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Cognitive Control Disruption and Quality of Life in
Individuals with Obsessive-Compulsive Disorder

Isaac J. Hunt

A dissertation submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

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ABSTRACT

Cognitive Control Disruption and Quality of Life in Individuals with Obsessive-Compulsive Disorder

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Doctor of Philosophy

Obsessive-compulsive disorder (OCD) is associated with diminished quality of life and cognitive control dysfunction. Conflict adaptation is a reflection of cognitive control, and consists of the ability to detect conflict in previous trials and adjust performance on current trials. Conflict adaptation is thought to rely on interplay between the anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex (dlPFC) for detecting conflict and signaling for increases in control, respectively. We hypothesized that individuals with OCD would show reduced conflict adaptation effects in response times, error rates, ACC activation, and dlPFC activation when compared with healthy control subjects. We also expected diminished conflict adaptation to be associated with poorer quality of life in those with OCD. Nineteen individuals with OCD and twenty psychiatrically-healthy controls completed a Stroop task while response times, error rates, and fMRI data were recorded. 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent), x 2-Current Trial Congruency (congruent, incongruent) ANOVAs were conducted for both behavioral and fMRI data. Indices of conflict adaptation were correlated with quality of life scores. There was a significant response time conflict adaptation effect collapsed across groups; however, there were no between-groups interactions or main effects. No error rate conflict adaptation was observed at any level of the analysis. On fMRI analyses, the dlPFC showed increased activation on incongruent relative to congruent trials collapsed across groups; however, no ACC activation differences were observed between current incongruent and congruent trials. Conflict adaptation-related activation was noted in the ACC collapsed across groups. The between-groups ANOVA revealed a significant cluster in the ACC with control participants showing greater ACC, medial prefrontal cortex, and left orbitofrontal cortex conflict adaptation activation-related activation relative to individuals with OCD. No between-groups differences were seen in the dlPFC. Conflict adaptation was not significantly related to quality of life. Individuals with OCD may use different neural processes to achieve similar behavioral results to those of healthy controls. Alternative explanations of conflict adaptation effects such as temporal learning theory are also discussed. Our hypothesized model for the ACC and dlPFC functioning as the evaluative and regulative components of cognitive control was only partly supported. ACC and dlPFC activation appeared to highlight different roles, but these roles may be independent rather than existing in a feedback loop. Although quality of life is significantly diminished in individuals with OCD, this loss of quality of life does not appear to be mediated by conflict adaptation differences.

Keywords: conflict adaptation, cognitive control, obsessive-compulsive disorder, functional magnetic resonance imaging, quality of life

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Cognitive Control Disruption and Quality of Life in Individuals with Obsessive-Compulsive Disorder

Obsessive-compulsive disorder (OCD) is defined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) as the presence of obsessions or compulsions that are time-consuming and significantly interfere with social, occupational, and other areas of functioning (American Psychiatric Association, 2013). Obsessions consist of persistent thoughts, urges or images that are recurrent and distressing. Individuals with OCD may attempt to put these intrusive thoughts from their minds by performing a compulsive behavior — defined as a rigidly repetitive behavior meant to diminish anxiety or neutralize distress (Franklin & Foa, 2008). Most compulsive behaviors serve more than one function and are generally performed to relieve anxiety or distress (Starcevic et al., 2011). Some of the compulsive behaviors that have been described in OCD include ordering, checking, hoarding, and excessive cleaning (see Starcevic et al., 2011). Compulsive behaviors are often not realistically related to the distress they are meant to neutralize and can be seen as excessive and unreasonable (American Psychiatric Association, 2013). For example, some patients with OCD who perform excessive repetitive compulsions “fear that something bad will happen to a loved one but often cannot specify what particular disaster will befall them” (Franklin & Foa, 2008, p. 194). Obsessions and compulsions can become onerous, distressing, and time consuming for those who experience and perform them and, thus, it is not surprising that individuals with OCD tend to report diminished quality of life relative to psychiatrically-healthy individuals (see Coluccia et al., 2016).

OCD is a disabling condition with a considerable economic impact. In a given year in the United States, 1.2% of all adults meet full diagnostic criteria for OCD, and the disorder has a lifetime prevalence rate of 2.3% (Ruscio, Stein, Chiu, & Kessler, 2010). DuPont, Rice, Shiraki,

and Rowland (1995) estimated that in 1990 the total economic cost for OCD in the United States was approximately \$8.4 billion, comprising 5.7% of the total estimated costs for all mental disorders in that year. Eddy, Dutra, Bradley, and Westen (2004) conducted a meta-analytic review of the literature on the effects of psychotherapy and pharmacological interventions for OCD. They concluded that, although both pharmacotherapy and psychotherapy have substantial beneficial effects for individuals with OCD, there is a tendency for moderate obsessive-compulsive symptoms to remain even after successful treatment completion. They also concluded that no replicable evidence existed for long-term benefits of OCD-related treatment beyond a year following treatment. The pooled participants from the studies included in the meta-analysis had a mean duration of illness of 11.31 years \pm 2.29 (total n = 225; Eddy, Dutra, Bradley, & Westen, 2004). Therefore, it appears that individuals with OCD may incur significant and long-lasting economic costs spanning several years even after the completion of treatment.

Developing a greater understanding of the cognitive and neural processes that underlie OCD may help researchers and clinicians to more directly address the impact of this debilitating disorder. Cognitive control and executive functioning abilities are specific areas of cognition that are impacted by OCD (Olley, Malhi, & Sachdev, 2007) and may be related to treatment gains (McNamara et al., 2014; Vriend et al., 2013). Below we describe cognitive control component processes and then provide summaries of how these cognitive control processes may differ in individuals with OCD relative to psychiatrically-healthy individuals.

Cognitive Control and Conflict Adaptation

Cognitive control can be defined as an individual's ability to evaluate performance, recruit attentional resources, and adjust performance according to environmental demands (Miller & Cohen, 2001). Cognitive control is thought to represent the interaction between two

critical components: an evaluative component and a regulative component (Egner, Delano, & Hirsch, 2007). One of the most commonly used paradigms for studying the evaluative and regulative components of cognitive control is the Stroop task (Stroop, 1935). This task presents color-words in differing colors of ink creating conflict between two conflicting responses (reading the word or responding to the color of the ink). There is a high degree of reliability among fMRI studies showing common activations in response to the conflict of competing stimuli on the Stroop task. The areas of activation that are most commonly reported include the bilateral anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (dlPFC), precuneus, left inferior frontal region, left inferior parietal region, anterior insula, and middle occipital region (see Banich et al., 2000; Liu et al, 2004; & Roberts & Hall, 2008). Neumann and colleagues (2005) conducted a meta-analysis of fifteen fMRI studies using the Stroop task and showed a frontal activation network involving the pre-supplementary motor area, the inferior frontal sulcus extending into the middle frontal gyrus, the bilateral ACC, and the inferior frontal junction area (see also Neumann, von Cramon, & Lohmann 2008). A widely-held theory of cognitive control identifies the ACC as the primary site of activation for the evaluative component of cognitive control and the dlPFC as the primary site of activation for the regulative component (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Yeung, 2014).

Evaluative Component. As stated above, the evaluative component of cognitive control is thought to be responsible for detecting response conflict (i.e., the presence of competing response options) and monitoring performance for errors. The ACC is thought to be the primary brain region responsible for the detection of conflict (see Yeung, 2014) particularly when an automatic response needs to be overridden in order to provide a more effortful response. This theory was soon supported and replicated in several studies using both positron emission

tomography and fMRI modalities (Bush et al., 1998; Carter, Mintun, & Cohen, 1995; for a more complete review see Botvinick, Braver, Barch, Carter, & Cohen, 2001). ACC activation in automatic response inhibition has also been demonstrated using go/no-go tasks (Casey et al., 1997; Kawashima et al., 1996).

The evaluative component of cognitive control also plays an important role in the processing of errors. Botvinick, Braver, Barch, Carter, & Cohen, (2001) point out that the error-processing role of the ACC has been primarily demonstrated in electrophysiological research as opposed to neuroimaging modalities. For example, the error-related negativity (ERN) is a negative-going waveform component of the event-related potential that has been associated with performance monitoring and the processing of errors (Falkenstein, Hohnsbein, Hoormann, & Banke, 1991; Gehring, Coles, Meyer, & Donchin, 1990). The ERN has been localized to the ACC by converging electrophysiological, lesion, and neuroimaging studies (Brázdil, Roman, Daniel, & Rektor, 2005; Stemmer, Segalowitz, Witzke, & Schonle, 2004; van Veen & Carter, 2002). Enhanced ERN amplitudes are associated with elevated symptoms of anxiety (Weinberg, Klein, & Hajcak, 2012; Weinberg, Olvet, & Hajcak, 2010; Xiao et al., 2011). In summary, the evaluative component of cognitive control involves the process of detecting conflict and signaling the need for greater allocation of attentional resources to respond to conflict and errors and is localized primarily in the ACC.

Regulative Component. The regulative component of cognitive control includes the allocation and maintenance of attentional resources towards task performance (Botvinick, Braver, Barch, Carter, & Cohen, 2001). The dorsolateral prefrontal cortex (dlPFC) is thought to be a primary site associated with regulative control (Perlstein, Dixit, Carter, Noll, & Cohen, 2003). As mentioned above, the evaluative component (localized to the ACC) is responsible for

the detection of conflict and informs the regulative component (localized to the dlPFC; MacDonald & Carter 2003; Macdonald, Cohen, Stenger, & Carter, 2000; Perlstein Dixit, Carter, Noll, & Cohen, 2003) of the need to recruit, implement, and maintain additional attentional resources. In support of this conceptualization, Hanslmayr and colleagues (2008) showed increased coupling of the ACC and dlPFC on incongruent trials of the Stroop task relative to congruent trials.

Barch and colleagues (1997) provided early evidence for increased dlPFC activity in psychiatrically-healthy participants when context information had to be retained through a delay period relative to when context information was used immediately. MacDonald, Cohen, Stenger, and Carter (2000) later demonstrated increased dlPFC activity on a Stroop task when preparing for a high-conflict trial (color naming) relative to a low-conflict trial (word reading). MacDonald & Carter (2003) further demonstrated the importance of the dlPFC in regulative control in a comparison of patients with schizophrenia and healthy control subjects. They used a task that required participants to inhibit a learned response. As control participants prepared to inhibit a learned response, they showed significantly elevated dlPFC activation, whereas individuals with schizophrenia did not show a similar effect (see also Macdonald, Cohen, Stenger, & Carter, 2000). Thus, the dlPFC appears to play an important role in the regulative component of cognitive control, and there is evidence to show that psychiatric disorders may impair this functioning. A discussion of the evaluative and regulative components of cognitive control specific to individuals with OCD will follow in a section below.

Dissociating the Evaluative and Regulative Components. MacDonald and colleagues (2000) used a modified version of the traditional Stroop paradigm to demonstrate a double dissociation between the regulative and evaluative components of cognitive control while

collecting functional magnetic resonance imaging (fMRI) data. Prior to each trial in the Stroop task, participants were given an instruction to attend to either the word or the color of the trial stimulus. Responding to the word in a Stroop task is a more automatic response than responding to the color; responding to the color of a stimulus requires greater cognitive control in order to override the prepotent word-reading response (MacLeod & MacDonald, 2000). Individuals tend to show a slower, more deliberate response style for trials in which they are instructed to respond to the color rather than the word of a stimulus—a phenomenon referred to as the “Stroop effect” (MacLeod & MacDonald, 2000).

Following the presentation of the color or word instruction in MacDonald’s task (2000), a stimulus was presented after either a one-second or five-second delay. fMRI data were collected during control implementation (time between instructions and presentation of the stimuli) and during conflict (presentation of the Stroop stimulus). MacDonald and colleagues (2000) demonstrated greater left dlPFC activity during the preparatory period for trials in which participants were instructed to respond to the color of the stimulus relative to the preparatory period for trials in which participants were instructed to respond to the word of the stimulus. Thus, dlPFC activity was associated with greater implementation of control prior to high-conflict trials relative to low conflict trials. No activation differences were shown in the ACC for the preparatory period. Individuals who showed greater left dlPFC activation following instructions also showed a smaller Stroop interference effect. Macdonald and colleagues (2000) suggested that this supported the hypothesis of dlPFC-driven cognitive control implementation.

Following the presentation of stimuli, participants showed greater ACC activation in response for incongruent (e.g. GREEN written in red) relative to congruent (e.g. GREEN written in green) stimuli. Differential activation of the dlPFC for the presentation of congruent and

incongruent stimuli was not significant. Individuals who showed the largest Stroop interference effect tended to have greater ACC activation in response to presented stimuli, but this effect was not significant, likely due to the small sample size of the study ($n = 12$; $r = 0.38$, $p = .12$; MacDonald et al. 2000). Thus, MacDonald and colleagues (2000) provided support for the conclusion that control implementation occurs primarily in the dlPFC, and performance monitoring occurs primarily in the ACC of the brain.

Conflict Adaptation. The interactive nature of the evaluative and regulative components of cognitive control can also be assessed by examining what are known as conflict adaptation or congruency-sequence effects. For ease of reading, we will refer to these effects as conflict adaptation throughout this dissertation. Conflict adaptation is defined as the ability to detect conflict and adaptively respond with the recruitment of greater attentional resources and adjustments in performance (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Cohen, Botvinick, & Carter, 2000, see also Miller & Cohen, 2001). The evaluative and regulative components of cognitive control are both central components of conflict adaptation.

Conflict adaptation is often operationalized by considering differences in response times, error rates, and neurological activation as a function of sequencing effects (effects of different combinations of incongruent and congruent trials; Botvinick, Braver, Barch, & Cohen, 2001; Botvinick, Cohen, & Carter, 2004; Carter et al. 1998; Gratton, Coles, & Donchin, 1992;). For example, Kerns and colleagues (2004) evaluated conflict adaptation in psychiatrically-healthy control participants using a single-trial Stroop task. This task included congruent stimuli (color-words written in their own color; e.g., GREEN written in green) and incongruent stimuli (color-words written in a different color; e.g., GREEN written in red) presented every 1.5 seconds.

Participants were asked to respond quickly and accurately to the color of the word rather than the

word itself in order to elicit greater cognitive control processes. Kerns and colleagues (2004) demonstrated a double dissociation in response times between stimulus type (congruent vs. incongruent) and the effects of previous trials on current trials. Four trial-conflict types were considered in their analyses: congruent preceded by congruent trials (cC), congruent preceded by incongruent trials (iC), incongruent preceded by congruent trials (cI), and incongruent preceded by incongruent trials (iI). Kerns and colleagues (2004) showed that individuals tend to respond to cI trials with significantly slowed response times relative to iI trials. However, response times for iC trials were not significantly slower than response times for responses to cC trials. In other words, response times tended to be slower on incongruent trials in general, but this slowing is even more apparent when the conflict of an incongruent trial is preceded by a congruent trial (cI).

Thus, controlled adjustments in response times appear to be affected by the detection of conflict for which the regulative component has not already been activated. When an incongruent stimulus is encountered, there tends to be a delayed response as greater attentional resources are recruited to respond to the stimulus. However, when an incongruent stimulus is encountered following a previous incongruent stimulus (iI), the behavioral slowing of responses is not as pronounced, because increased control was already recruited in response to the previous trial, and the need for additional resource recruitment on the current trial is reduced.

In summary, Kerns and colleagues (2004) demonstrated significant increases in ACC activity in cI trials relative to iI trials, and they concluded that iI trials had relatively lower ACC activity because conflict in the previous incongruent trial had already resulted in the recruitment of greater attentional control. Thus, the need for the ACC to signal the dlPFC for greater attentional resources in these trials was reduced because these resources were already active. In

the cI trials, however, incongruent trials are preceded by congruent trials that did not require the recruitment of additional attentional resources; therefore, the conflict of the incongruent trial (cI) stimulates the cognitive control feedback loop (ACC to dlPFC) to respond adaptively to the conflict. As hypothesized, increased ACC activity in response to conflict was subsequently complemented with increased dlPFC activity on the following trial ($p < .01$; Kerns et al., 2004). The double dissociation of regulative and evaluative control in conflict adaptation has also been replicated in event-related potential (ERP) studies (Clayson & Larson, 2011a; Clayson & Larson, 2011b; Xue, Ren, Kong, Liu, & Qui, 2015;).

Alternative explanations for conflict adaptation effects have been presented including temporal learning theory, repetition priming and feature integration or feature binding (Puccioni & Vallesi, 2011; Schmidt, 2013; Schmidt, Notebaert, & Van Den Bussche, 2015; Schmidt & Weissman, 2016). These alternative explanations will receive greater attention in the Method and Discussion sections of this dissertation, but a brief outline will be presented here. Temporal learning theory suggests that individuals show conflict adaptation effects simply due to the phenomenon that individuals tend to vary response speed as a function of response speed on a previous trial (Grosjean, Rosenbaum, & Elsinger, 2001; Schmidt, 2013; Schmidt, Notebaert, & Van Den Bussche, 2015; Schmidt & Weissman, 2016). Puccioni and Vallesi (2011) have stated that Stroop tasks using only three colors were susceptible to repetition priming effects. With too few color options, repetitions and feature integration effects become unavoidable. To address this possible confound, Blais, Stefanidi, and Brewer (2014) demonstrated conflict adaptation while controlling for these effects using a four-choice vocal Stroop task that prevented repetitions of colors or features (parts of stimuli). Similar considerations need to be made in future studies of conflict adaptation effects. The design of the current study controlled for these confounds by

experimentally removing repetitions of colors or words in a modified Stroop task. Further detail can be seen in the Method section.

Cognitive Dysfunction in OCD

Individuals with OCD have deficits in inhibitory cognitive control processes that may contribute to their symptoms (Chamberlain, Blackwell, Fineberg, Robbins, & Sahakian, 2005). Specifically, individuals with OCD have difficulty inhibiting intrusive thoughts and shifting attention away from these intrusions. Non-symptomatic, first-degree relatives of individuals with OCD share this pattern of poor inhibition, cognitive inflexibility, and difficulty shifting attention (Chamberlain et al., 2007). Chamberlain and colleagues (2007) suggest that this cognitive inflexibility in individuals with OCD and their family members reflects an underlying, genetic predisposition to irregular neurocognitive function.

Aydin, Güleç and Öyekçin (2013) report that the two cognitive deficits in OCD that have the greatest clinical impact on overall cognitive functioning are executive dysfunction (including difficulties with cognitive control) and visuo-spatial memory impairment (see also Abramovitch, Abramowitz, & Mittelman, 2013). Aydin and colleagues (2013) concluded that although the executive dysfunction in individuals with OCD has been well documented, the relationship between the clinical features of the disorder and cognitive functions has not been elucidated. Therefore, Aydin and colleagues (2013) called for studies that combine both neuropsychological testing and brain imaging to address this gap in the research.

The Evaluative Component of Cognitive Control in OCD. Over-activation of the ACC and related areas is associated with obtrusive thoughts and compulsive, repetitive behaviors in OCD (Grundler, Cavanagh, Figueroa, Frank, & Allen, 2009). Maltby, Tolin, Worhunsky, O'Keefe, and Kiehl (2005) considered the evaluative component of cognitive processing in both

psychiatrically-healthy control participants and participants with OCD using a Go/No-Go task. They demonstrated significantly increased activation of the caudal and rostral ACC, left lateral orbito-frontal cortex, left lateral prefrontal cortex, bilateral posterior cingulate cortex, caudate, and thalamus in response to the commission of errors and conflict-related tasks (Maltby, Tolin, Worhunsky, O'Keefe, & Kiehl, 2005).

Mathews, Perez, Delucchi, and Mathalon (2012) conducted a meta-analytic review of the research literature on the ERN in OCD. They quantitatively demonstrated a significant mean difference (Cohen's d) between healthy control ERN amplitudes and OCD ERN amplitudes showing enhanced ERN amplitudes in individuals with OCD compared to the control participants ($d = -0.62$, $p = 0.001$; Mathews, Perez, Delucchi, & Mathalon, 2012). This initial result, however, had a good deal of heterogeneity due to task type. When the meta-analysis was limited to studies that used response conflict tasks (e.g. flanker, Stroop, GoNoGo), the enhancement of ERN amplitudes in individuals with OCD relative to healthy controls was even more pronounced, ($d = -0.86$, $p < 0.001$) and was not significantly heterogeneous (Mathews, Perez, Delucchi, & Mathalon, 2012). According to Cohen's criteria for interpreting mean difference effect sizes (Cohen 1988), this effect for OCD on ERN amplitudes in response to conflict tasks was large with individuals with OCD showing increased ERN amplitudes relative to psychiatrically-healthy controls.

