed attenuated principal-component N2 amplitudes among individuals with GAD for incongruent but not congruent trials and no principal-component N2 conflict adaptation effects for those with GAD; groups did not differ on scalp-channel N2 waveform amplitudes. The reduction in the principal-component N2 was most pronounced in individuals with increased anxiety and depressive symptoms. These findings can be interpreted in the context of a reduction in the general detection of conflict in those with GAD, as they showed decreased principal-component N2 amplitudes for incongruent, but not congruent, trials when collapsed across previous trial congruency. Thus, it appears that the conflict adaptation reductions in those with GAD in comparison to controls are influenced by inefficiencies in conflict detection, not just by decreased adjustments on a trial-by-trial basis.

Ours is the first study to use the temporal sensitivity of ERPs in examining conflict adaptation in individuals with GAD, but our findings are consistent with one study of the N2 ERP in high trait anxiety participants and a growing body of research showing altered GAD-related conflict adaptation processes. Dennis and Chen (2009) showed reduced scalp-channel N2 amplitudes following threat stimuli in highly anxious participants following threatening, but not other face stimuli presentation. Responses to neutral face stimuli did not differ between high and low anxiety participants. Etkin et al. (2010) and Etkin and Schatzberg (2011) reported reduced ACC activity in individuals with GAD relative to controls on a face-Stroop conflict adaptation paradigm leading them to conclude that those with GAD fail to adapt to emotional conflict. Increased anxiety levels are also associated with decreased conflict processing abilities, similar to our findings (e.g., Etkin et al., 2010). The key difference between our study and the previous work, however, is in the nature of the stimuli. Prior to our study it was unclear whether GAD-related deficits in conflict adaptation were due to the emotional nature of the tasks used or are primarily the result of poor conflict detection and resolution mechanisms regardless of emotional content. Our results suggest that decreased conflict adaptation in GAD is present in cognitive tasks without an emotional component. That is, GAD-related deficits in conflict adaptation appear to be independent of emotional processing. Such deficits are primarily present when the amplitude of the N2 is isolated in a TFSF, rather than in the more traditional scalp-channel N2, potentially suggesting multiple contributing sources to the N2.

These findings have implications for studies that suggest pathological compensation to emotional stimuli or emotional processes as a mechanism for GAD (e.g., Etkin & Schatzberg, 2011). Specifically, individuals with GAD may poorly compensate for many types of stimuli of both emotional and non-emotional content indicating a fundamental deficit in conflict processing. This possibility does not preclude findings by the Etkin group that decreased ACC activity fails to dampen amygdala response, but rather are consistent with a wider-spread dysregulation of ACC-related neural processes. Such ACC deficits may be related to amygdala activity in some, but not all, instances. Several studies show ACC-related activity in conflict adaptation paradigms (e.g., Kerns et al., 2004; Sheth et al., 2012). Similarly, recent studies report altered ACC morphology and activity in those with GAD including altered white matter connectivity in those with GAD compared to controls (Zhang et al., 2013), positive correlations between ACC volume and GAD-related worry (Schienele, Ehner, & Schafer, 2010), and longer ACC-related activity in mood induction paradigms that emphasize worry relative to other non-anxious conditions (Paulesu et al., 2010). Indeed, one study suggested that uncertainty as to response accuracy may be a key component in GAD-related developmental processes (Krain et al., 2006) and another showed that the magnitude of pretreatment ACC activity predicted subsequent treatment response to venlafaxine even though overall ACC activity was not fully differentiated from controls (Whalen et al., 2008). Taken together, the alterations in ACC functioning relative to controls appears to be a contributor to GAD-related pathology.

