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Abstract

Obsessive compulsive disorder (OCD) is a debilitating, chronic condition that affects up to 3% of the population. A significant number of patients do not respond or still have residual symptoms even after completing empirically supported treatments. The study of neurocognitive functioning has been identified as one path toward developing a better understanding of underlying mechanisms and identifying new treatment targets. Response inhibition (RI), the ability to suppress inappropriate or irrelevant responses, is a neurocognitive process that may be particularly relevant to OCD. RI deficits have been found in adults with OCD, however questions remain regarding the nature and specificity of the relationship between individual RI domains and OCD. This dissertation addresses such questions across three chapters. Chapter 1 investigates whether OCD symptomatology is related to RI deficits in an analogue sample of 222 participants. OCD symptomatology was a significant and unique predictor of one RI domain, action cancellation, controlling for ADHD, impulsivity, anxiety, and depressive symptomatology, supporting the possibility that action cancellation is an endophenotype or trait-based marker of OCD. In 99 of these participants, Chapter 2 explores whether cognitive processing speed mediates the relationship between depressive symptomatology and individual RI domains, a relationship that has been shown in previous research with clinical samples and referred to as evidence against the specificity of an RI deficit in OCD. RI domains, as well as cognitive processing speed, were unrelated to depressive symptomatology suggesting that neither RI nor cognitive processing speed are trait-based deficits underlying depressive disorders. In Chapter 3, 28 treatment-seeking youth with OCD were compared to 27 treatment-seeking youth with anxiety disorders on the three RI domains. No significant differences emerged between groups across RI domains and RI was unrelated to OCD, anxiety, or depressive severity but was correlated with age. Results from this study indicate that youth with OCD may not possess RI deficits, differing from adults with OCD. Possible explanations for this inconsistency related to neurodevelopmental processes are discussed.

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RESPONSE INHIBITION IN OBSESSIVE COMPULSIVE DISORDER AND
CO-OCCURRING PSYCHOPATHOLOGY

Sarah Herrick Morris

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ABSTRACT

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Sarah Herrick Morris

Martin E. Franklin

Obsessive compulsive disorder (OCD) is a debilitating, chronic condition that affects up to 3% of the population. A significant number of patients do not respond or still have residual symptoms even after completing empirically supported treatments. The study of neurocognitive functioning has been identified as one path toward developing a better understanding of underlying mechanisms and identifying new treatment targets.

Response inhibition (RI), the ability to suppress inappropriate or irrelevant responses, is a neurocognitive process that may be particularly relevant to OCD. RI deficits have been found in adults with OCD, however questions remain regarding the nature and specificity of the relationship between individual RI domains and OCD. This dissertation addresses such questions across three chapters. Chapter 1 investigates whether OCD symptomatology is related to RI deficits in an analogue sample of 222 participants. OCD symptomatology was a significant and unique predictor of one RI domain, action cancellation, controlling for ADHD, impulsivity, anxiety, and depressive symptomatology, supporting the possibility that action cancellation is an endophenotype or trait-based marker of OCD. In 99 of these participants, Chapter 2 explores whether cognitive processing speed mediates the relationship between depressive

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INTRODUCTION

Obsessive compulsive disorder (OCD) is a debilitating, chronic condition that affects up to 3% of the population (Ruscio, Stein, Chi, & Kessler, 2010, Zahar, 1999). It is associated with significant impairment in social, academic, and family functioning (Piacentini, Bergman, Keller, & McCrackern, 2003) and is considered one of the ten most handicapping conditions by the World Health Organization (Bobes et al., 2001). OCD is characterized by symptoms that include intrusive thoughts, images and urges that are persistent and unwanted and cause marked anxiety or distress (i.e., obsessions) as well as repetitive mental or behavioral rituals (i.e., compulsions) that are performed in response to obsessions in order to reduce, avoid, or prevent the associated anxiety or distress (American Psychiatric Association, 2013). OCD presents similarly in children, adolescents and adults (Kalra & Swedo, 2009) and rarely remits without treatment (Stewart et al., 2004).