Researchers in the field of psychosurgery have also demonstrated the important role of the ACC in severe, treatment-refractory cases of OCD. Specifically, neuroablative surgeries (including: capsulotomy, subcaudate tractotomy, limbic leucotomy, and stereotactic cingulotomy; Shah, Pesiridou, Baltuch, Malone, & O'Reardon, 2008), can be highly effective, last-resort treatments for individuals struggling with severe obsessive-compulsive symptoms

(Cosgrove 2000; Eljamel, 2008; Cosgrove & Rauch, 2003; Price, 2001). The behavioral and functional gains from stereotactic ablation of the ACC in individuals with severe OCD are both significant and long-lasting due to the permanent nature of the procedures (Dougherty et al., 2002; Sheth et al., 2013;). For example, Sheth and colleagues (2013) showed that thirty-five percent of individuals with OCD who underwent cingulotomy demonstrated a full response to treatment (as measured by the Yale-Brown Obsessive Compulsive Scale [YBOCS] and the Beck Depression Inventory [BDI]). After follow-up repeat cingulotomy, this rate rose to forty-seven percent with an additional twenty-two percent reporting partial improvements in obsessive-compulsive and depressive symptoms. Thus, surgically-induced reductions in ACC activation may be associated with reduced symptom severity for many individuals with OCD. This provides support for the idea that relative hyperactivity of the ACC may play an important contributory role in the symptoms of the disorder.

Ursu, Stenger, Shear, Jones, and Carter (2003) also demonstrated hyperactivity in the ACC in individuals with OCD relative to healthy controls in response to both errors and high-conflict correct trials in a modified continuous performance task. Their task consisted of single letters presented briefly every twelve seconds. Participants were instructed to respond with a button press to every “X” target preceded by an “A” cue. Participants were to respond to all other stimuli by pressing an alternate “non-target” button. Trials with the correct cue but the incorrect target (e.g. “A” followed by “Y”) or incorrect cues but correct targets (e.g. “B” followed by “X”) elicited conflict. This task allowed the researchers to evaluate ACC activity in response to both errors in performance and stimulus-related conflict. As expected, Ursu and colleagues (2003) found significantly increased ACC activation in individuals with OCD relative to healthy controls following errors. They also demonstrated greater conflict-related ACC activity in

individuals with OCD relative to healthy controls for “X” targets preceded by “B” compared with “X” targets preceded by “Y”. Thus the hyperactivity of the evaluative component of cognitive control does not appear to be limited to the detection and processing of errors in OCD, but encompasses a broader function of conflict monitoring.

In a study of pediatric OCD, Huyser, Veltman, Wolters, de Haan, and Boer (2011) provided evidence that hyperactivity of the ACC may be a trait characteristic for OCD patients that does not change with reductions in symptoms following cognitive-behavioral therapy (CBT). Huyser and colleagues (2011) administered an arrow flanker task to twenty-five pediatric outpatients with OCD before and after participation in sixteen manualized sessions of CBT. Although CBT resulted in significant symptom reductions for OCD patients as measured by the child version of the YBOCS, ACC activity following errors was not reduced post-treatment. Relative ACC-hyperactivity in OCD has also been shown to be unresponsive to pharmacological treatment (Stern et al., 2010). Aouizerate and colleagues (2004) provided a review of the literature on the role of the ACC in the pathophysiology of OCD. They concluded that the dysfunctional activity of the ACC in OCD could explain not only hyperactive conflict monitoring processes, but also the mismanagement of the emotional consequences of performance. In summary, the ACC appears to be hyperactive in individuals with OCD compared to psychiatrically-healthy individuals. Dysfunctional hyperactivity of the ACC in people with OCD is a stable trait even following successful treatment, and it may be an underlying factor that contributes to many OCD-related symptoms and cognitive difficulties.

The Regulative Component in OCD. Individuals with OCD also show deficits in executive/regulative control associated with dlPFC activity including poor planning, task-switching, inhibition, and initiation (Olley, Malhi, & Sachdev, 2007; van den Heuvel et al.,

2005). General reductions in dlPFC activation in OCD have been documented in the neuroimaging literature and may explain the extreme difficulty individuals with the disorder experience in trying to regulate their compulsive behaviors (Aouizerate et al., 2004). For example, Martinot and colleagues (1990) demonstrated relative hypoactivity of the dlPFC in individuals with OCD compared to healthy controls in response to a Stroop task. However, Schlösser and colleagues (2010) demonstrated increased bilateral activation of the dlPFC (as well as the dorsal ACC) in response to incongruent vs. congruent Stroop trials in individuals with OCD relative to healthy controls. Schlösser and colleagues (2010) also used dynamic causal modeling to demonstrate greater connectivity from the dorsal ACC to the left dlPFC in individuals with OCD relative to healthy controls on incongruent trials suggesting increased activity of both the evaluative and regulative components of cognitive control. Therefore, it is important to consider dlPFC activity as a function of congruency as done in the current dissertation using conflict adaptation.

One possible explanation for the seemingly contradictory findings of the Martinot and colleagues (1990) and Schlösser and colleagues (2010) studies is that regulative cognitive control processes may be differentially impacted by certain dimensions of obsessive-compulsive symptoms. For example, Hough and colleagues (2016) showed that individuals with hoarding disorder showed increased right dlPFC and ACC activation on a Go/No-Go task relative to healthy control subjects. In this study, individuals with hoarding disorder also showed greater right dlPFC activation (but not ACC activation) relative to individuals with OCD who did not have hoarding symptoms. Individuals with OCD without hoarding symptoms did not differ significantly from healthy controls on the same Go/No-Go task. Hough and colleagues (2016) also administered a Stroop task in the same experiment showing no brain activation differences

between non-hoarding OCD participants and healthy controls during conflict processing (presentation of congruent vs. incongruent trials). Individuals with hoarding disorder, however, showed a relative decrease in medial prefrontal cortex activation relative to individuals with non-hoarding OCD. Thus, future researchers will need to carefully consider the differing contributory processes underlying the symptoms of OCD that result in abnormal regulative cognitive control in OCD.

Seo and colleagues (2016) showed that repetitive transcranial magnetic stimulation over the right dlPFC resulted in OCD symptom relief as well as depressive symptom relief for patients with OCD after three weeks of treatment. They suggested that increased dlPFC activation might have activated inhibitory pathways to downregulate hyperactive orbitofrontal functioning in OCD; however, their results were preliminary and based on a relatively small sample (27 total participants). In light of the hypothesized cognitive control feedback loop between the dlPFC and the ACC described above, it is also possible that a similar increase in dlPFC activity could result in downregulation of relative hyperactivity of the ACC in OCD.

In summary, the existing literature provides no consensus on whether dlPFC activation is generally increased (as suggested by Martinot et al., 1990; Seo et al. 2016) or decreased (as suggested by Schlösser et al., 2010) in individuals with OCD relative to healthy controls during conflict processing. Schlösser and colleagues (2010) concluded that theories described in the current literature about the exact mechanisms of the ACC and dlPFC feedback loop must be regarded as preliminary until further evidence is presented. The present dissertation was designed to help contribute to this area of inquiry.

Conflict Adaptation in OCD. An important concept underscoring both the evaluative and regulative components of cognitive control is conflict adaptation. As discussed above,

conflict adaptation is dynamic responding to high-conflict cues that require the recruitment of greater attentional resources (Botvinick, Braver, Barch, Carter, & Cohen, 2001). Conflict adaptation measured by response times, has been used to dissociate the regulative and evaluative components in pediatric OCD (Liu, Gehring, Weissman, Taylor, & Fitzgerald, 2012). Liu and colleagues evaluated post-error slowing and conflict adaptation in a pediatric sample with OCD relative to psychiatrically-healthy controls. Liu and colleagues' (2012) experimental task was a multisource interference task in which participants were instructed to respond to the unique digit in a set (using digits 1, 2, and 3). Participants were to press a separate button for 1, 2, or 3 with their index, middle, and ring fingers respectively. Three-digit numbers (e.g. 121, 332, 133, 112) were presented to participants. Congruent trials consisted of numbers in which the unique digit was aligned with the left-to-right order of buttons (i.e. 1xx, x2x, xx3). Incongruent trials consisted of numbers with the unique digit was not aligned with the left-to-right order of buttons (e.g. x1x, 2xx, 3xx).

Similar to Kerns et al. (2004), Liu and colleagues (2012) were interested in sequence effects of trial congruency (iI, iC, cI, cC), but were also interested in post-error slowing effects. Post-error slowing refers to the tendency for individuals to slow behavioral responses in order to increase accuracy following the commission of errors (Botvinick, Braver, Barch, Carter, & Cohen, 2001). Liu et al. (2012) observed that response time conflict adaptation was present in healthy controls, but not in youth with OCD. Specifically, healthy controls tended to respond faster to iI trials relative to cI trials, whereas OCD participants tended to respond slightly slower (though not significantly so) to iI trials relative to cI trials. The authors concluded that there may be a failure in the cognitive control feedback loop between the lateral prefrontal cortex and the ACC in youth with OCD. We hypothesized that this same conflict-adaptation effect

demonstrated by Liu and colleagues (2012) in pediatric samples would generalize to the adult OCD population.

Recent research on adults with OCD, however, was not concordant with the results of Liu and colleagues (2012). Marsh and colleagues (2014) compared both behavioral and fMRI BOLD responses to conflict between twenty-two adults with OCD and twenty-two psychiatrically healthy controls. Contrary to the results of Liu et al. (2012), they did not find any behavioral response time (RT) or error rates differences between groups. Individuals with OCD did show significantly greater BOLD activation in the putamen, insula, and inferior frontal gyrus relative to control participants on conflict-laden trials. Interestingly, this finding was not driven primarily by the conflict on the current trial, but rather by the sequencing of trials (i.e., the alternation of congruent and incongruent trials). Conflict adaptation as it is defined in the current study and in the existing literature (Kerns et al., 2004; Liu et al., 2012) was not directly measured by Marsh and colleagues (2014). In the absence of an adult study of conflict adaptation in OCD, we expected that the results from the pediatric OCD sample (Liu et al., 2012) would provide the most reliable prediction of conflict adaptation in adults with OCD, though the findings of Marsh and colleagues (2014) provide some potential evidence against this hypothesis.

A recent study of seventy adults with OCD and seventy matched healthy control participants provides further contrast with the pediatric findings of Liu and colleagues (2012; Riesel, Klawohn, Kathmann, & Endrass, 2017). This study was published following data collection and analysis of the current dissertation, and thus was not considered in the hypotheses or current aims. Riesel and colleagues (2017) found increased anterior N2 amplitudes in individuals with OCD relative to controls that were particularly pronounced in trials preceded by a trial of different congruency (i.e. cI, iC trials). The anterior N2 is a negative-going waveform

component of the event-related potential that is thought to reflect cognitive control processes such as processing no-go trials on a Go/NoGo task (for review see Folstein & Van Petten, 2008). Riesel and colleagues (2017) also showed increased response time conflict adaptation in individuals with OCD relative to healthy controls. They concluded that individuals with OCD have hyperactive conflict monitoring processes that could be related to general distress and obsessive-compulsive symptoms. Thus, contrasting evidence from two studies of congruency sequence effects in adult OCD (Marsh et al., 2014; Riesel, Klawohn, Kathmann, & Endrass, 2017) and a study of pediatric OCD (Liu et al., 2012) suggest important neurological differences between pediatric and adult OCD.

Cognitive Control Dysfunction and Quality of Life in OCD

To date, conflict adaptation has not been specifically considered as a contributor to the diminished quality of life seen in individuals with OCD. However, there is evidence to suggest that cognitive control dysfunction generally may contribute to poor quality of life. Ursu, Stenger, Shear, Jones, and Carter (2003) demonstrated a positive relationship between increased ACC conflict- and error-related activity and obsessive-compulsive symptom severity as measured by total scores on the YBOCS in individuals with OCD ($r = .51, p = .06$; $r = .46, p = .08$ respectively). This study may have lacked the statistical power to detect significant relationships between ACC activity and obsessive-compulsive symptom severity; however, the correlation may also be an overestimate due to sampling error (total OCD $n = 11$, total healthy control $n = 13$). In the absence of further evidence, however, Ursu and colleagues (2003) have provided preliminary evidence for an association between ACC activity and OCD symptom severity.

Ozdemir, Atmaca, Yildirim, and Gurok (2013) demonstrated no structural gray matter differences in the dlPFC between psychiatrically-healthy controls and individuals with OCD;

however, Alvarenga and colleagues (2012) provided evidence that gray matter differences in the dlPFC may exist not as a function of the disorder alone, but of symptom dimensions within the disorder. Alvarenga and colleagues (2012) examined gray matter differences in 38 treatment-naïve individuals with OCD to determine whether certain obsessive-compulsive symptom dimensions correlated with structural volumes in the brain. They found that sexual/religious obsessions were positively correlated with gray matter volume of the right dlPFC and negatively correlated with bilateral gray matter volumes of the ACC. Other obsessive-compulsive symptom dimensions (aggression, hoarding, contamination, and symmetry) were found to correlate with gray matter volumes of various regions (e.g., orbitofrontal cortex & right parahippocampal gyrus), but not with the ACC or the dlPFC (Alvarenga et al., 2012).

Obsessive-compulsive symptom severity has been shown to be related to quality of life in individuals with OCD (Coluccia et al., 2016; Masellis et al., 2003). Thus, if there is indeed a relationship between ACC and dlPFC activity and severity of obsessive-compulsive symptoms, there may also be a relationship between ACC and dlPFC activity and quality of life. The World Health Organization defined quality of life as an individual's perception of his or her health in four major domains: physical well-being, cognitive well-being, psychological well-being, and social well-being (World Health Organization, 1995). Although other definitions of quality of life have been described, we operationalized quality of life according to its definition by the World Health Organization (1995) in order to be consistent with previous research on quality of life in OCD. Quality of life is impacted for individuals suffering from OCD due to its chronic, disabling course which affects the well-being of both the afflicted individual and their families (Cicek, Cicek, Kayhan, Uguz, & Kaya, 2013; Subramaniam et al., 2013). In their meta-analysis, Coluccia and colleagues (2016) demonstrated a moderate effect size for OCD on quality of life.

Specifically, individuals with OCD show diminished quality of life relative to psychiatrically-healthy controls. This effect was moderated by sex (studies with greater proportions of female patients with OCD showed worse quality of life) and OCD symptom severity (patients with less severe symptoms reported significantly lower quality of life outcomes). The authors speculated that patients with mild symptoms may have reported worse quality of life than patients with more severe symptoms due to relatively poor insight in the patients with severe symptoms.

It remains unclear whether quality of life is most negatively impacted by the severity of obsessions or by the severity of compulsions. Masellis and colleagues (2003) demonstrated a significant relationship between obsessions, but not compulsions and quality of life. However, Stengler-Wenzke, Kroll, Riedel-Heller, Matschinger, and Angermeyer (2007) reported the opposite effect with compulsions rather than obsessions being associated with significant declines in quality of life in individuals with OCD. Thus, the exact means by which symptoms of OCD diminish quality of life are unknown.

The negative impact of OCD on quality of life is further compounded by the relatively frequent presence of additional comorbid psychiatric diagnoses (Macy et al., 2013). Quality of life in OCD has primarily been assessed using the following measures: The Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q; Endicott, Nee, Harrison, Blumenthal, 1993); the World Health Organization Quality of Life Brief Measurement Tool (WHOQOL-BREF; World Health Organization, 1995); and the Health-related Quality of Life Questionnaire (von Lehe et al., 2006). In assessing specific domains of quality of life in OCD, Moritz and colleagues (2005) demonstrated significant correlations between total YBOCS scores and the following domains of quality of life: physical functioning, vitality, social functioning, role-emotional, and mental health. Cicek, Cicek, Kayhan, Uguz, and Kaya (2013) also showed

significant correlations between YBOCS total scores and the quality of life for caregivers of individuals with OCD in the following domains: physical health ($r = -.33$), psychological health ($r = -.37$), social relationships ($r = -.33$), and environment ($r = -.39$).

In summary, OCD symptom severity is significantly related to quality of life for both individuals with OCD and their caretakers. There is also preliminary evidence for a possible relationship between hyperactivity of the ACC and OCD symptom severity (see Ursu et al. 2003); however, this effect may be overstated. In the current dissertation, we sought to describe the correlational relationships among OCD-related ACC activity, dlPFC activity, OCD symptom severity, and OCD-related quality of life. In doing so, we hope to meaningfully describe some of the neuropathological underpinnings of OCD-related declines in quality of life. The current study, therefore, includes the following specific aims:

Aims of the Current Study

Aim 1. Determine if there are differences between OCD and psychiatrically-healthy control participants on behavioral manifestations (median response times and mean error rates) of conflict adaptation.

Hypothesis 1. Individuals with OCD will have greater difficulty adjusting performance to adapt to task demands. This will be manifest in a median response time interaction between group, current trial congruency, and previous trial congruency with decreased calculated (see formula in method below) conflict adaptation times in participants with OCD relative to psychiatrically-healthy control participants. This will also be manifest in a similar interaction for error rates and decreased calculated error conflict adaptation rates in OCD relative to healthy controls.

Aim 2. Dissociate the neural manifestations of evaluative and regulative components of cognitive control in individuals with OCD and compare cognitive control component processes to psychiatrically-healthy control participants.

Hypothesis 2. Individuals with OCD will show relatively greater conflict detection compared to controls, and will subsequently show impairments in their ability to adjust performance to adapt to task demands. These alterations in cognitive control will be seen in fMRI as relative hyperactivity of the ACC and relative hypoactivity of the dlPFC compared to healthy control participants in response to conflict. Individuals with OCD will also show diminished conflict adaptation relative to healthy controls analogous to that seen in behavioral data. These differences will be particularly evident in calculated conflict adaptation beta weights and will correspond to indices of conflict adaptation in the behavioral data.

Aim 3. Assess the possible relationship between cognitive control dysfunction and quality of life in individuals with OCD.

Hypothesis 3. We expect to see a convergence of multiple sources between quality of life and conflict adaptation. Specifically, we hypothesize that quality of life will be associated with all of the following: response time conflict adaptation, error rate conflict adaptation, ACC conflict adaptation, dlPFC conflict adaptation, and decreased obsessive-compulsive symptoms. Additionally, decreased conflict adaptation (as manifest in both behavioral and fMRI indices) will be associated with increased symptoms of OCD and deficits in neuropsychological functioning.

Method

The complete data set and fMRI scripts can be found at <https://osf.io/5u8nu/> on the Open Science Foundation.

Participants

Participants included 20 individuals with OCD (males = 13) and 20 psychiatrically-healthy controls (males = 13) matched for age and years of education. Participants in both groups were generally high-functioning. For the OCD group, eighteen individuals reported White/Caucasian ethnicity and two individuals reported Hispanic ethnicity. Similarly, for the control group eighteen individuals reported White/Caucasian ethnicity, one individual reported mixed ethnicity, and one individual reported Pacific Islander ethnicity. Sixteen individuals in the OCD group reported that they were full-time students, whereas thirteen individuals in the control group reported that they were full-time students ($X^2 = 1.13$, $df = 1$, $p = .29$). With the exception of one individual in the control group, all participants denied any history of tobacco or alcohol use. The individual who did report alcohol use reported consuming only one alcoholic beverage per week. One individual in the OCD condition was excluded from all fMRI analyses due to excessive motion artifact. This individual had ten motion events (defined as $> .6\text{mm}$ translation or $>.3^\circ$ rotation). There is no established rule for quality control of motion events; however, it has been demonstrated that even with advanced motion correction techniques, the influence of head motion cannot be entirely controlled for; therefore, in cases of excessive motion events, the best course of action is to disregard the entire scan (Goto et al., 2016; for further discussion of motion artifact correction see Poldrack, Mumford, & Nichols, 2011). The average age of included participants was 23.0 years (± 3.1) and the average years of education of included participants was 14.8 years (± 1.6). There were no significant differences between the OCD and control groups in age or in years of education (p values $> .05$; see Table 1 for all values). In the OCD group, total scores on the YBOCS-2 averaged 18.65 (± 7.69 ; min = 9, max = 31) indicating that our participants' symptom severity was at least one standard deviation below the normed means for individuals with OCD (for normative data see Storch et al. 2010; Wu, McGuire,

Hornig, & Storch, 2016). Only two of our participants with OCD were treatment naïve. Most of our participants with OCD had a history of past and current treatment for their OCD symptoms (medications: past [n = 2]; current [n = 13]; psychotherapy: past [n = 11]; current [n = 3]).