The precise nature and mechanism of altered conflict processing and ACC activity in individuals with GAD and high levels of anxiety, however, remains somewhat unclear. For example, a study that examined individuals with high trait levels of anxiety (but not diagnosed GAD) and a non-emotional face-Stroop task (i.e., a gender discrimination task) showed increased, rather than decreased, ERP indices of ACC-mediated conflict adaptation associated with high trait anxiety (Osinsky, Alexander, Gebhardt, & Hennig, 2010). A follow-up study that used a similar gender discrimination task with three separate conditions – word only, face only, and face-word overlay – showed faster conflict adaptation RTs in individuals with high trait anxiety for face only stimuli, but not face-word overlay and word only stimuli (Osinsky, Gebhardt, Alexander, & Hennig, 2012). For ERPs, there were no significant correlations between conflict-related ERPs and trait anxiety symptoms in the face-word overlay condition, but there were significant negative correlations between anxiety symptoms and face and word-processing ERPs in the face and word only conditions. There were, however, differences between overlaid face-word stimuli and the more cognitive face and word alone stimuli, supporting the premise of the current study to examine conflict adaptation processes without emotional content. We note that these studies were done in healthy individuals with high trait anxiety and used face-word stimuli. Taken together, there appears to be some variability in findings across studies of conflict adaptation in high anxiety. Whereas our study adds to previous research supporting altered conflict related processing associated with clinical levels of anxiety, it is unclear...
how high levels of trait anxiety influence the processing of conflict.

Three studies show increased amplitude of the error-related negativity (ERN) component of the ERP in those with GAD compared to control and GAD plus comorbid MDD participants (Weinberg, Olvet, & Hajcak, 2010; Weinberg, Klein, & Hajcak, 2012; Xiao et al., 2011). The ERN is a fronto-central response-locked ERP that is thought to reflect ACC-related conflict activity between error and correct trials just after an erroneous response (Danielmeier et al., 2009; Falkenstein, Hoehnsbein, Hoermann, & Banke, 1991; Gehring, Goss, Coles, Meyer, & Donchin, 1993; Nieuwenhuis, Ridderinkhof, Blom, Band, & Kok, 2001; Yeung et al., 2004); whereas the N2 is thought to represent the detection of stimulus-related conflict between the flanker and target stimuli (Folstein & Van Petten, 2008; Nieuwenhuis et al., 2003; Yeung et al., 2004; Yeung & Cohen, 2006). Both the N2 and ERN are source localized to the ACC (Brazdil, Roman, Daniel, & Rektor, 2005; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004; van Veen & Carter, 2002a; Yeung et al., 2004), are thought by some to reflect the same conflict related processes, with the ERN reflecting the conflict between correct and error responses and the N2 reflecting the conflict between target and flanker processing (Yeung et al., 2004), and show an inverse relationship with each other based on the amount of previous trial conflict (Larson et al., 2012b).

Our current results indicate decreased-amplitude conflict-related principal-component N2 in GAD, which seems counterintuitive considering findings of enhanced ERN amplitude in GAD (Weinberg et al., 2010, 2012; Xiao et al., 2011). Previous research has evidenced a functional dissociation between the ERN and N2. For example, previous findings indicated reduced ERN and enhanced N2 in a participant with a left-ACC lesion (Swick & Turken, 2002), reduced ERN and normal N2 after alcohol consumption (Ridderinkhof et al., 2002), reduced ERN and enhanced N2 with increased proximity of flankers to the target stimulus (Danielmeier et al., 2009), and increased ERN and normal N2 during a flanker trial with a bright target stimulus relative to dim target stimulus (Yeung, Ralph, & Nieuwenhuis, 2007). Indeed, other research on conflict processing has shown normal stimulus-locked ERP amplitude, indexed by the Stroop N450, between controls and individuals with mild (Larson, Farrer, & Clasen, 2011) and severe traumatic brain injury (TBI; Larson et al., 2009b), despite research showing an attenuated ERN in mild (Pontifex, O’Connor, Broglio, & Hillman, 2009) and severe TBI (Larson, Kaufman, & Perlstein, 2009a). Thus, considering that the N2 putatively indexes selective attention as it requires the biasing of attention away from the flankers and the ERN is contingent upon the conflict generated by continued stimulus processing following an erroneous response, GAD may be associated with impaired selective attention processes requiring the ability to filter out distracting information and enhanced target-stimulus processing following erroneous responses.

The RT and error rate data show generally intact reflections of conflict adaptation in those with GAD, despite differences in the principal-component N2 relative to controls. There were no significant-between-groups differences in error rates as a function of current or previous trial congruency and RTs showed intact conflict adaptation in anxiety and slowed task switching in controls. These findings differ from those of Etkin et al. (2010) who observed increased RTs on il trials compared to cl trial in controls but not individuals with GAD. The follow-up study by Etkin and Schatzberg (2011) showed a lack of RT-related conflict adaptation in both the GAD only and comorbid groups relative to the MDD only and control groups, suggesting that GAD, regardless of comorbidity is associated with a reduction in RT-related conflict adaptation. All of these studies have shown different neural correlates of conflict adaptation between GAD and control participants. Other studies suggest that negative emotion regardless of pathology may reduce behavioral manifestations of conflict adaptation (Padmala, Bauer, & Pessoa, 2011), but these results are not consistent across studies (van Steenbergen, Band, & Hommel, 2010).