Fortunately, significant advances have been made over the past twenty years in the development of treatments for this disorder. Both exposure and response prevention (ERP), a type of cognitive behavioral therapy (CBT), and pharmacotherapy with a serotonin reuptake inhibition (SSRI), have proved efficacious in the treatment of OCD in both adults (see Romanelli et al., 2014, for review) and children (see Watson & Rees, 2008 for review). Although many patients have benefited substantially from these interventions, there are still a significant number who either do not respond or still have residual symptoms after completing empirically supported treatments (Franklin & Foa, 2011). For example, a meta-analysis of long-term outcomes of pediatric OCD found that

following treatments, persistence rates were 41% for full OCD and 60% for full or subthreshold OCD (Stewart et al., 2004).

As stated in the National Institute of Mental Health's (NIMH) Research Domain Criteria (RDoC) project, defining and studying the "mechanisms of complex behaviors" across mental disorders are essential steps in improving such outcomes. Neurocognitive functioning has been identified as one type of such a mechanism, as it may serve as a link between brain functioning and the phenomenology of a disorder. Accordingly, examining neurocognitive functioning that may be implicated in the etiology and maintenance of OCD was the overarching goal of this dissertation research. There are a number of pathways by which this type of research may lead to reduced suffering related to OCD symptomatology.

First, identifying neurocognitive impairments that are present in OCD may provide new treatment targets. A treatment target is a "mechanism of action" that may "modify disease, behavior, or functional outcomes" (NIMH, 2017). Once a hypothesized target is identified, precise interventions aimed at that target can be developed and tested. Such interventions could be added to established treatments to make them more efficient or effective, could be used as an adjunctive treatment for those who do not have satisfactory response to traditional CBT or pharmacotherapy, or could be used to tailor treatment if it is found that the deficit is particularly pronounced in a subset of patients. Next, it is hoped that identifying neurocognitive processes related to OCD will allow psychologists to predict the development of symptoms before they become impairing. Subtle changes in behavior and cognition may be precursors to the development of

mental illness and if they can be measured, preemptive interventions become a possibility. In addition to the potential to predict onset of illness, neurocognitive processes that are found to be related to OCD may be studied as potential predictors of treatment response, allowing treatment providers to select the likeliest successful intervention for an individual. Finally, studying impairments in neurocognitive functioning in one disorder such as OCD may reveal abnormal basic processes that are shared across other disorders. This revelation would aid in increasing the precision of diagnostic categories and therefore treatment.

Response inhibition (RI) is one neurocognitive function that may be particularly relevant to OCD. RI is defined as the ability to suppress inappropriate but inadvertently activated, prepotent responses to stimuli (Barkley, 1997; Nigg, 2000; Verbruggen & Logan, 2008). The ongoing feedback loop in which intrusive, uncontrollable obsessions trigger repetitive, habitual compulsions may represent a deficit in RI (e.g., Bannon, Gonsalves, Croft, & Boyce, 2006; Chamberlain et al., 2008; Menzies et al., 2007; Watkins et al., 2005).

RI can be broken down into three subcomponents or domains. First, interference control refers to the ability to resolve a conflict in which competing response tendencies are co-activated due to incongruent stimulus dimensions (Chamberlain & Sahakian, 2007; Sebastian, et al., 2013). Second, action restraint is the effortful control of a response in compliance with changing context cues (Morein-Zamir, Fineberg, Robbins, & Sahakian, 2010; Sebastian, et al., 2013). Finally, action cancellation is the inhibition of an ongoing motor response (Logan, 1994; Sebastian et al., 2013). Functional magnetic

imaging (fMRI) has shown that these subcomponents share a common neural network but differ in the degree of brain regional involvement, validating this subcomponent model of RI, and suggesting the possibility that each domain may be differentially related to specific mental illnesses or disease processes (Sebastian et al., 2013). A variety of paradigms have been developed and used to study RI in the lab. Although many of these tasks were initially employed using non-computerized methods (e.g., Beers et al., 1999) computerized tasks are now standard (Sebastian et al., 2013). Stroop tasks capture interference control, go/no-go tasks measure action restraint, and stop signal tasks gauge action cancellation.