Individuals with OCD reported taking the following psychotropic medications at the time of their participation in the study: fluoxetine (n = 5), sertraline (n = 3), escitalopram (n = 2), paroxetine (n = 1), bupropion (n = 1), fluvoxamine (n = 1), and methylphenidate (n = 1, the participant taking methylphenidate denied any diagnosis of attention-deficit/hyperactivity disorder). All but one of the participants were right-handed (there was one left-handed individual in the OCD group) to reduce heterogeneity due to possible differences in brain organization from individuals who are left handed (Estévez-González, García-Sánchez, & Junqué, 1996).

Participants were native English speakers due to studied differences in performance on neuropsychological tests between native and non-native English speakers and the lack of standardized neuropsychological tests across multiple languages (Kisser, Wendell, Spencer, & Waldstein, 2012). Other exclusionary criteria included: color-blindness as assessed by the Ishihara pseudoisochromatic plates (Ishihara, 1917; Ishihara et al., 2014) pregnancy (due to unknown potential risks associated with MRI), previous psychiatric diagnosis (for psychiatrically-healthy controls), alcohol abuse in the past year, current antiepileptic medication use, learning disorder, attention-deficit hyperactivity disorder, or any neurologic injury or disease such as traumatic brain injury, stroke, or epilepsy that could affect results.

Power Analysis

We conducted an *a priori* power analysis using G*Power 3 analysis software to determine the number of participants that would be necessary to detect the hypothesized effects (Faul, Erdfelder, Lang, & Buchner, 2007). Our analysis for conflict adaptation included two

groups with four factors (see below). As stated above, no studies have directly tested conflict adaptation effects using fMRI in individuals with OCD. Liu, Gehring, Weissman, Taylor, and Fitzgerald (2012), however, used conflict adaptation to examine conflict monitoring in response times in pediatric OCD. Although their study cannot provide estimates of effect sizes for OCD on brain activation in the ACC and dlPFC, their analysis of conflict adaptation response times is comparable to the analysis used in adults with OCD in the current study. Liu and colleagues (2012) reported an effect size of $F = 0.27$ for conflict adaptation between those with OCD and psychiatrically-healthy controls. Using this effect size, we completed a power analysis with alpha set to .05, estimated correlation between repeated measures set to .475, and power set to .90. This power analysis indicated that a total sample size of twenty-eight (fourteen per group) was required to detect the effects of interest. We ran forty participants (twenty in each group) to ensure adequate power for the study and to account for possible lost data due to equipment malfunction, excessive motion artifact, or other unexpected events (one participant was ultimately lost due to motion artifact as described above).

Procedure

The Brigham Young University (BYU) Institutional Review Board approved all study procedures. Each participant provided written informed consent before taking part in the study. An fMRI pre-screen provided by the BYU MRI Research Facility and required for all participants was initially administered to ensure that participants were eligible for participation and were not at risk during MRI procedures. A diagnostic/screening interview was then administered to all participants (see below) along with the Ishihara pseudoisochromatic plates to ensure participants were not colorblind (Ishihara, 1917; Ishihara, et al. 2014). Following pre-screening and interviewing, participants filled out several self-report questionnaires assessing

quality of life and behavioral/emotional functioning (described below). Next, research personnel administered a neuropsychological battery prior to structural scanning and completion of the fMRI task. The total average time required to run each participant was approximately 2.5 hours.

Diagnosis & Severity of OCD Symptoms

All participants had a diagnosis of OCD as provided by a medical or mental health practitioner in the community prior to enrolling in the study. Diagnosis of OCD was confirmed at the time of testing by a graduate student in clinical psychology according to DSM-IV criteria (American Psychiatric Association, 2000) using the MINI International Neuropsychiatric Interview (MINI; Sheehan et al., 1998). Sensitivity and specificity for diagnoses with the MINI of all disorders in a mixed sample of psychiatric patients and healthy controls is good or very good with the exception of poor sensitivity for agoraphobia (0.59; Lecrubier et al., 1997).

All healthy control participants meeting DSM-IV criteria (as assessed by the MINI) for a psychological disorder were excluded during prescreening (excluded for: depression/anxiety = 3, attention-deficit/hyperactivity disorder = 2). These participants were not run through the MRI protocol. OCD rarely occurs in isolation. Approximately 90% of individuals meeting DSM-IV criteria for OCD in their lifetime will also meet full criteria for at least one other lifetime disorder (Ruscio, Stein, Chiu, & Kessler, 2010). Ruscio and colleagues (2010) further reported that the majority of these comorbid disorders are anxiety disorders and mood disorders. Therefore, individuals in the OCD group with comorbid anxiety and mood disorders were not excluded from participation. All comorbid diagnoses (assessed using the MINI interview and previous professional diagnoses) were recorded for characterization of the sample and are presented below (see Psychiatric Data heading in the Results section).

Severity of obsessive-compulsive symptoms was assessed using the YBOCS-2 (Storch et al., 2010). The original YBOCS (Goodman et al., 1989) is considered the gold standard for assessment of the severity of obsessive-compulsive symptoms (Frost, Steketee, Krause, & Trepanier, 1995; Kim, Dysken, & Kuskowski, 1990). The YBOCS-2 is an updated, psychometrically-improved version of the original YBOCS that integrates avoidance into the scoring of the severity scale items. The creators of the YBOCS-2 revised the Severity Scale items (both content of the items and scoring framework) in order to improve upon problematic areas on the original YBOCS identified by psychometric studies of the measure (Storch et al., 2010). For example, Storch and colleagues (2010) cited Purdon and Clark (2000) as well as Rassin and colleagues (2000) for the removal of the Resistance to Obsessions item. They reported that this item was removed in the development of the YBOCS-2, because it was originally intended to be an index of psychological health, but actually proved to be associated with greater impairment in individuals with OCD. The YBOCS-2 has good psychometric properties with strong interrater reliability with an intraclass correlation coefficient (ICC) of .96, test-retest reliability ($ICC > .85$) and internal consistency (Cronbach's α ranges from .75 to .89; see Storch et al., 2010; Wu, McGuire, Horng, & Storch, 2016).

Questionnaire Measures

Quality of Life. Quality of life was assessed in all participants using the Q-LES-Q (Endicott, Nee, Harrison, & Blumenthal, 1993) and the WHOQOL-BREF (World Health Organization, 1995). The Q-LES-Q consists of ninety-three self-report items that comprise five subscales. Subscales for the Q-LES-Q include physical health, subjective feelings, leisure time activities, social relationships, and general activities. Each of the subscales has excellent internal consistency ($\alpha > .90$) and good test re-test correlations ($r = .63$ to $.89$; Endicott, Nee, Harrison, &

Blumenthal, 1993). The WHOQOL-BREF consists of twenty-six items comprising four subscales: physical health, psychological health, social relationships, and environment. Internal consistency for the WHOQOL-BREF is acceptable ($\alpha > .70$; World Health Organization, 1995).

Emotional and Behavioral Functioning. Emotional and behavioral functioning were assessed using the following questionnaires: Beck Depression Inventory-2nd Edition (BDI-2; Beck, Steer, & Brown, 1996); State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983); and the Behavior Rating Inventory of Executive Function for adults (BRIEF-A; Roth, Isquith, & Gioia, 2005). The BDI-2 is a twenty-one-item measure of the severity of several depressive symptoms experienced by a participant in the preceding two weeks. The BDI-2 has excellent internal consistency ($\alpha = .94$; Arnau, Meagher, Norris, & Bramson, 2001) and excellent test-retest reliability ($r = .93$; Beck, Steer, & Brown, 1996). The STAI consists of forty items designed to differentiate trait anxiety from state anxiety. The STAI has good internal consistency and good test-retest reliability ($\alpha = .89$; $r = .88$; Barnes, Harp, & Jung, 2002). The BRIEF-A was used to assess each participant's self-reported behavioral regulation and metacognition. The behavioral regulation scale for the BRIEF-A consists of five subscales including: inhibition, ability to shift attention, emotional control, self-monitoring, and initiation. The metacognition scale includes four subscales: working memory, planning and organizational ability, task monitoring, and organization of materials. The BRIEF-A has excellent internal consistency and test-retest reliability ($\alpha = .93$ to $.96$; $r = .94$; Roth, Isquith, & Gioia, 2005).

Neuropsychological Measures

A neuropsychological assessment battery was administered to all participants to determine whether study effects might be specific to deficits in cognitive control processes or to generalized decrements in cognitive functioning. The assessment battery for each participant

included the following tests: Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998), Wechsler Test of Adult Reading (WTAR; Wechsler, 2001), and the Trail Making Test Parts A and B (TMT-A, TMT-B; Reitan 1955; Reitan 1958).

The RBANS is useful for detecting major cognitive impairment and has good specificity for mild neurocognitive disturbance such as mild cognitive impairment (MCI). The RBANS is a practical and time-efficient screener (see Suhr, 2015) for major neurocognitive impairments. The RBANS has good test-retest reliability ($r = .88$) and high internal consistency (α between .86 and .94; Strauss, Sherman, & Spreen, 2006). To supplement RBANS, TMT-A and TMT-B were administered. The Trail Making Tests provide a rapid assessment of an individual's processing speed and attention switching ability (Reitan 1955; Reitan 1958). TMT-B has been shown to be sensitive to neurocognitive deficits in a variety of disorders (Strauss, Sherman, & Spreen, 2006).

Administration of the WTAR allows clinicians to accurately estimate an individual's intellectual functioning and served to determine if there were unexpected differences between OCD and control groups in overall intellectual capacities (Wechsler, 2001). The WTAR provides a stable measure of intellectual functioning that is minimally affected by neurological change or insult such as TBI (Green et al., 2008). We used this information to determine if groups were similar in estimated intelligence. All together, these measures provided a useful estimate of each individual's neuropsychological functioning across several domains.

Magnetic Resonance Imaging

All fMRI data were collected using a Siemens 3T Tim Trio scanner located at the BYU Magnetic Resonance Imaging Research Facility (BYU MRI RF) in Provo, Utah. All functional images were collected using echo planar imaging (EPI) that is sensitive to blood oxygenation level dependent (BOLD) contrast (TR = 2000ms, TE = 28ms, flip angle = 90°, matrix size =

64×64, FoV = 192mm × 192mm, slice thickness = 3mm, 39 slices, voxel size = 3× 3×3mm).

Slices were acquired in ascending alternating order oriented to the anterior commissure and posterior commissure.

Trained research personnel (Level III certified at the BYU MRI RF) placed participants in the scanner and positioned a twelve-channel Siemens phased array head coil prior to imaging. The following high-resolution sequences were collected for cortical reconstruction and subsequent structural analysis (not part of the current dissertation, except MP-RAGE): 3D MP-RAGE, 3D TSE T2-weighted, diffusion tensor imaging (DTI), and field map sequence for offline distortion correction. The MP-RAGE was used to localize functional activations. DTI acquisition were completed using a product single-shot, spin echo, EPI imaging pulse sequence with diffusion weighting as provided by the Siemen's group with the MRI scanner. Only the functional and MP-RAGE scans were used in the current dissertation, and all other scans were collected for use in follow-up studies.

Experimental fMRI Task

After structural scans were acquired, each participant completed a computerized single-trial Stroop task while fMRI data were collected (task was a near reproduction of the Stroop task in Kerns et al., 2004 with our task using 4 colors instead of 3 but similar to Kerns et al., 2004 in all other respects). The task consisted of 264 total trials divided into three blocks of eighty-eight trials each. Four monosyllabic colors and color-words were used as stimuli for the task (red, green, blue, and gray). Each stimulus was either congruent or incongruent. Congruent stimuli consisted of a color-word presented in its own color (e.g. "GREEN" written in green). Incongruent stimuli consisted of a color-word written in a different color (e.g. "GREEN" written in blue). Participants were instructed to respond to the color of the stimulus while ignoring the

color-word as quickly and accurately as possible via a button press of the right hand (right index finger = red, right middle finger = green, right ring finger = blue, right pinky = gray).

Puccioni and Vallesi (2011) identified a possible risk for a confounding repetition priming effect in a Stroop task using three colors (see also Schmidt, 2013 for a review of alternative explanations for conflict adaptation effects). When only three colors are used, it is impossible to have a transition of consecutive incongruent trials in which no feature is repeated (either the word or the color of the stimulus). In order to avoid this confound, we used four colors and grouped them into alternating pairs of RED/GRAY (the words “red” and “gray” displayed in either red or gray text) and BLUE/GREEN (the words “blue” and “green” displayed in either blue or green text; see Jimenez & Amavia, 2013; see also Blais, Stefanidi, & Brewer, 2014). Thus, no two consecutive trials included repetitions of either color or word.

Prior to being placed in the scanner, participants had to complete a practice Stroop task with 90% accuracy to ensure task understanding and correct color mapping of response buttons. Each trial was three seconds long. A color-word was shown for 1.5s followed by a fixation cross (+) for 1.5s (as in Kerns et al., 2004). Trials were presented in random order to allow for analyses despite the hemodynamic response not yet being fully resolved. In keeping with the previous version of the task (Kerns et al., 2004), the first and last four trials of each block were constrained to be congruent trials to increase conflict effects.

fMRI Data Preprocessing

All fMRI data were preprocessed and analyzed using Analysis of Functional Neuroimages (AFNI) software (Cox, 1996; Cox & Hyde, 1997; Gold et al., 1998). Functional scans were slice time corrected to account for differences in acquisition time within a given TR. In each block, functional images were motion corrected to align with the sixty-sixth acquisition

volume (middle of 132 total volumes per block). The functional images from each block were also corrected to align with the mean image of the first run. TRs with significant motion events (defined as $> .6\text{mm}$ translation or $> .3^\circ$ rotation) were excluded from the analysis. Additionally, TRs immediately preceding and following TRs with significant motion events were excluded from the analysis. Structural scans were coregistered with functional scans. Six motion regressors (three translations: x, y, and z; and three rotations: pitch, roll, and yaw) were created for use in single subject regression analyses. Additional regressors for scanner drift were also created for each block. Each block included behavioral regressors coding for trial type (congruent, incongruent) or for sequencing of trial types (cC, iC, cI, and iI), depending on the statistical model (see below for further details). These were modeled in a regression analysis by convolving a standard hemodynamic response function with a 1.5-second boxcar function. Resulting parameter estimates (beta) maps were smoothed with a 5mm full width half-max (FWHM) Gaussian kernel. The scans were then aligned to an in-house template in Talairach space (Talairach & Tournoux, 1988) using Advanced Neuroimaging Techniques (ANTs; Avants, Epstein, Grossman, Gee, 2008). Functional data were resampled to $3\times 3\times 3\text{mm}$. To control for type I error, we conducted Monte Carlo simulations (10,000) to determine a priori cluster extent thresholds using the AFNI program 3dClustSim. The voxel-wise threshold of $p < .02$ was set based on the volume of the whole-brain anatomical mask and a 5mm full width half-maximum (FWHM) spatial blur and a spatial extent threshold of forty contiguous voxels ($1,080\text{mm}^3$) to maintain a family-wise error rate of $p < .05$.

Statistical Analysis

We first tested hypothesis one that individuals with OCD would have greater difficulty adjusting their performance to adapt to task demands than control participants. This would have

been manifest in decreased conflict adaptation response times as well as decreased conflict adaptation error rates in individuals with OCD relative to healthy controls. In replication of the analysis conducted by Liu and colleagues (2012), we conducted a 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) repeated measures analysis of variance (ANOVA) on median response times. We used median response times rather than means because of the tendency for response times to be positively skewed and for the mean to be heavily influenced by outliers (Ratliff, 1993). This decision was made prior to conducting the response time analysis as described below. We checked the response time distributions for normality and found that median (p values: $cC = .25$, $iC = .50$, $cI = .12$, $iI = .82$) response times were normally distributed for all of the trial types. Partial η^2 was reported as an estimate of effect size for all repeated measures ANOVA analyses.

Error rates (percentages of incorrect responses) were also considered in a parallel 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) repeated measures ANOVA. Error rates were calculated on an individual basis as a percentage of errors made on each type of trial (cC , iC , cI , and iI). We checked the error rates distributions for normality and found that error rates for cC , cI , and iI trials were significantly skewed (p values: $cC < .01$, $cI = .02$, $iI < .01$). There was also a trend for the distribution of error rates on iC trials to be skewed, but this was not significant ($p = .09$). To address this non-normality in the error rates, the individual data for all four trial types were square-root transformed prior to the statistical analyses below. This transformation eliminated all significant skewing (p values: $cC = .37$, $iC = .30$, $cI = .16$, $iI = .58$) from the error rates for all four trial types.

Mean conflict adaptation effects were calculated for both behavioral and fMRI data (response times and beta weights from differing trial types respectively) using the following formula: (see Clayson & Larson, 2012; Nieuwenhuis et al., 2006; van Steenbergen, Band, & Hommel, 2010).

$$RT\text{Conflict Adaptation} = (\text{Median } cI \text{ RT} - \text{Median } cC \text{ RT}) - (\text{Median } iI \text{ RT} - \text{Median } iC \text{ RT})$$

$$fMRI \text{ Conflict Adaptation} = (cI \text{ beta weights} - cC \text{ beta weights}) - (iI \text{ beta weights} - iC \text{ beta weights})$$

We also calculated mean conflict adaptation effects for error rates using the same formula.

Our second hypothesis stated that individuals with OCD would show hyperactive conflict detection and subsequent impairment in their ability to adapt to task demands. This would have been manifest by increased activation of the ACC and decreased activation of the dlPFC on high-conflict trials in participants with OCD relative to controls. To test this hypothesis, we first conducted a contrast between current congruent and current incongruent trials to test whether the manipulation had produced the expected Stroop effect for incongruent relative to congruent trials. Second, we conducted a 2-Group (OCD, control) x 2-Current Trial Congruency (congruent, incongruent) repeated measures ANOVA to test whether the Stroop effect differed by group.

Next, we conducted a 2-Current Trial Congruency (congruent, incongruent) x 2-Previous Trial Congruency (congruent, incongruent) repeated measures ANOVA to test for conflict adaptation effects collapsed across group. For this model, we originally used the same thresholds as in other analyses (voxel-wise $p < .02$ and $k > 40$ contiguous voxel spatial extent). This model produced ten significant clusters with the largest being about three-thousand voxels. For improved interpretability and given the robust findings, we then applied a more stringent

threshold ($p < .001$, $k > 30$ voxels) to provide more specificity for areas of differential activation. We did not use this more stringent threshold for any of the other models.

Finally, we conducted a 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) whole-brain voxel-wise repeated measures ANOVA to determine how conflict adaptation effects (effects of previous and current trial congruency) differed between groups. This 3-way ANOVA was conducted separately from the 2-Group (OCD, control) x 2-Current Trial Congruency (congruent, incongruent) ANOVA, as well as from the 2- Current Trial Congruency (congruent, incongruent) x 2-Previous Trial Congruency (congruent, incongruent) ANOVA, because of the influence of including Previous Trial Congruency or Group factors in the model on the hemodynamic response function.

We tested our third hypothesis that quality of life would be negatively associated with indices of conflict adaptation and severity of OCD symptoms using zero-order correlations. We also tested the relationships among indices of conflict adaptation, neuropsychological measures, and psychiatric measures using zero-order correlations. To reduce the number of correlations and Type I error, all correlational analyses were restricted to outcomes that differed significantly by group in the analyses for aims one and two (as per Table 1 and Table 2). In addition, we adjusted our p value threshold to $< .01$ for all zero-order correlations to better control for Type I error.