The disconnect between neurologic correlates of conflict adaptation and behavioral performance in several of these studies parallels the current findings. Etkin and Schatzberg (2011) suggest that intact behavioral performance can be seen in individuals with pathology despite abnormalities in neurologic circuitry primarily due to compensatory processes that are engaged at the expense of traditional conflict-adaptation pathways. Thus, ACC and dPFC-mediated conflict adaptation may be supported by other, unmeasured, areas that serve to hinder the presentation of the N2 in those with GAD. For example, a recent study in individuals with social anxiety showed increased insula activity to emotional content, but decreased connectivity with the ACC potentially leading to decreased ACC-related activity (Klumpp, Angstadt, & Phan, 2012). The hypothesis of compensatory processes influencing conflict adaptation needs future testing by examining conflict adaptation in an fMRI-type scanning session without the confound of emotional stimuli that is present in the research to date. The finding that the principal-component N2 showed differences, but more traditional scalp–channel N2 amplitude did not supports this possibility. That is, when isolated using PCA, the N2 was smaller in those with GAD, but when multiple contributors were possible there were no differences between the GAD and control groups.

5. Limitations

The current results should be considered within the context of several strengths and limitations. The study sample consisted of individuals diagnosed with GAD both in the community and confirmed by a structured clinical interview and well-matched control participants similar in age and education and identical in sex distribution. However, given the community-based nature of the sample the majority of the GAD participants were taking psychotropic medications. Thus, it is possible that medications played a role in the current findings, though analyses suggest that comorbidity did not significantly influence our results. Similarly, a small percentage of the GAD participants had a comorbid depressive disorder, although comorbidity did not appear to significantly influence the current findings. We also cannot fully rule out the influence of feature integration effects on the conflict adaptation findings given that on the flanker task utilized there were no way to achieve complete alternations between trials; however, previous research using an identical flanker task showed behavioral and ERP conflict adaptation robust against removal of repetition trials (Clasen & Larson, 2011b). There is the possibility that the timing of the RTs influenced group differences in the N2; however, we find this unlikely as we excluded all error and post-error trials and previous research shows correct-trial response-locked ERPs do not differ between individuals with GAD and controls (Weinberg et al., 2010, 2012; Xiao et al., 2011). In addition, the control participants did not show significant RT-related conflict adaptation, despite intact electrophysiological indicators of conflict adaptation. Finally, we were not able to disentangle the relative contributions of dimensional depressive and anxiety symptoms in the current study design given the multicollinearity of our depression and anxiety inventories. A study specifically examining depression and anxiety comorbidity is needed to further understand the relative contributions of depressive and anxious symptoms.

6. Summary and conclusion

In summary, our findings indicated that electrophysiological indicators of conflict adaptation, specifically the
principal-component N2, are diminished in individuals with GAD relative to demographically similar control participants in a purely cognitive task with no emotional stimuli. More traditional scalp-channel N2 amplitude and behavioral indices did not differ between groups. Results suggest that it is likely that poor adjustments to conflict in GAD are not solely due to poor regulation of emotion-related neural processes likely involving the amygdala, but are more far reaching and involve poor conflict detection and conflict adaptation as well as contributions from multiple sources. Future research is necessary to disentangle whether previous findings of impaired emotional conflict adaptation effects (Etkin et al., 2010; Etkin & Schatzberg, 2011) represent generalized cognitive control dysfunction or a contribution of impaired cognitive and emotional conflict monitoring processes as well as the possibility of compensatory systems influencing cognitive control functions in those with GAD.

Acknowledgment

We are grateful to Tracy Brown, Christina Catron, Joseph Fair, Isaac Prows, Isaac Hunt, Kirsten Mikael, and William David Walker for their assistance with data collection. This study was supported by funds from the Brigham Young University College of Family, Home, and Social Sciences, the Brigham Young University Counseling Center, and a Brigham Young University Mentored Environment Grant. We thank the BYU Comprehensive Clinic and Counseling Center for assistance in participant recruitment. The authors report no conflicts of interest.