Table 1. Demographics and Psychiatric Data

	Control Group ($n = 20$)	OCD Group ($n = 20$)	t score ($df = 39$)	Cohen's d	p value
Average Age (Years)	23.00 (± 2.96)	23.95 (± 3.38)	0.05	0.02	0.96
Average Education (Years)	14.95 (± 1.54)	14.60 (± 1.64)	0.70	0.22	0.49
YBOCS-2: Obsessions	0.95 (± 1.96)	9.35 (± 4.13)	-8.21	2.60	$< 0.01^*$
YBOCS-2: Compulsions	0.85 (± 1.63)	7.60 (± 3.02)	-8.80	2.78	$< 0.01^*$
YBOCS-2: Total Score	1.80 (± 3.33)	18.65 (± 7.69)	-9.00	2.84	$< 0.01^*$
BDI-2: Total Score	2.45 (± 3.15)	13.65 (± 11.79)	-4.10	1.30	$< 0.01^*$
STAI: State Score	27.85 (± 6.76)	39.60 (± 13.57)	-3.47	1.10	$< 0.01^*$
STAI: Trait Score	31.20 (± 6.64)	47.00 (± 13.79)	-4.62	1.46	$< 0.01^*$

* p value ≤ 0.01 ; OCD = obsessive-compulsive disorder; YBOCS-2, Yale-Brown Obsessive Compulsive Scale, second edition; BDI-2 = Beck Depression Inventory, Second Edition; STAI = State-Trait Anxiety Inventory

Table 2. Neuropsychological Testing and Quality of Life Results

Neuropsychological Measures	Control Group (n = 20)	OCD Group (n = 20)	t score (df = 39)	Cohen's d	p value
BRIEF-A: BRI	42.35 (\pm 5.87)	53.00 (\pm 11.07)	-3.80	1.20	< 0.01**
BRIEF-A: MI	46.85 (\pm 6.40)	55.00 (\pm 12.13)	-2.66	0.84	0.01**
BRIEF-A: GEC	44.50 (\pm 5.94)	54.40 (\pm 12.09)	-3.29	1.04	< 0.01**
RBANS: Total Scale	105.80 (\pm 14.70)	101.20 (\pm 11.65)	1.10	0.35	0.28
RBANS: Imm. Mem. Scale	106.40 (\pm 19.87)	100.10 (\pm 13.38)	1.18	0.37	0.25
RBANS: Vis./Constr. Scale	97.95 (\pm 13.47)	101.40 (\pm 17.81)	-0.69	0.22	0.49
RBANS: Language Scale	107.25 (\pm 15.55)	100.35 (\pm 17.04)	1.34	0.42	0.19
RBANS: Attention Scale	105.85 (\pm 12.75)	101.10 (\pm 14.30)	1.11	0.35	0.27
RBANS: Del. Mem. Scale	103.05 (\pm 10.98)	102.85 (\pm 11.21)	0.06	0.02	0.95
WTAR: Standard Score	115.00 (\pm 6.58)	108.80 (\pm 10.06)	2.31	0.73	0.03*
Trails A (z)	0.92 (\pm 0.39)	0.60 (\pm 0.68)	1.87	0.59	0.07
Trails B (z)	0.70 (\pm 0.56)	0.40 (\pm 0.80)	1.34	0.42	0.19
Stroop: Word (T)	51.70 (\pm 7.93)	52.55 (\pm 11.62)	0.27	0.09	0.79
Stroop: Color (T)	50.50 (\pm 6.11)	46.60 (\pm 9.34)	-1.56	0.49	0.13
Stroop: Color-Word (T)	58.65 (\pm 11.75)	54.20 (\pm 10.24)	-1.28	0.40	0.21
Stroop: Interference (T)	59.85 (\pm 10.04)	56.65 (\pm 6.49)	-1.20	0.38	0.20
Quality of Life Measures					
Q-LES-Q: Total Score	82.76 (\pm 8.32)	73.83 (\pm 14.26)	2.44	0.77	0.02*
WHOQOL-BREF: Physical	18.20 (\pm 1.95)	16.03 (\pm 3.03)	2.70	0.85	0.01**
WHOQOL-BREF: Psych.	16.57 (\pm 2.02)	13.77 (\pm 3.17)	3.33	1.05	< 0.01**
WHOQOL-BREF: Social	16.13 (\pm 3.69)	14.87 (\pm 3.97)	1.04	0.33	0.30
WHOQOL-BREF: Enviro.	15.71 (\pm 1.53)	14.44 (\pm 1.75)	2.42	0.77	0.02*

* p value ≤ 0.05 ; ** p value ≤ 0.01 ; OCD = obsessive-compulsive disorder; BRIEF-A = Behavior Rating Inventory of Executive Functioning, Adult version; BRI = Behavioral Rating Index; MI = Metacognitive Index; GEC = General Executive Composite; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; WTAR = Wechsler Test of Adult Reading; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire; WHOQOL-BREF = World Health Organization Quality of Life Brief Measurement Tool

Results

Psychological Data & Quality of Life

Psychiatric Data. Psychological diagnoses using the MINI showed that all participants in the OCD group met criteria for a current diagnosis of OCD. Of these participants, nine also met criteria for generalized anxiety disorder (45%), three met criteria for either a current or past major depressive disorder (15%), one met criteria for post-traumatic stress disorder (5%), and

one met criteria for social anxiety disorder (5%). Participants in the control group did not meet criteria for any psychological disorders.

As expected, individuals with OCD scored significantly higher than controls on the YBOCS-2, a measure of OCD severity (see Table 1). Total scores on the YBOCS-2 for individuals with OCD had a mean of 18.7 (\pm 7.7) indicating that most of these participants were experiencing mild-to-moderate OCD symptoms. Participants with OCD also scored significantly higher on the BDI-2 relative to the age-matched control participants indicating relatively elevated symptoms of depression in the OCD group. Furthermore, individuals with OCD scored significantly higher than control participants on both state and trait anxiety as measured by the STAI. Taken together, these results indicate that individuals with OCD had significant elevations in obsessive-compulsive symptoms, depressive symptoms, trait anxiety, and state anxiety relative to healthy controls.

Neuropsychological Functioning. Between-groups comparisons of neurocognitive domains generally did not show significant differences (Table 2). Test scores that did not differ between groups included the overall RBANS cognitive functioning score, all RBANS domain scores, Trail Making Tests A & B, and the Stroop Color-Word Test (see Table 2). There was, however, a significant difference between groups for WTAR standard scores, with individuals with OCD performing slightly below control participants. Scores on the WTAR for both groups were generally in the above average range for their respective ages (Wechsler, 2001). On a survey measure of executive functioning (BRIEF-A), individuals with OCD reported significantly greater perceived and self-reported difficulties in both behavioral and metacognitive domains of executive functioning as well as in executive functioning generally (see Table 2). In summary, individuals with OCD and healthy control participants differed only in estimated

intellectual functioning and self-reported executive functioning as measured by the WTAR and BRIEF-A, respectively.

Quality of Life. On the WHOQOL-BREF and the Q-LES-Q questionnaires, individuals with OCD rated their overall quality of life as lower than the control participants (see Table 2). Individuals with OCD showed specific comparative deficits in the following domains of quality of life: physical health, psychological wellbeing, environmental factors, and overall quality of life. No significant between-groups differences were seen in the social relationships scale of the WHOQOL-BREF.

Behavioral Results

Response Time Analysis. Grand mean (mean of medians) response times for the four types of trial (cC, iC, cI, and iI) by group can be seen in Table 3 (see also Figure 1). The Stroop effect (incongruent > congruent; main effect of current trial congruency) was significant and had a large effect size with $F(1,38) = 94.25, p < .001, \eta_p^2 = .71$. The main effect for previous trial congruency was not significant, $F(1,38) = 0.04, p = .84, \eta_p^2 = 0.001$. The interaction effect between current trial congruency and group was not significant, $F(1,38) = 0.01, p = .93, \eta_p^2 = .00$, suggesting that the Stroop effect did not differ by group. The interaction effect between previous trial congruency and group was also not significant with $F(1,38) = 1.23 (p = .27, \text{partial } \eta_p^2 = .03)$.

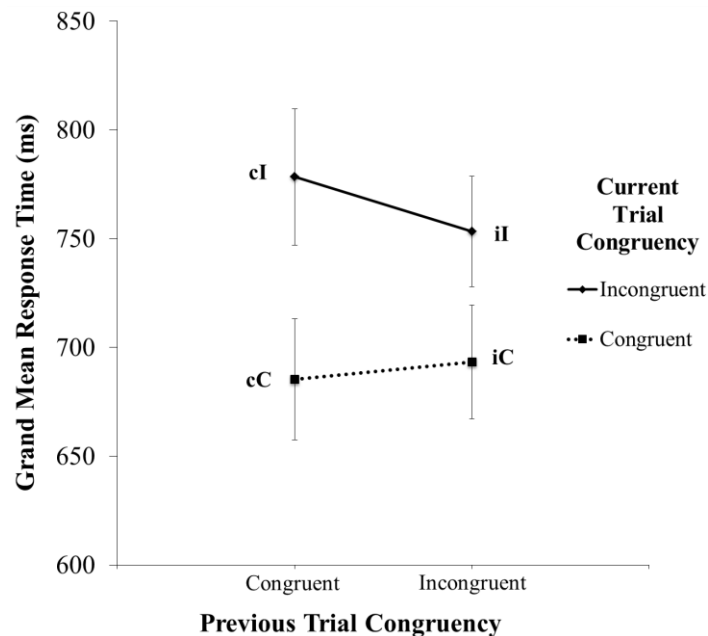
Table 3. Response Times (Means of Medians) and Error Rates (Means)

Response Times (ms)	Control Group (n = 20)	OCD Group (n = 20)	Combined (n = 40)	t score (df = 38)	Cohen's d	p value
cC Trials	664.65 (±99.31)	685.28 (±124.33)	674.96 (±111.56)	0.58	0.18	0.57
iC Trials	676.45 (±91.45)	693.33 (±116.59)	684.89 (±103.78)	0.51	0.16	0.61
cI Trials	748.63 (±111.67)	778.38 (±140.12)	763.50 (±125.97)	0.74	0.23	0.46
iI Trials	748.58 (±96.92)	753.33 (±113.83)	750.95 (±104.37)	0.14	0.04	0.89
Error Rates (%)						
cC Trials	3.99% (±5.48%)	4.25% (±4.52%)	4.12% (±4.96%)	0.16	0.05	0.87
iC Trials	3.35% (±3.04%)	4.01% (±3.39%)	3.68% (±3.20%)	0.65	0.21	0.52
cI Trials	6.82% (±5.86%)	6.17% (±4.47%)	6.50% (±5.16%)	-0.40	0.13	0.69
iI Trials	5.79% (±4.87%)	5.27% (±4.20%)	5.53% (±4.50%)	-0.36	0.11	0.72

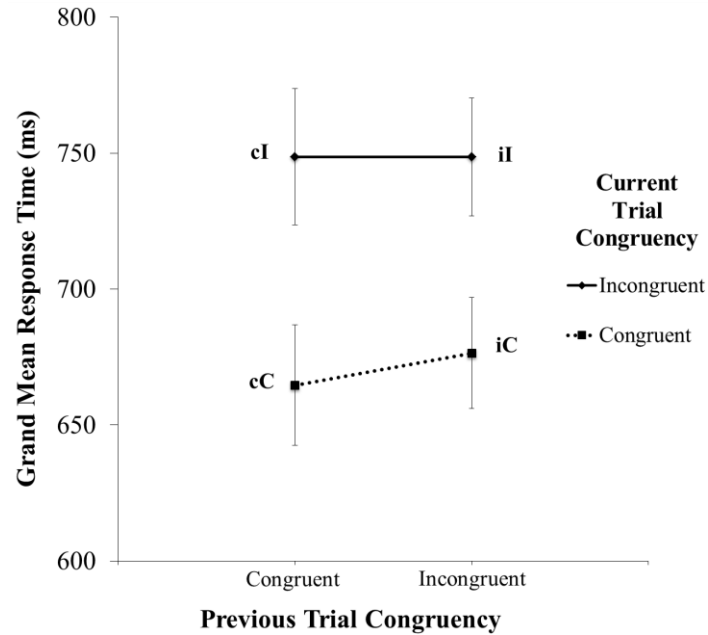
p* value ≤ 0.05; *p* value ≤ 0.01; OCD = obsessive-compulsive disorder; cC = congruent-congruent trials; iC = incongruent-congruent trials; cI = congruent-incongruent trials; iI = incongruent-incongruent trials

Figure 1. Median Response Times by Group

Response Times for the OCD Group



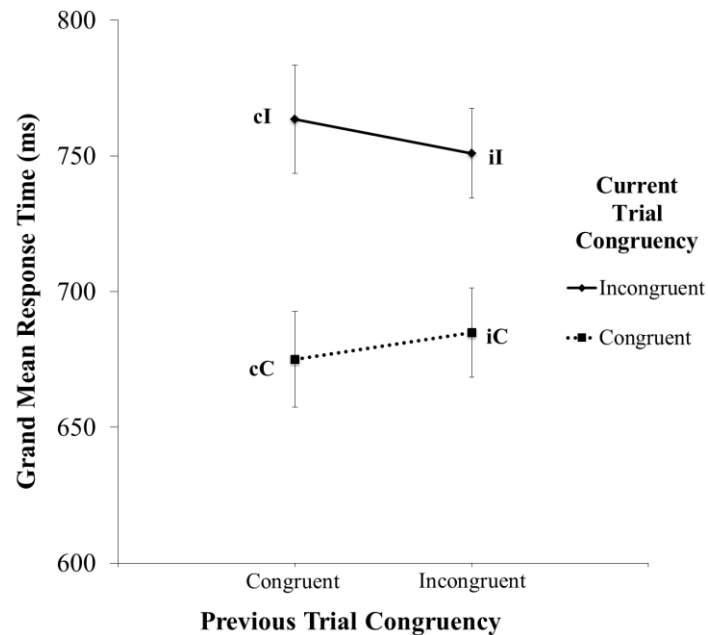
Response Times for the Control Group



OCD = obsessive-compulsive disorder; cC = congruent-congruent trials; iC = incongruent-congruent trials; cI = congruent-incongruent trials; iI = incongruent-incongruent trials

For conflict adaptation, there was a significant interaction between the previous and current trials collapsed across group of small effect size, $F(1,38) = 4.29, p = .04, \eta_p^2 = .04$ (see Figure 2), with the difference between congruent trials ($iC - cC$) being greater than the difference between incongruent trials ($iI - cI$); $t(39) = 2.09, p = .04, d = 0.34$. There was a tendency for iC trials to have longer RTs than cC trials and for cI trials to have longer RTs than iI trials (as would be predicted by conflict adaptation theory), but these differences were not significant, $t(39) = 1.44, p = .16, d = 0.23$, and $t(39) = 1.29, p = .20, d = 0.87$, respectively. The three-way interaction effect for the repeated measures ANOVA was not significant, $F(1,38) = 0.98, p = .33, \eta_p^2 = .03$. For individuals with OCD, the calculated mean conflict adaptation time was 33ms (± 65 ms). For psychiatrically-healthy control participants, the calculated mean conflict adaptation time was 12ms (± 70 ms).

Figure 2. Median Response Times for Current by Previous Trials Collapsed Across Group
Response Times Collapsed Across Group



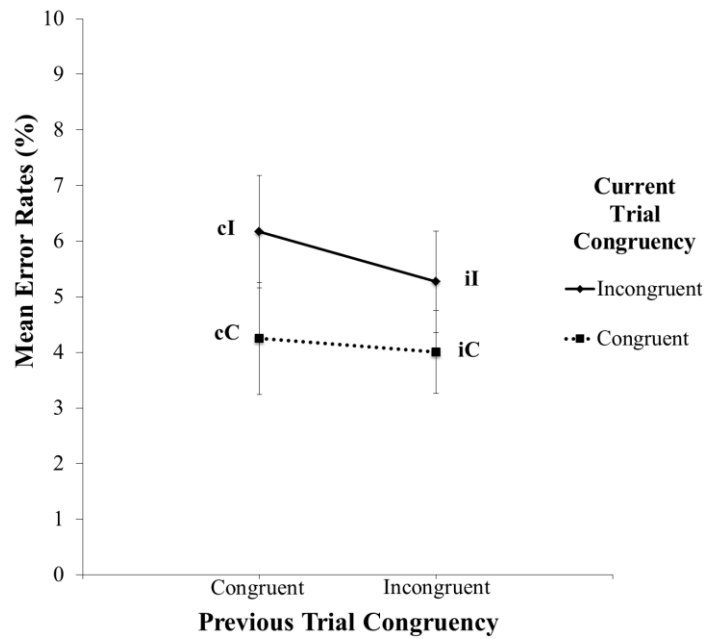
cC = congruent-congruent trials; *iC* = incongruent-congruent trials; *cI* = congruent-incongruent trials; *iI* = incongruent-incongruent trials

Error Rate Analysis. Mean error rates by group (percentage of incorrect responses) for the different trial types can be seen in Table 3 (see also Figure 3). The Stroop effect (incongruent > congruent; main effect for current trial congruency) was significant and had a large effect size with incongruent trials tending to have greater error rates than congruent trials, $F(1,38) = 13.95$, $p = .001$, $\eta^2 = .27$. The main effect for previous trial congruency was not significant, $F(1, 38) = 0.17$, $p = .69$, $\eta^2 < 0.01$. Neither current nor previous trial congruency had any significant interaction with group, $F(1, 38) = 0.49$, $p = .49$, $\eta^2 < 0.01$, and, $F(1, 38) = 0.22$, $p = .64$, $\eta^2 = 0.01$, respectively.

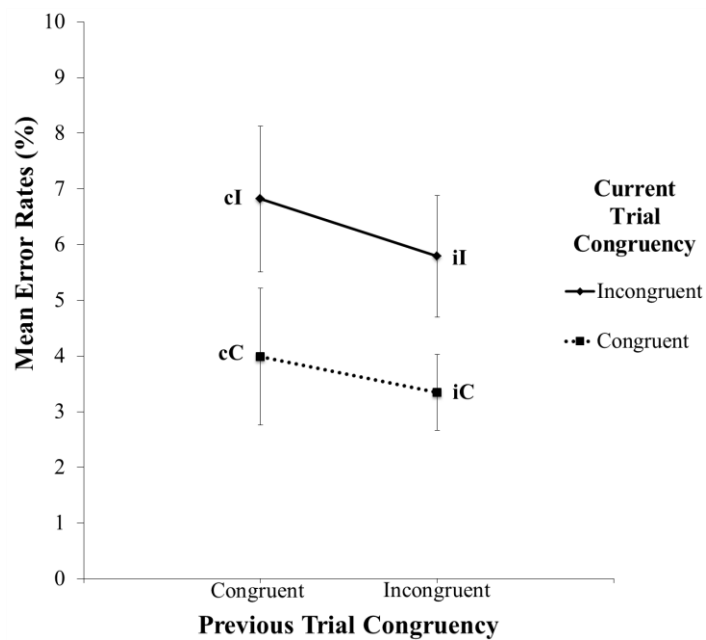
For conflict adaptation, there was no significant interaction between the previous and current trials collapsed across group with $F(1, 38) = 0.24$, $p = .63$, $\eta^2 = .01$, (see Figure 4).

Figure 3. Mean Error Rates by Group

Error Rates for the OCD Group

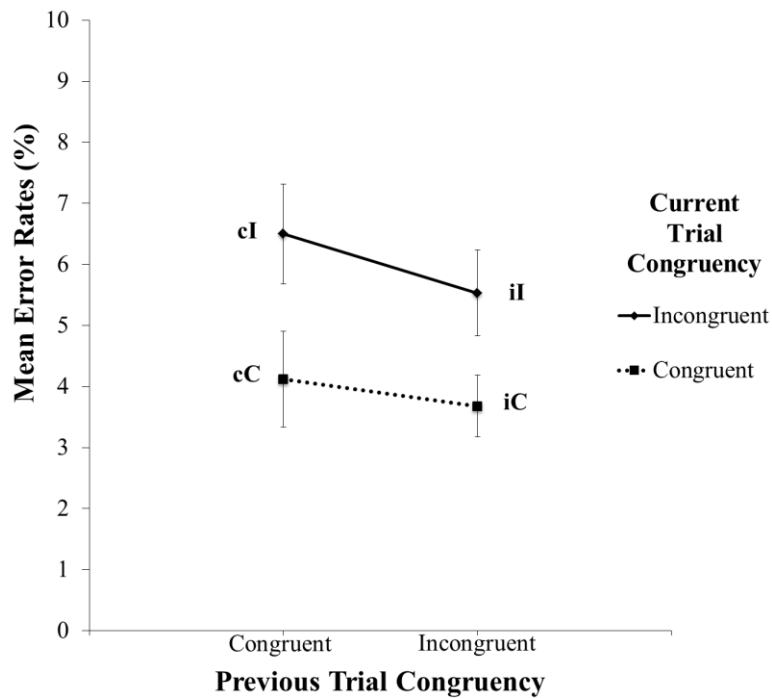


Error Rates for the Control Group



OCD = obsessive-compulsive disorder cC = congruent-congruent trials; iC = incongruent-congruent trials; cI = congruent-incongruent trials; iI = incongruent-incongruent trials

Figure 4. Mean Error Rates for Current by Previous Trials Collapsed Across Group
Error Rates (%) Collapsed Across Group



cC = congruent-congruent trials; *iC* = incongruent-congruent trials; *cI* = congruent-incongruent trials; *iI* = incongruent-incongruent trials

The 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) interaction effect was also not significant, $F(1, 38) = 0.01, p = .91, \eta_p^2 < .01$.

fMRI Results

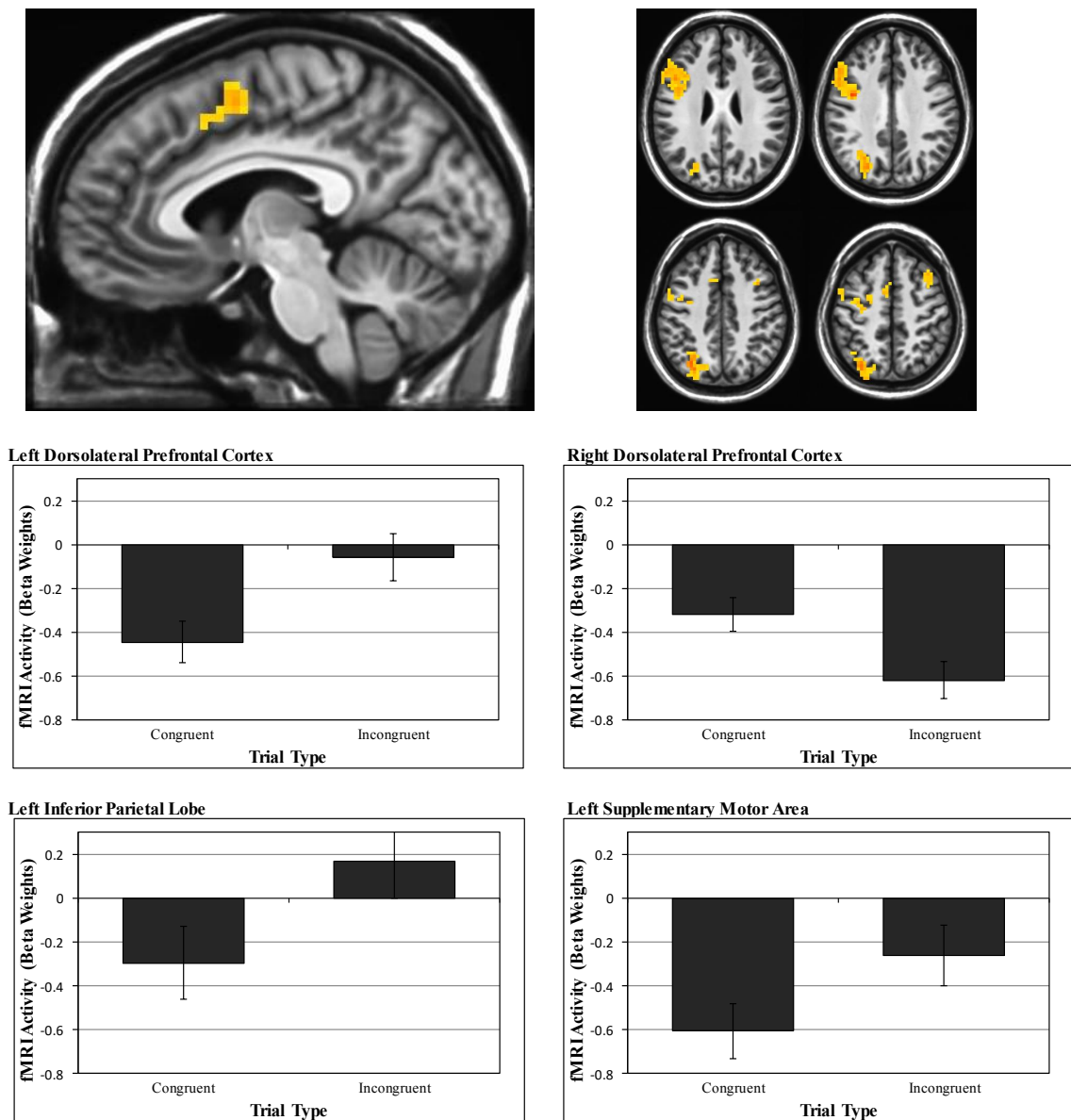
For the brain response, we first conducted a voxel-wise whole-brain analysis of congruent vs. incongruent trials to test for a Stroop effect. This analysis yielded four significant clusters in the following regions: left dlPFC, right dlPFC, left inferior parietal lobe, and left supplemental motor area (see Table 4 for statistics, see Figure 5 for graphical presentation).

Table 4. Significant fMRI Clusters by Model for the Congruent-Incongruent Trial Contrast

	<i>df</i>	<i>t</i>	<i>p</i>	Cohen's <i>d</i> (Within Subjects)
Congruent-Incongruent Contrast				
Left Dorsolateral Prefrontal Cortex (dlPFC)	76	-5.04	< .001**	0.45
Right Dorsolateral Prefrontal Cortex (dlPFC)	76	3.94	< .001**	0.60
Left Inferior Parietal Lobe	76	-4.51	< .001**	0.35
Left Supplemental Motor Area	76	-3.75	.001**	0.29

p* < .05, *p* ≤ .001

Figure 5. Stroop Effect Clusters from the Contrast between Congruent and Incongruent Trials



As expected, each of these regions showed significantly greater BOLD signal change on incongruent trials relative to congruent trials, with the exception of the right dlPFC which showed the opposite effect (congruent greater than incongruent). The regions for these effects were consistent with previous research (Banich et al., 2000; Liu, Banich, Jacobson, & Tanabe, 2004; Neumann, Lohmann, Derrfuss, & von Cramon, 2005); however, we also expected a significant contrast in the ACC with greater activation on incongruent relative to congruent trials that was not present (see Neumann, Lohmann, Derrfuss, & von Cramon, 2005).

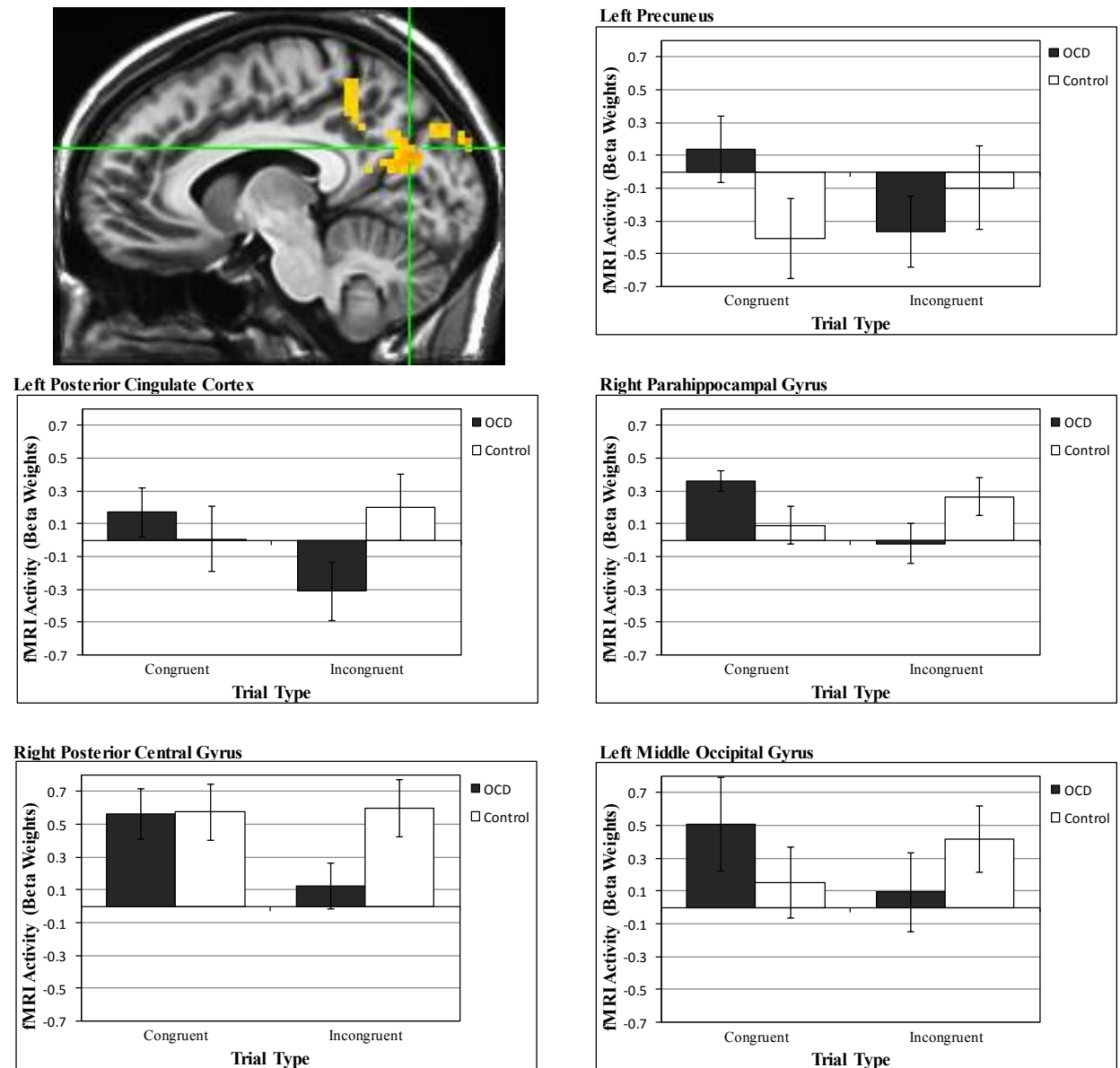
Second, we conducted a 2-Group (OCD, Control) x 2-Current Trial Congruency (congruent, incongruent) voxel-wise repeated measures ANOVA to test for differences in the Stroop effect between groups. Significant clusters for the 2-Group (OCD, control) by 2-Current Trial Congruency (congruent, incongruent) interactions were found in the following regions: left precuneus, left posterior cingulate cortex, right parahippocampal gyrus, right postcentral gyrus, and left middle occipital gyrus (see Table 5 for statistics, see Figure 6 for graphical presentation).

Table 5. Significant fMRI Clusters by Model for the 2-Group (OCD, control) x 2-Current Trial Congruency ANOVA, and the 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) ANOVA

	<i>df</i>	<i>F</i>	<i>p</i>	Partial η^2
2-Group x 2-Current				
Left Precuneus	1, 37	23.35	< .001**	.39
Left Posterior Cingulate Cortex	1, 37	26.72	< .001**	.42
Right Parahippocampal Gyrus	1, 37	19.89	< .001**	.35
Right Postcentral Gyrus	1, 37	22.49	< .001**	.38
Left Middle Occipital Gyrus	1, 37	12.95	.001**	.26
2-Previous x 2-Current				
Left Anterior Cingulate Cortex (ACC) 1	1, 38	25.25	< .001**	.40
Left Anterior Cingulate Cortex (ACC) 2	1, 38	26.05	< .001**	.41
Left Fusiform Gyrus	1, 38	46.16	< .001**	.55
Right Inferior Occipital Gyrus	1, 38	27.22	< .001**	.42
Left Globus Pallidus	1, 38	29.78	< .001**	.44
Left Orbitofrontal Cortex	1, 38	30.44	< .001**	.45
2-Group x 2-Previous x 2-Current				
Anterior Cingulate Cortex (ACC)	1, 37	20.89	< .001**	.36
Medial Prefrontal Cortex	1, 37	18.12	< .001**	.33
Left Orbitofrontal Cortex	1, 37	22.90	< .001**	.38

* $p < .05$, ** $p \leq .001$; *OCD = obsessive-compulsive disorder*

Figure 6. Occipital/Parietal Interaction Effect Clusters from the 2-Group (OCD, Control) x 2-Current Trial Congruency (congruent, incongruent) Voxel-wise Repeated Measures ANOVA (collapsed across previous trial)



OCD = obsessive-compulsive disorder

For these clusters, we compared differences between beta weights for incongruent trials and congruent trials (incongruent minus congruent) between groups. In every case, the control group showed larger beta differences between incongruent and congruent trials than the OCD group:

left precuneus $t(37) = 4.83, p < .001, d = 1.55$; left posterior cingulate $t(37) = 5.17, p < .001, d = 1.66$; right parahippocampal gyrus $t(37) = 4.46, p < .001, d = 1.43$; right postcentral gyrus $t(37) = 4.74, p < .001, d = 1.52$; and left middle occipital gyrus $t(37) = 3.60, p = .001, d = 1.15$. Thus, control participants showed greater activation on incongruent relative to congruent trials across all significant clusters in the model.

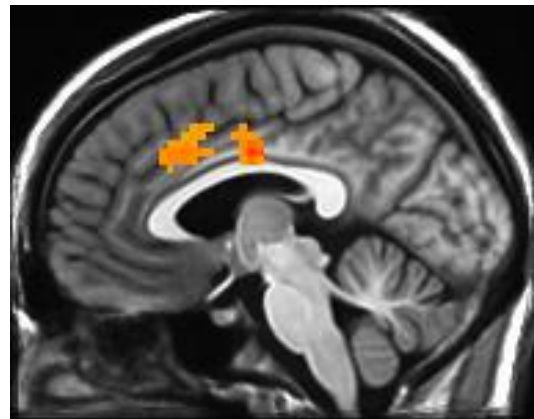
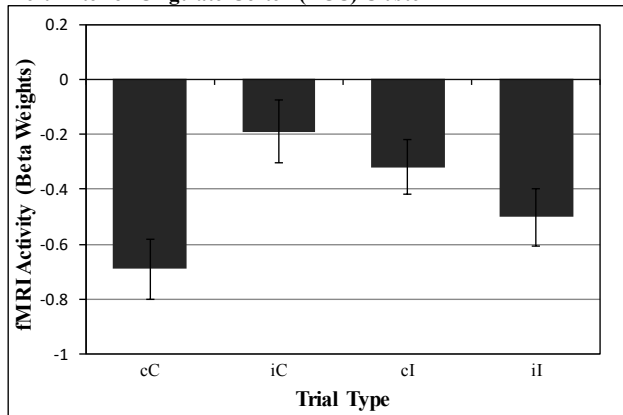
Third, we conducted a 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) voxel-wise repeated measures ANOVA to test for conflict adaptation collapsed across group. This model showed two significant clusters in the left ACC (see Table 5 for statistics, see Figure 7 for graphical presentation) as well as clusters in the left fusiform gyrus, right inferior occipital gyrus, left globus pallidus, and left orbitofrontal cortex (see Table 5 for statistics, see Figure 8 for graphical presentation).

Consistent with a cognitive control interpretation of conflict adaptation effects (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Cohen, Botvinick, & Carter, 2000, see also Miller & Cohen, 2001), both of the clusters in the left ACC on this model showed significantly greater ACC activation in cI trials relative to iI trials: ACC cluster 1, $t(38) = 2.16, p = .04, d = 0.35$; and ACC cluster 2, $t(38) = 2.57, p = .01, d = 0.41$. Additionally, both of the clusters in the left ACC showed greater ACC activation for iC trials relative to cC trials: ACC cluster 1 $t(38) = 4.30, p < .001, d = 0.69$; and ACC cluster 2 $t(38) = 3.33, p = .002, d = 0.50$. We found similar effects for greater activation in cI relative to iI trials in the following regions: left fusiform gyrus, $t(38) = 2.49, p = .02, d = 0.40$; left globus pallidus, $t(38) = 4.44, p < .001, d = 0.71$; and left orbitofrontal cortex, $t(38) = 3.34, p = .002, d = 0.54$. The difference between cI and iI trials was not significant in the right inferior occipital gyrus, $t(38) = 1.27, p = .21, d = 0.20$. We showed greater activation for iC trials relative to cC trials in the following regions: left fusiform gyrus,

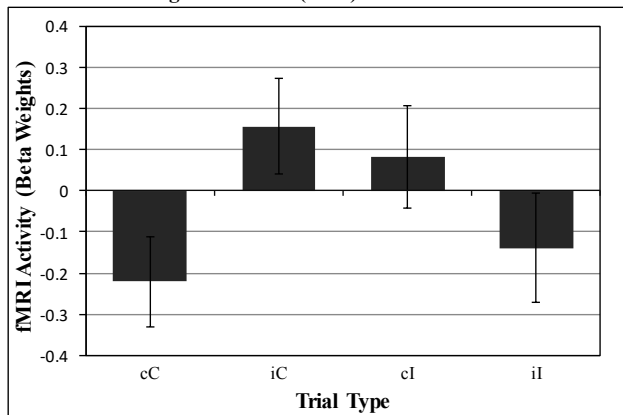
$t(38) = 4.61, p < .001, d = 0.74$; right inferior occipital gyrus, $t(38) = 3.84, p = .001, d = 0.66$; left globus pallidus, $t(38) = 3.59, p = .001, d = 0.58$; and left orbitofrontal cortex, $t(38) = 3.94, p < .001, d = 0.64$. In summary, the 2-Previous Trial Congruency x 2-Current Trial Congruency ANOVA showed multiple effects across multiple brain regions for conflict adaptation collapsed across group, with conflict adaptation effects prominently shown in the ACC.

Figure 7. Left ACC Interaction Effect Clusters from the 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) Voxel-wise Repeated Measures ANOVA (collapsed across group)

Left Anterior Cingulate Cortex (ACC) Cluster 1

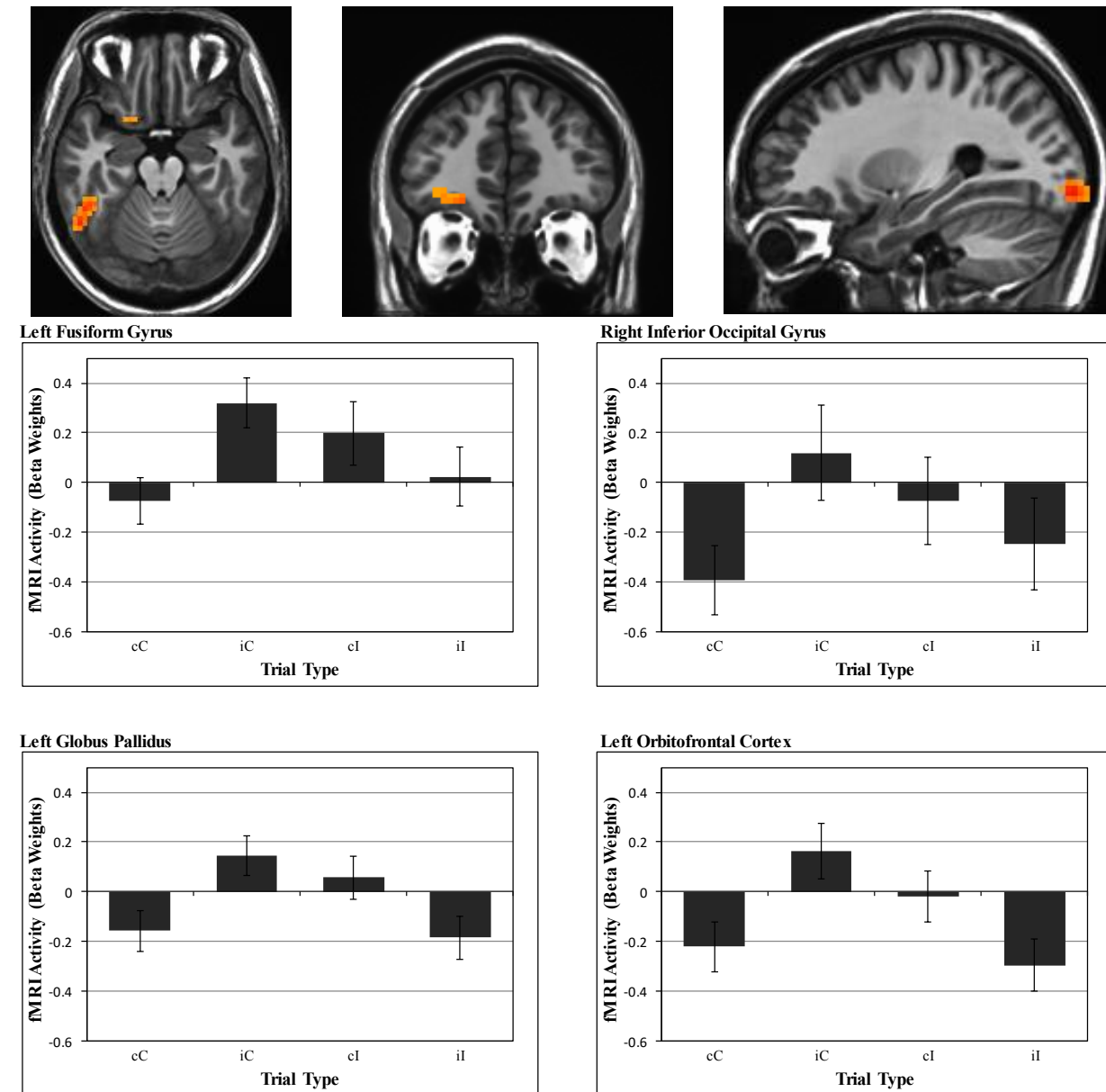


Left Anterior Cingulate Cortex (ACC) Cluster 2



cC = congruent-congruent trials; *iC* = incongruent-congruent trials; *cI* = congruent-incongruent trials; *iI* = incongruent-incongruent trials

Figure 8. Other Interaction Effect Clusters from the 2- Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) Voxel-wise Repeated Measures ANOVA (collapsed across group)

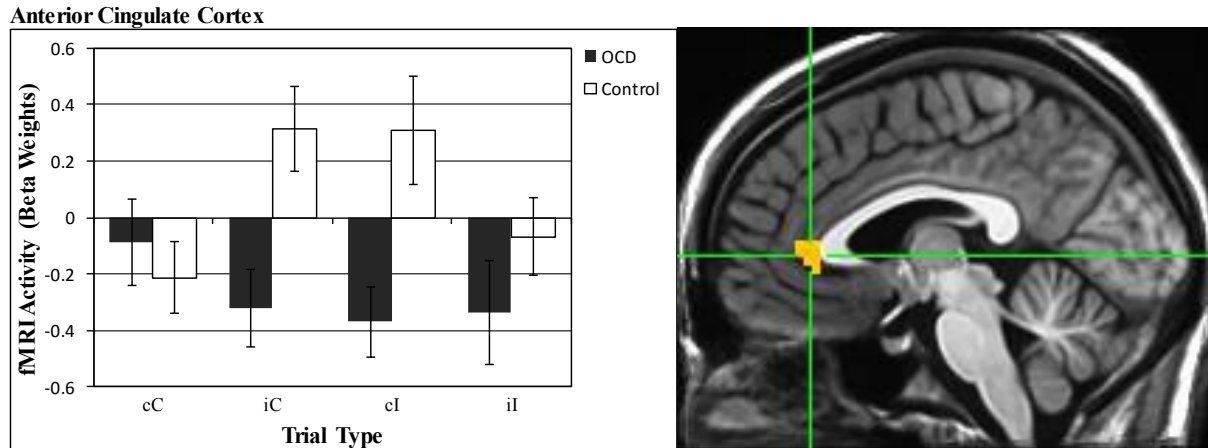


eC = congruent-congruent trials; *iC* = incongruent-congruent trials; *cI* = congruent-incongruent trials; *iI* = incongruent-incongruent trials

Finally, we conducted a 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) voxel-wise repeated measures ANOVA to consider sequencing effects between previous trial congruency

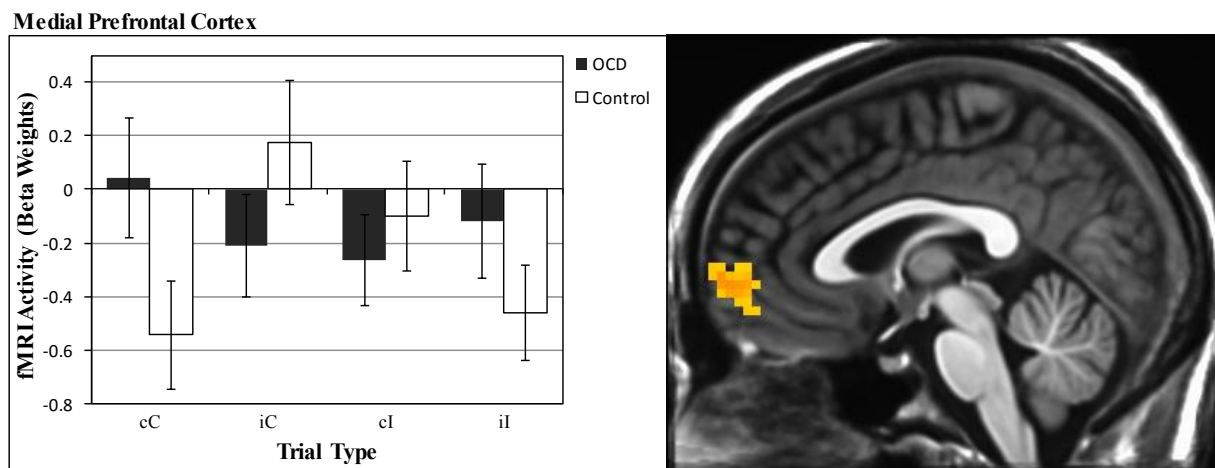
and current trial congruency with group as a between-subjects factor. This model had three suprathreshold clusters of activation in the ACC (see Figure 9), medial prefrontal cortex (see Figure 10), and left orbitofrontal cortex (see Figure 11; see Table 5 for statistics).

Figure 9. Anterior Cingulate Cortex Interaction effect of the 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) voxel-wise repeated measures ANOVA



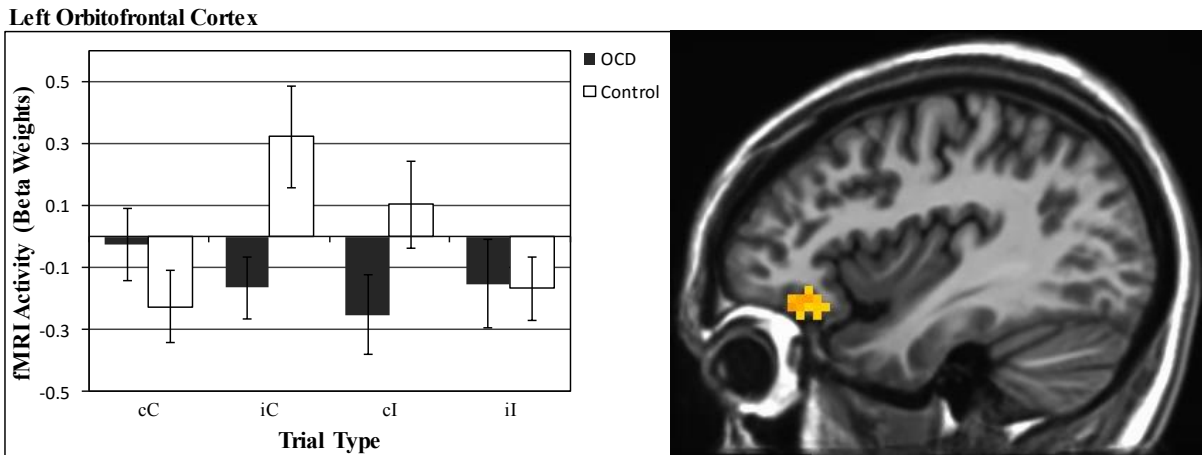
OCD = obsessive-compulsive disorder; cC = congruent-congruent trials; iC = incongruent-congruent trials; cI = congruent-incongruent trials; iI = incongruent-incongruent trials

Figure 10. Medial Prefrontal Cortex Interaction effect of the 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) voxel-wise repeated measures ANOVA



OCD = obsessive-compulsive disorder; cC = congruent-congruent trials; iC = incongruent-congruent trials; cI = congruent-incongruent trials; iI = incongruent-incongruent trials

Figure 11. Left Orbitofrontal Cortex Interaction Effect Cluster of the 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) Voxel-wise Repeated Measures ANOVA



OCD = obsessive-compulsive disorder; cC = congruent-congruent trials; iC = incongruent-congruent trials; cI = congruent-incongruent trials; iI = incongruent-incongruent trials

Contrary to our hypothesis, no significantly differing voxels for the three-way interaction were seen in dlPFC regions. We observed greater ACC activation in the control group on both cI and iC trials relative to the OCD group with $t(38) = 2.91$, ($p = .01$, $d = 0.93$), and $t(38) = 3.09$, ($p < .01$, $d = 0.99$), respectively. There was no difference between groups in ACC activation for cC and iI trials with $t(37) = -0.65$ ($p = .52$, $d = 0.21$) and $t(37) = 1.18$ ($p = .25$, $d = 0.38$), respectively. Control participants showed greater ACC activation on cI relative to iI trials (cI minus iI betas) than participants with OCD, $t(37) = 2.17$, $p = .04$, $d = 0.69$. Similarly, control participants showed greater ACC activation on iC relative to cC trials (iC minus cC betas) than participants with OCD, $t(37) = 5.29$, $p < .001$, $d = 1.69$. Control participants also showed greater conflict adaptation-related ACC activation (calculated from beta weights according to the formula presented in the Method section) relative to participants with OCD, $t(38) = 4.57$, $p < .001$, $d = 1.46$ (mean control beta weight = 0.91, mean OCD beta weight = -0.27).

The findings for the medial prefrontal cortex and the left orbitofrontal cortex were not the primary focus of this dissertation; therefore, the following results should be considered as *post-hoc* analyses only. For the significant cluster in the medial prefrontal cortex, activation did not differ significantly between groups for any of the trial types: cC trials, $t(37) = -1.94, p = .06, d = 0.62$; iC trials, $t(37) = 1.29, p = .21, d = 0.41$; cI trials, $t(37) = 0.61, p = .54, d = 0.2$, and iI trials, $t(37) = -1.24, p = .22, d = 0.4$. Control participants showed a non-significant trend for greater medial prefrontal cortex activation on cI relative to iI trials (cI minus iI betas) relative to participants with OCD, $t(37) = 1.96, p = 0.06, d = 0.63$. For iC relative to cC trials (iC minus cC betas), control participants showed significantly greater relative medial prefrontal cortex activation, $t(37) = 3.27, p = 0.002, d = 1.05$. Healthy controls also showed greater conflict adaptation-related (formula in Method section) activation in the medial prefrontal cortex relative to individuals with OCD, $t(38) = 4.26, p < .001, d = 1.36$ (mean control beta weight = 1.08, mean OCD beta weight = -0.40).

For the cluster in the left orbitofrontal cortex, control participants showed greater activation on iC trials relative to participants with OCD, $t(37) = 2.49, p = .02, d = 0.80$. The two groups did not differ on the other 3 trial types: cC trials $t(37) = -1.21, p = .24, d = 0.39$; cI trials $t(37) = 1.86, p = .07, d = 0.60$; and iI trials, $t(37) = -0.09, p = .93, d = 0.03$. Control participants showed greater left orbitofrontal cortex activation on cI relative to iI trials (cI minus iI betas) relative to participants with OCD, $t(37) = 2.50, p = 0.02, d = 0.80$. Similarly, control participants showed greater activation on iC relative to cC trials (iC minus cC betas) relative to participants with OCD, $t(37) = 3.92, p < .001, d = 1.25$. Finally, individuals with OCD showed reduced conflict adaptation-related activation (formula in the Method section) in the left orbitofrontal cortex relative to controls, $t(38) = 4.79, p < .001, d = 1.53$ (mean control beta weight = 0.82,

mean OCD beta weight = -0.24). Thus, control participants showed consistently greater conflict adaptation-related activation across all significant clusters from the 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent), x 2-Current Trial Congruency (congruent, incongruent) ANOVA. This was concordant with our prediction of reduced neurological conflict adaptation in individuals with OCD.

In summary, the significant interaction effects from the 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent), x 2-Current Trial Congruency (congruent, incongruent) ANOVA, appeared to have been primarily driven by greater cluster activations in the control group relative to the OCD group (in individual trial types, in trial type differences, and in conflict-adaptation differences). These findings support our hypothesis for reduced conflict adaptation-related activation in individuals with OCD.

Correlations with Quality of Life

Mean behavioral response time conflict adaptation as well as mean error rate conflict adaptation were not significantly correlated with quality of life (as measured by Q-LES-Q total score, WHOQOL-BREF Physical Scale, WHOQOL-BREF Psychological Scale, and WHOQOL-BREF Environmental Scale; see Table 6). Similarly, estimates of conflict adaptation from the significant fMRI clusters in the 2-Group (OCD, control) x 2-Previous (congruent, incongruent) x 2-Current (congruent, incongruent) model were not significantly correlated with the same indicators of quality of life listed above with the exception of the Environmental Scale from the WHOQOL-BREF. Conflict adaptation beta weights in the medial prefrontal cortex and left orbitofrontal cortex were also associated with environmental quality of life (WHOQOL-BREF Environmental Scale); however, these findings were *post-hoc* (these regions were not the primary focus of the study).

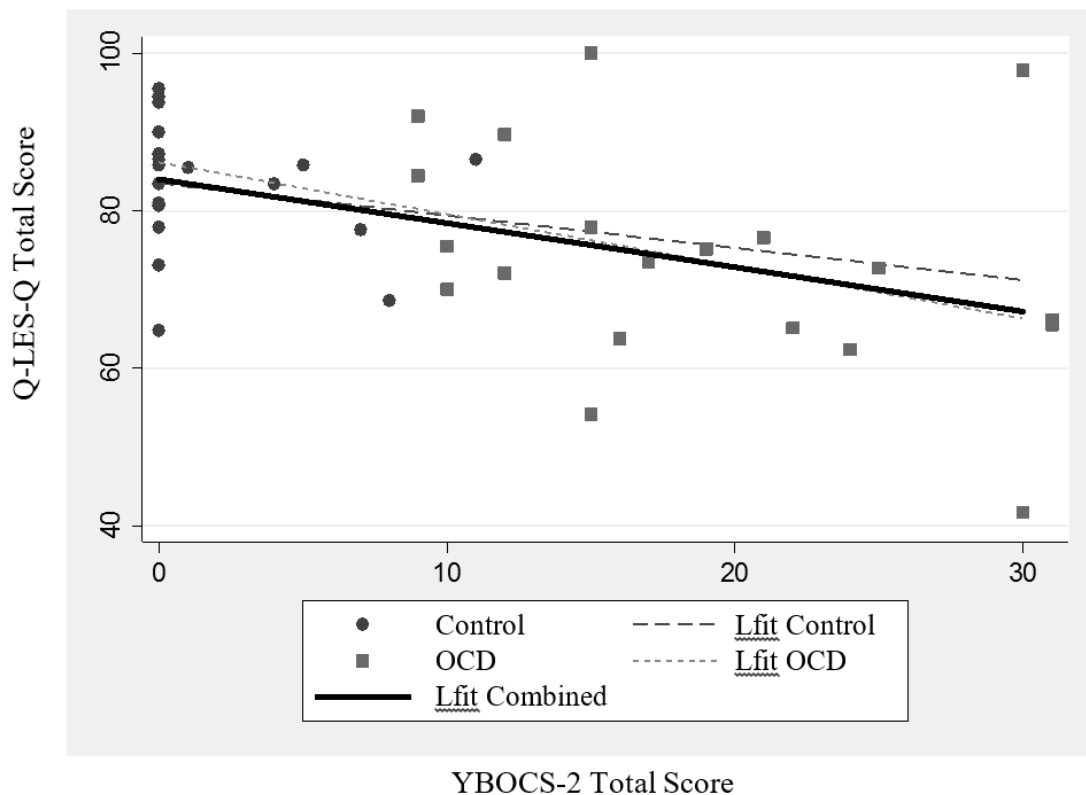
Table 6. Quality of Life: Zero-Order Correlations with Conflict Adaptation, Neuropsychological Functioning, and Psychiatric Functioning

		Q-LES-Q Total	WHOQOL-BREF Physical	WHOQOL-BREF Psychological	WHOQOL-BREF Environmental
Conflict Adaptation	Behavioral Response Times CA	$r = 0.02$ $p = .88$	0.18 .26	-0.08 .63	0.09 .56
	Behavioral Error Rate CA	$r = 0.16$ $p = .32$	0.25 .11	0.19 .25	0.07 .69
	2x2x2 Interaction Effect CA (ACC)	$r = 0.25$ $p = .12$	0.32 .04	0.22 .17	0.39 .01*
	2x2x2 Interaction Effect CA (medial PFC) #	$r = 0.39$ $p = .02$	0.38 .02	0.32 .04	0.47 .002*
	2x2x2 Interaction Effect CA (left OFC) #	$r = 0.25$ $p = .12$	0.31 .06	0.24 .15	0.42 .009*
	Psychiatric	YBOCS-2 Total Score	$r = -0.47$ $p = .002*$	-0.53 < .001**	-0.65 < .001**
YBOCS-2 Obsessions Scale		$r = -0.50$ $p = .001**$	-0.56 < .001**	-0.66 < .001**	-0.45 .004*
YBOCS-2 Compulsions Scale		$r = -0.40$ $p = 0.01*$	-0.45 0.004**	-0.54 < .001**	-0.38 .02
STAI State Total Score #		$r = -0.76$ $p = < .001**$	-0.68 < .001**	-0.81 < .001**	-0.50 0.001**
STAI Trait Total Score #		$r = -0.86$ $p = < .001**$	-0.76 < .001**	-0.91 < .001**	-0.65 < .001**
BDI-2 Total Score #		$r = -0.83$ $p = < .001**$	-0.76 < .001**	-0.86 < .001**	-0.58 < .001**
Neuropsychological	WTAR Standard Score#	$r = -0.28$ $p = .08$	-0.25 .12	-0.26 .11	-0.16 .31
	BRIEF-A: Behavioral Rating Index#	$r = -0.67$ $p = < .001**$	-0.66 < .001**	-0.73 < .001**	-0.59 < .001**
	BRIEF-A: Metacognitive Index#	$r = -0.73$ $p = < .001**$	-0.70 < .001**	-0.78 < .001**	-0.60 < .001**
	BRIEF-A: General Executive Composite#	$r = -0.76$ $p = < .001**$	-0.73 < .001**	-0.81 < .001**	-0.64 < .001**

* $p < .01$; ** $p \leq .001$; #Post hoc analyses; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire; WHOQOL-BREF = World Health Organization Quality of Life Brief Measurement Tool; CA = conflict adaptation calculated using the following formula $(cI - cC) - (iI - iC)$; ACC = anterior cingulate cortex, PFC = prefrontal cortex; OFC = orbitofrontal cortex; WTAR = Wechsler Test of Adult Reading; BRIEF-A = Behavior Rating Inventory of Executive Functioning, Adult version; STAI = State-Trait Anxiety Inventory; BDI-2 = Beck Depression Inventory, second edition

The YBOCS-2 Total Score and Obsessions Scale were negatively associated with all four included indices of quality of life (those indices that differed between groups, see Table 6). A scatterplot of Q-LES-Q Total Scores with YBOCS-2 Total Scores is shown in Figure 12. The negative association between these two variables was no longer significant when broken down by group (OCD group $r = -0.36, p = .12, r^2 = 0.13$; control group $r = -0.16, p = .49, r^2 = 0.03$). The YBOCS-2 Compulsions Scale was negatively associated with overall quality of life (Q-LES-Q Total Scale), physical quality of life (WHOQOL-BREF Physical Scale), and psychological quality of life (WHOQOL-BREF Psychological Scale), but not with environmental quality of life (WHOQOL-BREF Environmental Scale).

Figure 12. Scatterplot of Q-LES-Q Total Scores with YBOCS-2 Total Scores



OCD = obsessive-compulsive disorder; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire; YBOCS-2 = Yale-Brown Obsessive-Compulsive Scale, Second Edition

Correlations with Conflict Adaptation

Neither response time conflict adaptation nor error rate conflict adaptation were significantly associated with any psychiatric measures (see Table 7). ACC conflict adaptation beta weights from the three-way fMRI interaction were negatively associated with both the YBOCS-2 Total Score (see scatterplot in Figure 13) and the YBOCS-2 Obsessions Scale (see scatterplot in Figure 14).

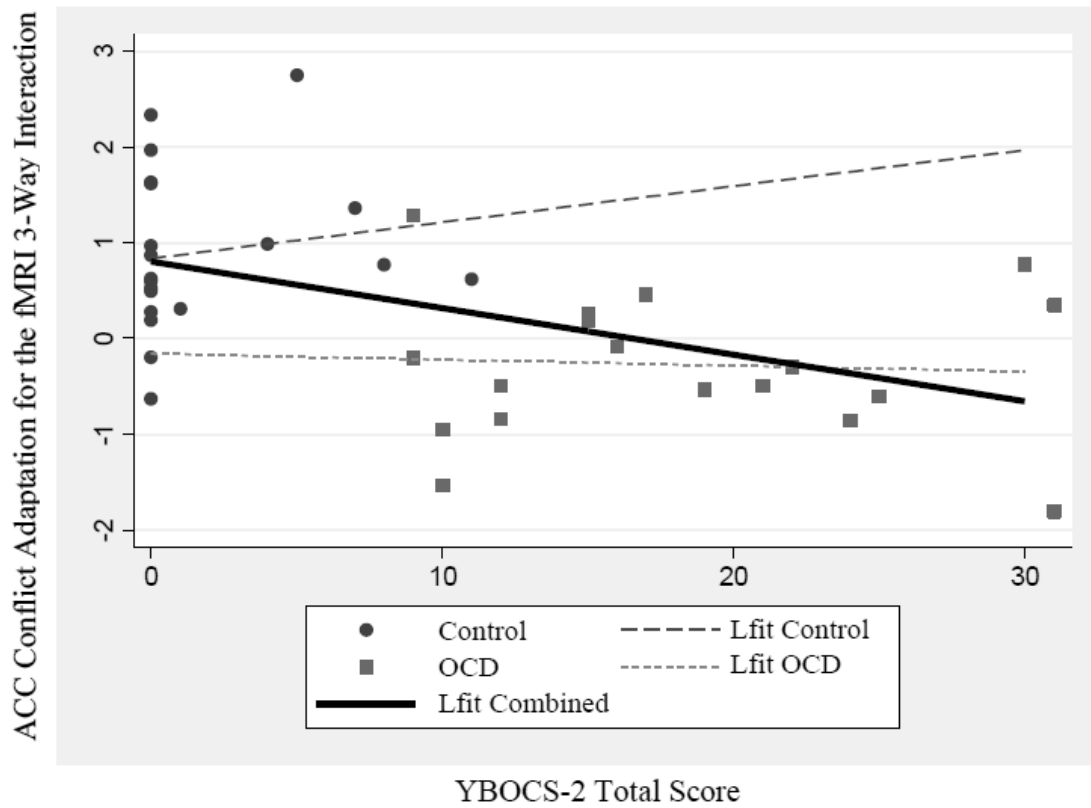
The association between YBOCS-2 Total Scores and ACC conflict adaptation beta weights was no longer significant when broken down by group (OCD group $r = -0.06$, $p = .81$, $r^2 = 0.00$; control group $r = 0.15$, $p = .52$, $r^2 = 0.02$). The same was true of the association between the YBOCS-2 Obsessions Scale and ACC conflict adaptation beta weights (OCD group $r = 0.02$, $p = .93$, $r^2 = 0.00$; control group $r = 0.03$, $p = .89$, $r^2 = 0.00$). ACC conflict adaptation beta weights were not significantly correlated with any other psychiatric or neuropsychological measures.

Table 7. Conflict Adaptation: Zero-Order Correlations with Psychiatric Functioning and Neuropsychological Functioning

		Calculated CA for Behavioral Data		Calculated CA for significant fMRI Clusters from the 2-Group x 2-Previous x 2-Current Interaction		
		Response Time CA	Behavioral Error Rate CA	2x2x2 Interaction Effect CA (ACC)	2x2x2 Interaction Effect CA (medial PFC)#	2x2x2 Interaction Effect CA (left OFC)#
Psychiatric	YBOCS-2 Total Score	$r = 0.19$ $p = .24$	-0.04 .79	-0.49 < .002*	-0.52 <.001**	-0.53 <.001**
	YBOCS-2 Obsessions Scale	$r = 0.24$ $p = .14$	-0.03 .84	-0.47 .003*	-0.47 .003*	-0.52 .001**
	YBOCS-2 Compulsions Scale	$r = 0.24$ $p = .14$	0.07 .67	-0.38 0.02	-0.40 .01*	-0.48 .002*
	STAI State Total Score #	$r = -0.02$ $p = .89$	0.06 .72	-0.24 .14	-0.23 .16	-0.17 .31
	STAI Trait Total Score #	$r = 0.05$ $p = .77$	0.01 .94	-0.31 .05	-0.41 <.01*	-0.38 0.02
	BDI-2 Total Score #	$r = 0.03$ $p = .88$	-0.08 .62	-0.31 .06	-0.45 .004*	-0.42 .007*
Neuropsychological	WTAR Standard Score	$r = -0.29$ $p = .07$	-0.32 .04	0.18 .27	0.24 .15	0.27 .10
	BRIEF-A: Behavioral Rating Index	$r = 0.10$ $p = .54$	-0.08 .62	-0.29 .08	-0.36 .02	-0.29 .07
	BRIEF-A: Metacognitive Index	$r = -0.01$ $p = .98$	-0.42 .01*	-0.32 .05	-0.37 .02	-0.29 .07
	BRIEF-A: General Executive Composite	$r = 0.04$ $p = .82$	-0.29 .07	-0.32 .05	-0.39 .01*	-0.31 .05

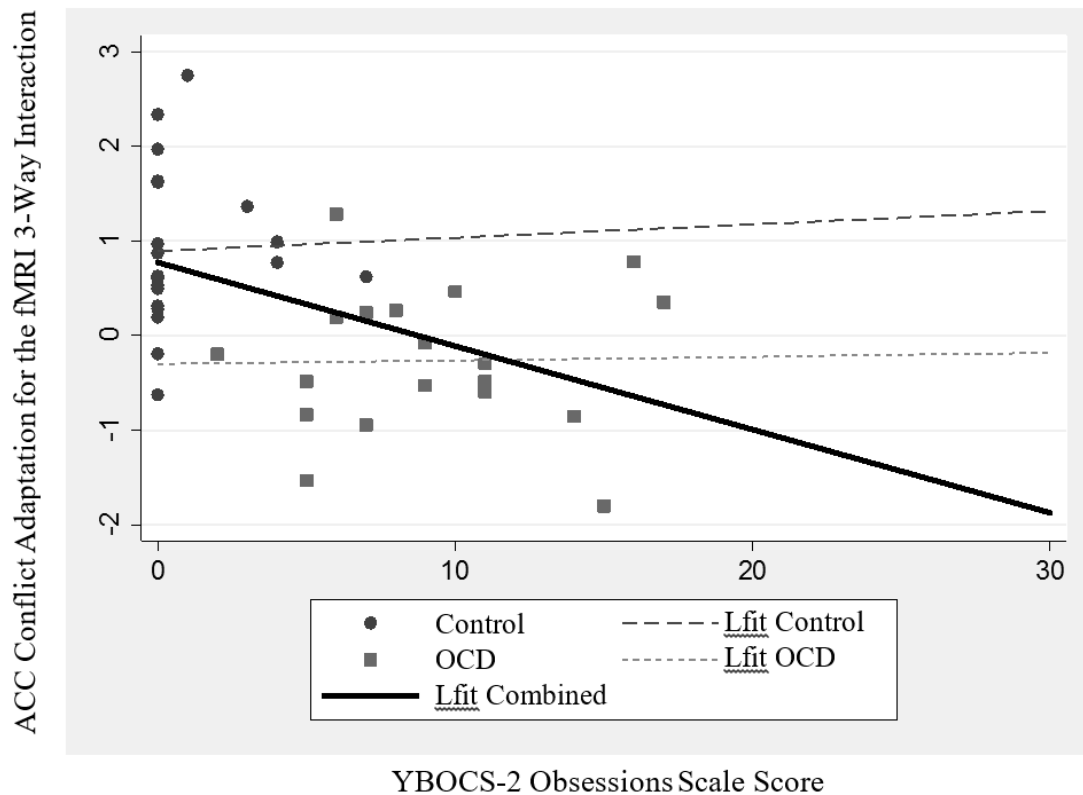
* $p < .01$, ** $p \leq .001$; #post hoc analyses; CA = conflict adaptation calculated using the following formula $(cI - cC) - (iI - iC)$; ACC = anterior cingulate cortex, PFC = prefrontal cortex; OFC = orbitofrontal cortex; YBOCS-2 = Yale-Brown Obsessive Compulsive Scale, second edition; STAI = State-Trait Anxiety Inventory; BDI-2 = Beck Depression Inventory, second edition; WTAR = Wechsler Test of Adult Reading; BRIEF-A = Behavior Rating Inventory of Executive Functioning, Adult version

Figure 13. Scatterplot of Conflict Adaptation Values for the 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) ANOVA with YBOCS-2 Total Scores



Conflict adaptation values calculated using the following formula $(cI - cC) - (iI - iC)$; OCD = obsessive-compulsive disorder; YBOCS-2 = Yale-Brown Obsessive-Compulsive Scale, Second Edition

Figure 14. Scatterplot of Conflict Adaptation Values for the 2-Group (OCD, control) x 2-Previous Trial Congruency (congruent, incongruent) x 2-Current Trial Congruency (congruent, incongruent) ANOVA with YBOCS-2 Obsessions Scale Scores



Conflict adaptation values calculated using the following formula $(cI - cC) - (iI - iC)$; OCD = obsessive-compulsive disorder; YBOCS-2 = Yale-Brown Obsessive-Compulsive Scale, Second Edition

Discussion

Our study had three specific aims. First, we sought to determine if there are differences between individuals with OCD and psychiatrically-healthy controls in behavioral (RT and error rate) manifestations of conflict adaptation. Second, we aimed to dissociate the neural manifestations of the evaluative and regulative components of cognitive control between groups. Finally, we sought to assess any possible relationship between cognitive control dysfunction and quality of life in individuals with OCD relative to healthy controls. Discussion of each of these aims will be sequentially considered below.

Behavioral manifestations of conflict adaptation were seen in our overall sample; however, conflict adaptation did not differ between groups as expected. We had expected that individuals with OCD would show worse conflict adaptation relative to psychiatrically-healthy controls similar to previous findings in a pediatric sample of OCD (Liu, 2012). If anything, there was actually a non-significant trend for individuals with OCD to show greater response time conflict adaptation relative to controls. Increased reaction time conflict adaptation in OCD would be consistent with the findings of Riesel and colleagues (2017). It is possible that the lack of conflict adaptation differences in our adult sample may be due to neurodevelopmental differences between pediatric and adult samples with OCD. For example, Abramovitch and colleagues (2013) conducted a meta-analysis of studies of pediatric OCD that did not show expected differences in neuropsychological functioning that had previously been documented in the adult literature (see Aydın, Güleç & Öyekçin 2013). They concluded that low persistence rates of pediatric OCD into adulthood along with possible neurodevelopmental changes over the lifespan might account for the differences seen between pediatric and adult populations in neuropsychological functioning. Thus, it may not be surprising that the current results differed from that of a pediatric OCD sample. In a psychiatrically-healthy population, there appears to be no difference in the magnitude of behavioral conflict adaptation between pediatric and adult samples (see Larson, Clawson, Clayson, & South, 2012); therefore, this neurodevelopmental difference between pediatric and adult individuals with OCD may be specific to the disorder.

Marsh and colleagues (2014) showed a lack of significant differences in trial sequencing effects between adults with OCD and healthy controls that was similar to our own results. Although they did not consider conflict adaptation specifically, they did consider congruency and sequencing effects (whether a trial was preceded by a trial of the same or opposite

congruency) in a way that is comparable to our own analysis. In their study adults with OCD did not differ from controls in RTs for trials with preceding trials of the same or opposite congruency. Similarly, our study showed no differences between groups for congruency or sequencing effects in an adult sample. We chose not to replicate the exact analyses of Marsh and colleagues (2014), because sequencing effects are more commonly addressed using conflict adaptation methods and the addition of more analyses beyond the scope of the current aims would have greatly elevated the risk for Type I error. However, many of our fMRI findings appeared to highlight differences in so-called “change trials” (cI and iC) relative to trials with similar preceding trials (cC and iI) in a manner that would be consistent with the model used by Marsh and colleagues (2014). Future studies should take these seemingly concordant findings into account when determining design and analyses.

Riesel and colleagues (2017) demonstrated increased reaction time conflict adaptation in adults with OCD relative to healthy controls that appeared to be strongly related to increased N2 ERP amplitudes. Localization of components of the event-related potential is somewhat limited, but the N2 is associated with cognitive control processes and is thought to be mediated by frontal lobe functioning, and more specifically the ACC (van Veen & Carter, 2002). Thus, if individuals with OCD are showing relatively heightened response time conflict adaptation (as non-significant trends may suggest in the current dissertation), they would be expected to also show increased activation in regions of the prefrontal cortex. As will be discussed below, individuals with OCD in our study may have processed the sequencing of trials differently from controls with a greater focus on current trials and less processing of the context of previous trials. On current congruent trials, individuals with OCD tended to show greater activation in the left posterior cingulate cortex, but not in the ACC.

As demonstrated by Liu (2012), individuals with OCD differ from their peers in conflict adaptation in childhood, but it is possible that they adaptively adjust their behavior to match that of healthy controls by adulthood. As seen in the current study (and as discussed below), neurological manifestations of conflict adaptation were significantly different between groups, and it may be that adults with OCD show similar behavioral responses to controls, yet arrive at these responses via different neurological processes.

With regard to error rates, the expected Stroop effect was significant (greater error rates on incongruent relative to congruent trials); however, contrary to hypotheses, no conflict adaptation was seen in error rates at any level of the analysis. This may have been due to the limited range of errors made on our Stroop task. In our sample, 9 individuals made 4 or fewer errors and 1 individual made no errors at all, and thus our range for statistical comparison of error rate conflict adaptation was very poor. Many studies with adequate ranges of errors and among different populations have demonstrated significant error rate conflict adaptation (Clawson, Clayson, & Larson, 2013; Clayson, & Baldwin, 2013; Clayson & Larson, 2011a; Larson et al., 2016; Larson, Clawson, Larson, South, Clayson, & Clawson, 2012; Larson, Farrer, & Clayson, 2011); however, one study did not show error rate conflict adaptation (Larson, Clawson, Clayson, & South, 2012). Reported error rates for the latter study (Larson, Clawson, Clayson, & South, 2012) generally appeared low relative to the other studies (cited above) that showed a significant effect. Thus, studies with lower error rates such as the current dissertation may be underpowered to detect error rate conflict adaptation due to limited number of errors made.

In summary, our task manipulation was successful and response time conflict adaptation was seen collapsed across groups. Individuals with OCD showed no difference in response time

conflict adaptation relative to healthy controls, but differences in brain activation (discussed below) suggest that they may have achieved this behavioral result through different neurological processes. Our task may not have been difficult enough to produce enough errors for meaningful analysis.

Our second aim was to dissociate the neural manifestations of the evaluative (ACC) and regulative (dlPFC) components of cognitive control between groups. Interestingly, the ACC did not show differential activation for current congruent relative to incongruent trials. Furthermore, there were no ACC differences between groups for current trial congruency. However, when conflict adaptation (sequencing of trials by congruency) was considered, the ACC did differ significantly as expected with greater activation for trials following a change in congruency (i.e. ACC activation: cI > iI trials and iC > cC trials). Thus, the hypothesis that the ACC serves as the primary location for the evaluative component of cognitive control was partially supported by our data. Specifically, the ACC appeared to play an evaluative role for detecting conflict in the form of changes in sequential trial congruency, but did not appear to play a role in differentially processing current congruent relative to incongruent trials.

The lack of differential activation in the ACC in response to current-trial congruency was contrary to our expectations and to the results of Macdonald (2000). Although this result was not expected, it is not unprecedented. Liu and colleagues (2004) demonstrated dlPFC activation differences on a Stroop task without accompanying ACC differences comparable to our results. They concluded that the dlPFC and ACC may actually have independent roles in cognitive control rather than functioning in an evaluative-regulative feedback loop. In support of this conclusion, they pointed to findings from Cohen and colleagues (1999) and from Ochsner and colleagues (2001) who demonstrated that individuals who had undergone stereotactic

cingulotomy (ablation of the ACC) showed no changes in performance on a Stroop task. Thus, it may reasonably be concluded that the ACC does not play a major role in processing congruent vs. incongruent stimuli on Stroop tasks. Although this is contrary to our hypothesis, our current data appear to provide support for this interpretation.

Riesel and colleagues (2017) demonstrated relatively larger conflict adaptation-related N2 amplitudes in individuals with OCD relative to controls suggestive of relatively increased ACC activation. This contrasts with our findings for diminished conflict-adaptation-related ACC activity in individuals with OCD relative to controls. Riesel and colleagues (2017) concluded that this heightened ACC activation in OCD may be beneficial in processing tasks requiring a high degree of control to resolve conflict. The longer periods between trials on the current fMRI task in contrast with Riesel's EEG flanker task may have been important in this process. It has already been established that individuals with OCD tend to show relatively hyperactive cognitive control processes (see Grundler, Cavanagh, Figueroa, Frank, & Allen, 2009; Maltby, Tolin, Worhunsky, O'Keefe, & Kiehl, 2005; Mathews, Perez, Delucchi, & Mathalon, 2012). It could be that longer inter-trial stimulus times (having to process these trials for longer periods) had the potential to overload the cognitive control systems of individuals with OCD, and therefore they adaptively began attending to current trials with less regard for the context of previous trial congruency. Future research is needed to test this possibility.

Conflict adaptation analyses by group yielded significant clusters in the ACC with participants in the control group showing greater ACC activation on both cI and iC trials relative to individuals with OCD. If the ACC's role in cognitive control is particularly salient to sequencing effects, (as suggested above), then individuals with OCD showed diminished capacity to adaptively process changes in trial congruency, or at least, they did not process trial

sequencing in the same way as controls. Surprisingly, this did not result in expected behavioral differences between groups, and individuals with OCD appear to have arrived at similar behavioral responses to healthy controls but by differing neurological means. Unexpected findings for conflict adaptation by group in the medial prefrontal cortex and the left orbitofrontal cortex may shed some light on how individuals with OCD processed conflict adaptation differently. For both of these regions, conflict adaptation-related activation (as calculated by the formula in the Method section) was also diminished in individuals with OCD.

Previous researchers (Marsh et al., 2014; Neumann, Lohmann, Derrfuss, & von Cramon, 2005) have demonstrated differences in inferior frontal and middle frontal regions of the brain that may be analogous to our findings in the medial prefrontal cortex and the orbitofrontal cortex. Marsh and colleagues (2014) suggested that OCD-mediated differences in fronto-striatal circuits might be related to cognitive inflexibility in individuals with the disorder. They specifically reported that individuals with OCD showed increased activation of the inferior frontal gyrus in response to sequential changes in trial congruency on a Simon task. Interestingly, our sample actually showed diminished conflict adaptation-related medial prefrontal cortex activation for individuals with OCD relative to healthy controls. Direct comparisons of cI and iC trials between groups were not significant, but actually trended in the opposite direction of reported effects from those of Marsh and colleagues (2014). This contradictory finding is difficult to interpret, but may highlight a need to understand further mediating factors affecting activation of this brain region.

As was suggested above in the discussion of relatively diminished ACC activation, the longer inter-trial periods between stimuli on our task may have caused individuals with OCD to change strategies to avoid overloading the cognitive control system. Another potential mediating

factor explaining the contrast between current findings and those of Marsh and colleagues (2014) could be symptom severity. Marsh and colleagues (2014) did not report the severity of symptoms for their sample, but the mild symptoms in our sample could potentially account for this difference. It is also possible that this difference was related to differences in task. The Simon task used by Marsh and colleagues (2014) is a task of directional/spatial conflict, whereas the Stroop task used in the current study utilizes conflict between color and color-words. This explanation seems less likely as both tasks elicited sequencing-related conflict and neurological activation differences in similar regions. If the contrasting results were due simply to task differences, the similarities in localization between studies could be coincidental. On our task healthy control participants appeared more able to recruit additional cognitive resources in the medial prefrontal cortex as well as the orbitofrontal cortex than individuals with OCD.

Maltby and colleagues (2005) showed relative left orbitofrontal hyperactivity for individuals with OCD on high-conflict trials of a Go/No-Go task for which responses were correctly withheld. Our results showed that individuals with OCD actually had relatively low activation of the left orbitofrontal cortex relative to healthy controls on iC (high conflict) trials. Thus, our results for both the medial prefrontal cortex and the orbitofrontal cortex in individuals with OCD contrasted with expectations based on previous literature.

One possible explanation for individuals with OCD showing relatively diminished conflict-adaptation-related activation in the ACC, middle prefrontal cortex, and orbitofrontal cortex may be that individuals with OCD neurologically disengage somewhat from the sequential processing of trials so as to avoid overloading the cognitive control system. The Introduction section of this dissertation has presented ample support for the conclusion that general cognitive control processes tend to be hyperactive in individuals with OCD (for

examples see Maltby, Tolin, Worhunsky, O’Keefe, & Kiehl, 2005; Mathews, Maltby, Tolin, Worhunsky, O’Keefe, & Kiehl 2005; Sheth et al., 2013). Therefore, individuals with OCD may have a greater need to develop alternative neurological processes to avoid overwhelming the cognitive control system. This could require a greater focus for individuals with OCD relative to controls on each trial individually rather than processing trials in the context of preceding trials. If individuals with OCD tended to attend to current trials on a more trial-by-trial basis, we might expect to see increased activation on current trials independent of previous trials. Our group by current trial analysis showed significant differences in activation for the left precuneus, left posterior cingulate, right parahippocampal gyrus, and the left middle occipital gyrus. On incongruent trials, individuals with OCD tended to show relatively diminished activation in all of the regions noted above. Conversely, on congruent trials individuals with OCD tended to show greater activation of all of these same regions except for the right posterior central gyrus. Thus, individuals with OCD did differ in neural activation in response to current trial congruency independent of previous trial. The tendency to show relatively increased activation on congruent (low conflict trials) provides support for the theory that individuals with OCD were processing each trial on a trial-by-trial basis rather than in the context of previous trial.

As mentioned earlier, alternative explanations for conflict adaptation effects (the tendency to respond differentially to trials due to trial sequencing) have been presented. One theory that may be relevant to the current results is temporal learning (see Schmidt, 2013; Schmidt, Notebaert, & Van Den Bussche, 2015; Schmidt & Weissman, 2016). This theory posits that individuals learn to adjust temporal responses based on the duration of previous responses, thus following along with a learned “rhythm” of the task (Grosjean, Rosenbaum, & Elsinger, 2001). According to temporal learning theory, participants tend to respond more quickly

following faster responses and more slowly following slower responses. Responses to incongruent trials tend to be slower than responses to congruent trials (simple Stroop effect). Thus, it is not surprising that a cI trial would be responded to more slowly than would a cC or iC trial. According to temporal learning theory, an individual next encountering an iI trial, may respond more slowly than an individual encountering an iC trial simply because he/she has just responded more slowly to an incongruent trial and has learned to slow his/her response.

Thus, a conflict-adaptation effect could be present, but actually be best explained in terms of temporal learning. It is also entirely possible that individuals with OCD and healthy controls use mutually exclusive strategies for adaptive responding (e.g. one group using conflict adaptation and one group using temporal learning). It is not known which brain regions may specifically be related to temporal learning processes, but if individuals with OCD responded using a different strategy from controls, the between-group contrasts for current trials (without regard to previous trial) could provide clues as to the localization of this strategy in the brain: left precuneus, left posterior cingulate, right parahippocampal gyrus, and the left middle occipital gyrus.

It has been established that pediatric OCD is characterized by reduced response time conflict adaptation (Liu, Gehring, Weissman, Taylor, & Fitzgerald, 2012). Thus, individuals with OCD may initially show diminished behavioral conflict adaptation responses in their younger years, but as they age into adulthood there appear to be structural and metabolic neurological changes (outlined below) that result in alternative neurological processes allowing for similar behavioral responses to healthy peers. Interestingly, these alternative processes actually require less conflict adaptation-related activation (thus serving to avoid overwhelming an already

hyperactive cognitive control system). A possible mechanism for such metabolic and structural changes from youth to adulthood follows below.

We have already suggested that there may be neurodevelopmental changes accounting for the behavioral difference in pediatric vs. adult OCD. One such difference could lie in glutamatergic and GABAergic system changes that vary with length of illness and directly affect the ACC, orbitofrontal cortex, and medial prefrontal cortex (see Arnold et al., 2009; Ortiz et al., 2015; Simpson et al., 2012). Glutamate has been strongly associated with excitatory neurotransmission in previous literature (for review see Watkins, 2000), and the ACC has been shown to have a particularly high concentration for glutamate receptors relative to other regions of the brain (Bozkurt et al., 2005). Ortiz and colleagues (2015) demonstrated significant reductions in glutamate and glutamine (a precursor to glutamate) in individuals of longer illness duration relative to shorter illness duration in a sample of pediatric and adolescent OCD. Specifically, longer length of illness was related to diminished glutamate and glutamine in the ACC. Results from their overall pediatric sample (without regard to illness duration); however, did not show significant differences between children with OCD and healthy controls. Arnold and colleagues (2008) showed that differences in a gene affecting the glutamatergic system result in structural brain changes in OCD particularly in the right ACC, right orbitofrontal cortex, and right thalamus. Their study was also conducted with a pediatric sample, but to our knowledge, these findings have not yet been evaluated in adults with OCD.

Yücel and colleagues (2008) did show that adult women with OCD have reduced glutamate and glutamine in the ACC relative to healthy controls; however, there was no such difference seen in males with OCD. Another study showed no differences between adults with OCD and healthy controls for glutamate and glutamine in the rostral ACC; however, the study

did show reduced ACC activation in adults with OCD on an emotional Stroop task for OCD-specific words relative to neutral words (Brennan et al. 2015). Interestingly, Simpson and colleagues (2012) also saw no glutamate and glutamine differences in adults with OCD relative to healthy controls; however, they did see reduced γ -aminobutyric acid (GABA) relative to voxel tissue water in the medial prefrontal cortex for individuals with OCD relative to controls. In sharp contrast to glutamate, GABA has been shown to play an important inhibitory role in neurotransmission; however, research also suggests that the role of GABA shifts from excitatory to inhibitory as an individual ages from childhood to adulthood (Li, 2008). This relative GABA reduction was particularly pronounced in males relative to females and in individuals with older age of onset of OCD relative to individuals with a younger onset.

Kühn and colleagues (2016) recently published a study that described important differences in glutamate and GABA levels during a Stroop task. Their sample did not include individuals with OCD, but understanding their results may be instructive. They used fMRI-guided functional magnetic resonance spectroscopy to evaluate associations between regional activation and neurotransmitter concentrations in the ACC before, during, and after performance of a manual Stroop task similar to our own. GABA and glutamate levels were shown to have an inverted U-shape pattern for measurement points before, during, and after the task. Glutamine (precursor to glutamate) increased linearly and did not decrease following the task. A negative association was seen between GABA concentrations and ACC BOLD signal change suggesting that GABA did indeed play a significant role in inhibitory functioning. We propose that possible differences in glutamatergic and GABAergic systems for individuals with OCD may play an important role in differential ACC (and other regions) functioning when compared with healthy controls. It is particularly interesting that existing findings for changes in glutamate and GABA

in OCD overlap so well with our observed regions of conflict adaptation-related hypoactivity in OCD (ACC, medial prefrontal cortex, and orbitofrontal cortex). It is possible that due to the neurological differences described above, individuals with OCD may show altered inhibition (GABA) and excitation (glutamate) in response to stimuli that would normally elicit conflict adaptation processes.

Simpson and colleagues (2012) also considered the dlPFC as a region of interest in their analysis of GABA and glutamate concentrations, but they did not identify any significant proton magnetic resonance spectroscopy differences. This could be concordant with our lack of dlPFC findings for conflict adaptation. Future studies may benefit from considering conflict adaptation in the above regions using f-MRI guided functional magnetic resonance spectroscopy to evaluate metabolic factors related to neurological differences in OCD. The method used by Kühn and colleagues (2016) associating metabolic concentrations of neurotransmitters with BOLD signal change may be particularly helpful in this area of research.

In our study, the dlPFC showed an opposite pattern of activation to the ACC with significant differences in activation for processing current trials by congruency (greater activation for incongruent than congruent trials), but showing no differences in conflict adaptation analyses. We had expected the dlPFC to act as the regulative component of cognitive control signaling the need for increased cognitive resources to respond to conflict. Instead, the dlPFC appeared to be involved in the differential processing of current congruent vs. incongruent stimuli without regard for previous trial congruency.

Individuals with OCD have shown deficits in executive/regulative control associated with dlPFC activation including poor planning, task-switching, inhibition, and initiation (see Olley, Malhi, & Sachdev, 2007; van den Heuvel et al., 2005). The research comparing dlPFC activation

in response to Stroop tasks in individuals with OCD relative to healthy controls is mixed with some showing relatively increased activation (Schlösser et al., 2010) and others showing relatively decreased activation (Martinot et al., 1990). Hough and colleagues (2016) recently demonstrated that dlPFC activation in OCD may vary as a function of specific symptoms. Specifically, they demonstrated that individuals with hoarding symptoms showed increased dlPFC activation (without accompanying ACC differences) when compared with healthy control participants. Participants with OCD who did not have hoarding symptoms showed no such difference. Our sample of individuals with OCD did not report hoarding behaviors and did not differ significantly in dlPFC activation providing further support for the findings of Hough and colleagues (2016).

Overall, our hypothesized model for ACC activation as the evaluative component (i.e. conflict detection) and dlPFC activation as the regulative component of cognitive control appeared to be only partially supported by our results. For example, the ACC did appear to function as a conflict detector for sequencing changes (e.g. when trials changed from congruent to incongruent); however, it did not serve to process conflict for current trials. The dlPFC activation differences appeared only when processing current trial congruency and were not associated with the sequencing of trials in any analysis. Ultimately, our results appear to support the conclusion of Liu and colleagues (2004) that these regions of activity may play independent roles in cognitive control rather than existing in an evaluative-regulative feedback loop.

Other unexpected findings were seen in our fMRI analyses that may have been incidental, but some attempt at interpretation is warranted. For example, we saw greater activation for incongruent trials relative to congruent trials (Stroop effect only) in the left inferior parietal lobe and the left supplemental motor area. Although the differences in these two regions were not

expected, they may be reflections of the visual perception and motor planning required to respond manually with one of four buttons.

For conflict adaptation collapsed across groups, significant differences were also seen in the left fusiform gyrus, right inferior occipital gyrus, left globus pallidus, and left orbitofrontal cortex. These findings were not expected and we know of no similar results for the left fusiform gyrus, right inferior occipital gyrus, or left globus pallidus. As discussed above, the left orbitofrontal cortex has been highlighted as an important region for processing high-conflict trials in a Go/No-Go task, though the specific role it may play is not known at this time (Maltby et al., 2005). We echo Maltby and colleagues' (2005) conclusion that further research is needed to explore the role of the left orbitofrontal cortex in cognitive control processes.

Activation differences in all significant clusters of the previous by current model were particularly pronounced on change (iC and cI) trials relative to similar (cC and iI) trials. It has been suggested that left fusiform gyrus activation may be related to whole-word recognition reading (see Hirshorn et al., 2016; Roberts et al., 2013). Thus participants may have been relying more on whole-word reading processes when the congruency of a trial changed from the previous trial. The finding in the right inferior occipital gyrus is generally thought to have been associated with an unknown aspect of visual information processing, but occipital involvement in a Stroop task is not unprecedented (for example, see Markowska, Bydgoszcz, Malkowski, Wróbel, & Ziolkowski, 2015). We know of no right inferior occipital differences in conflict adaptation analyses specifically. Finally, a brief search of the literature yielded no apparent explanations for our observed conflict adaptation-related difference in left globus pallidus activation. Given the high number of analyses conducted in this dissertation, it is possible that some of our findings are attributable to type I error.

In summary, conflict adaptation differences were seen collapsed across groups in ACC but not dlPFC activation. ACC differences were also seen in conflict adaptation between groups with individuals in the control group showing greater conflict-adaptation-related activation than individuals with OCD. Thus, as Liu and colleagues (2004) suggested, the ACC and dlPFC appear to play separate roles in conflict adaptation. Individuals with OCD appear to have arrived at similar behavioral results to controls, but by different neurological means. One possible explanation is that individuals with OCD processed information as described in temporal learning theory whereas control participants used conflict adaptation processing. Another factor potentially accounting for OCD-related diminished conflict adaptation could be differences in metabolic concentrations in the ACC, medial prefrontal cortex, and orbitofrontal cortex of glutamate and GABA regulating excitation and inhibition in those regions. Our results suggest that the dlPFC may be primarily involved in distinguishing current trial congruency, whereas the ACC is primarily responsible for addressing conflict arising from sequencing effects. Our hypothesis of an evaluative-regulative feedback loop for cognitive control was not fully supported by the results.

Our final aim was to assess the relationship between cognitive control dysfunction and quality of life in individuals with OCD relative to healthy controls. Contrary to hypotheses, behavioral indices of conflict adaptation (i.e. reaction times and error rates) were not associated with quality of life. This may not be surprising as behavioral conflict adaptation reaction time differences were not seen between groups, and very few errors were made by participants. Most indices of quality of life were not associated with neurological indices of conflict adaptation; however, the WHOQOL-BREF Environmental Scale was positively related to the three-way interaction effect beta weights for the ACC. Contrary to hypotheses, no significant dlPFC

clusters were seen on the three-way model, and therefore beta weights for this region were not available for comparison with indices of quality of life.

It was not entirely clear why environmental quality of life, but not other domains of quality of life would have been significantly related to conflict-adaptation-related ACC activation between groups. This result may likely have been due to type I error. A study of the WHOQOL-BREF in a psychiatric sample showed that the environment scale (comprised of eight items) had the lowest internal reliability of the four subscales (Cronbach's $\alpha = .68$) and three of the eight items did not load onto the same factor as the other items (Oliveira, Carvalho, & Esteves, 2016). Furthermore, given the large number of analyses and the few that achieved statistical significance, the probability of Type I error is quite high. Thus, our finding of a significant relationship with this subscale, but not with other more reliable subscales in a psychiatric sample, appears to be a weak finding that limits interpretability.

As hypothesized, total YBOCS-2 scores were negatively associated with Physical and Environmental domains of quality of life. The overall severity of obsessive-compulsive symptoms for the current sample was in the mild range, but the absence of severe symptoms is clearly insufficient to mitigate the negative effects of OCD on quality of life. Coluccia and colleagues (2016) conducted a meta-analysis of obsessive-compulsive symptoms and quality of life and demonstrated that individuals with mild symptoms actually tended to report lower quality of life than did individuals with more severe symptoms of OCD. This finding was attributed to increased insight and awareness for individuals with mild symptoms into the impact of symptoms on their daily functioning. Thus, our findings for diminished quality of life in individuals with mild OCD symptoms were consistent with other results. If individuals with more severe symptoms of OCD had been included in our sample, the negative association

between YBOCS-2 scores and quality of life may have appeared very differently, resulting in altered correlational results with indices of conflict adaptation. A stronger study design would include a greater range of symptom severity in participants with OCD; however, this can also bring other confounding factors into play as severe OCD is often accompanied by additional pathology (Ruscio, Stein, Chiu, & Kessler, 2010).

The significant negative association between obsessive-compulsive symptoms and quality of life was not present in either the OCD or control groups when considered alone. This may be due to reduced power (nineteen or twenty participants in each group respectively), or to limitations in ranges of scores for comparison. Total YBOCS-2 scores for individuals with OCD tended to cluster around the mild end of the scale. Scores for healthy controls were generally flat with only a small number of individuals showing any symptoms at all. Only in comparing both groups together did a significant correlation emerge between obsessive-compulsive symptoms and quality of life. Thus, the correlational relationship between these variables may be best explained by a group split rather than a continuous association.

As outlined in the results section, differences between individuals with OCD and controls were minimal with regard to overall neuropsychological functioning. These were limited to a difference in estimated intellectual functioning (OCD WTAR < control WTAR standard scores) and a difference in self-reported executive functioning (OCD BRIEF-A > control BRIEF-A T scores). Although the difference between group mean standard scores for intellectual functioning (WTAR) were statistically significant, means for the two groups differed by only 6.2 points on a standard scale (scale with a mean of one-hundred and a standard deviation of fifteen; Wechsler, 2001). Thus, the functional impact of this difference may have been minimal. Importantly,

intellectual functioning was not associated with any indices of conflict adaptation or quality of life.

As expected, self-reported executive functioning was negatively associated with all considered indices of quality of life. The metacognitive index of executive functioning was negatively associated with behavioral error rate conflict adaptation, though given the minimal range of errors made in the Stroop task the meaning of this finding is likely not interpretable. The General Executive Composite scores for the BRIEF-A were negatively associated with the conflict adaptation effect for the medial prefrontal cortex. As executive functioning is generally believed to be mediated by frontal lobe functioning (see Banich, 2009; Miller & Cohen, 2001), it makes sense for executive dysfunction to be associated with diminished medial prefrontal cortex functioning. As individuals with OCD generally show deficits in aspects of executive functioning, (and as these symptoms were self-reported by our present sample), there appears to be a clear distinction in our results between executive functioning generally and conflict adaptation specifically (Olley, Malhi, & Sachdev, 2007).

In summary, it is interesting that although OCD symptom severity was predictive of quality of life, OCD-related differences in conflict adaptation generally were not. Overall, self-reported executive dysfunction was predictive of diminished quality of life, but this relationship appears to be mediated by processes other than conflict adaptation. Conflict adaptation may be a useful tool for better understanding the neurological processes underlying OCD; however, future researchers should be advised that a direct relationship between conflict adaptation and quality of life is not likely to emerge with repeated study, at least in individuals with mild symptoms of the disorder.

There are a number of limitations for the current dissertation. First, our sample of individuals with OCD was less symptomatic than is usually expected for individuals with the disorder. Specifically, our sample scored $18.65 (\pm 7.69)$ on the YBOCS-2 which was at least one standard deviation below the expected mean for individuals with OCD (compare mean scores of 30.55 ± 7.44 , Storch et al., 2010; and 26.54 ± 7.66 , Wu McGuire, Horng & Storch, 2016). Much of our sample had undergone treatment for their symptoms and, although they were still symptomatic at the time of participation in the study, the severity of their symptoms was well-managed by current medications and participation in psychotherapy. Although our sample demonstrated significant OCD-related declines in quality of life, it is possible that the neurological differences considered between individuals with OCD and psychiatrically-healthy controls would be more apparent in a sample with greater severity of symptoms. Second, our control sample showed significantly higher scores on a brief measure of estimated intellectual functioning; however, this measure did not significantly relate to quality of life or conflict adaptation. The difference between groups, while statistically significant, may not be clinically significant as the difference between mean standard scores was less than half of a standard deviation in the original normative sample as reported in the WTAR manual (Wechsler, 2001). Finally, due to the large number of analyses conducted in this dissertation, it is possible that Type I error may account for some of the significant findings, particularly in the correlation analyses.

Poor statistical power of general cognitive neuroscience research is an area of growing concern for many scientists. Szucs and Ioannidis (2017) recently analyzed over 26,000 statistical reports from 3,801 studies in cognitive neuroscience, psychology, and other related medical fields of study. They reported that the probability of false report (i.e. Type I error) is likely in

excess of 50% for the studies in question with cognitive neuroscience showing greater concerns than psychology or medical science. They particularly pointed out that small sample sizes and highly technical (often idiosyncratic) analyses in neuroimaging studies may be contributing to this problem. Of particular concern was a trend for study power to be negatively associated with high journal impact factors suggesting that underpowered studies have been finding unusual or interesting results, (likely due to error), that may receive undue attention in high impact factor journals. Eklund, Nichols, and Knutsson (2016) identified a significant problem in the default parametric statistical settings for common fMRI software packages resulting in a potential false positive rate of up to 70% for clusterwise inference. Thus, it is possible, (indeed probable), that many of the studies upon which current conflict adaptation theory has been built may be flawed, particularly in the case of neuroimaging studies with low power. We echo the sentiments of Eklund and colleagues (2016) and Szucs and colleagues (2017) that solutions to these methodological concerns may lie in: systematic data archiving, data sharing, refocusing research emphases on validating and improving existing cognitive neuroscience methods, preregistration of study methods, and raising the statistical significance threshold to a more robust level.

In conclusion, individuals with OCD showed similar behavioral responses to psychiatrically-healthy control participants, but arrived at these responses by different neurological processes. Given the current data, we cannot definitively determine whether these functions are independent of one another or parts of an evaluative-regulative feedback loop as hypothesized. The present data appear to support the former conclusion more than the latter. It is possible that individuals with OCD were able to show similar behavioral results to healthy controls by using an alternative processing system such as temporal learning. It is also possible that neurological differences in conflict adaptation could be related to metabolic differences

affecting excitatory and inhibitory functioning of observed regions of significant contrast between groups. Although individuals with OCD experience significantly diminished quality of life relative to healthy controls, this did not appear to be mediated by observed differences in conflict adaptation specifically; however, it was at least associated with self-reported deficits in executive functioning generally.

Future studies should focus on individuals with greater OCD symptom severity as the functional and neuropsychological profiles for these individuals differs markedly from those of individuals with mild symptoms. Additionally, future fMRI tasks should have a greater degree of difficulty to elicit more errors for useful comparisons between groups. We believe that the literature on glutamatergic and GABAergic system differences in OCD is possibly related to our conflict adaptation-related findings, and although this association could be merely circumstantial, further exploration of these factors may yield useful explanations for existing trends in the literature. Finally, there is a need for a greater understanding of the neuropsychological and neurological differences between pediatric and adult OCD samples, as our current results contrasted sharply with those of a prior pediatric study.

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