There have been several studies examining RI in adults with OCD using these types of tasks. Most have shown that adults with OCD perform poorly on RI tasks (e.g., Bannon et al., 2002; Bersani et al., 2013; Chamberlain et al., 2008; Enright et al., 1995; Gillan et al., 2011; Hartston, 1999; Lei et al., 2017; McLaughlin et al., 2016; Menzies et al., 2008; Penadés et al., 2007; Zhang et al., 2016). Based on these findings, as well as findings showing impaired RI in first-degree relatives of patients with OCD, RI has been proposed as a candidate endophenotype of OCD (Chamberlain et al., 2008). However, there have been studies that did not find RI impairment related to OCD (e.g., Bohne, Savage, Deckersbach, Kalanthroff et al., 2008; Boone et al., 1991; Kalanthroff et al., 2016; Krishna et al., 2011). Explanations for these inconsistencies are likely related to the heterogeneous nature of both RI and OCD. Studies have often used single RI tasks and have not been consistent in the tasks used, therefore tapping different RI domains, which may be differentially related to OCD. Additionally, OCD has high rates of co-morbidity

with disorders that are known to have executive functioning deficits including depression, disruptive behavior disorders (Geller, Biederman, Driffen, Jones, & Lefkowitz, 1996) and ADHD (Abramovitch, Dar, Mittelman, & Wilhelm, 2015; Boonstra et al., 2005). This has led some researchers to express skepticism that RI impairments are driven by obsessive compulsive symptomatology (e.g., Abramovitch & Abramowitz, 2014) and therefore may not be a “mechanism of action” that relates to OCD’s development, course, or outcome.

There are several gaps in the evidence base on the relationship between OCD and RI that, if addressed, would help to confirm the presence of an RI deficit specific to OCD as well as explain the nature of this relationship. First, very little research has been undertaken in analogue samples, a necessary population to establish a relationship between RI and obsessive compulsive symptomatology in order for RI to be considered an endophenotype of OCD (Abramovitch et al., 2015). Next, although many studies have excluded participants with major depressive disorder based on the belief that depression is associated with an RI deficit little research on RI in depression has been undertaken. Given the high rates of co-morbidity between OCD and depression (Ruscio et al., 2010), this belief has led to RI studies with samples that do not represent the true OCD patient population. Finally, scant attention has been paid to RI in pediatric OCD populations. Identifying an RI deficit in this population would suggest that that RI dysfunction is present temporally close to the onset of the disorder and refute the hypothesis that RI weakens over the course of a lifetime with OCD. This would increase the likelihood that impaired RI is a precursor to the development of pathology. It would also show how

relevant RI targeted interventions would be for children with OCD. These three specific gaps in the literature will be addressed in this dissertation in Chapters 1, 2, and 3, respectively.

Chapter 1 examines the three RI domains, interference control, action restraint, and action cancellation, and their independent relationships with OC symptomatology controlling for ADHD, impulsivity, anxiety and depressive symptoms in an analogue sample. This chapter addresses questions regarding the nature and specificity of an RI deficit related to OC symptomatology.

Chapter 2 addresses the question of how we might explain relationships between individual RI domains and disorders other than OCD, such as depression, that we would not expect to share this underlying vulnerability. It explores the relationship between RI and depressive symptomatology in an analogue sample as well as the role deficits in processing speed may play in RI impairment previously suggested to be present in depressed patients.

Chapter 3 examines RI in pediatric patients with OCD compared with pediatric patients with other anxiety disorders. This study seeks to extend RI research in adult OCD populations in order to determine whether RI impairment is relevant in youth with OCD. Evidence from this study will increase our understanding of pediatric OCD but will also speak to whether RI impairments are apparent relatively early in the disorder and are specific to OCD versus other anxiety disorders, and thus may be a useful predictor or precursor of the development of symptoms.

Together, this set of studies aims to provide evidence for a link between RI and the phenomenology of OCD using multiple methods that explore this relationship from a number of different angles. Establishing and understanding such a link could have important implications for improving the outcomes of individuals who are vulnerable to and suffer from OCD.

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Chapter 1: Response Inhibition and Obsessive Compulsive Symptomatology in a Non-clinical Sample

Abstract

Deficits in response inhibition (RI), the ability to suppress inappropriate or irrelevant responses, may play a role in the etiology and/or maintenance of obsessive-compulsive disorder (OCD). Many studies have demonstrated differences in RI between OCD patient groups and control groups, leading researchers to posit that deficient RI may be an endophenotype of OCD. Based on the current conceptualization of endophenotypes in psychiatric disorders, such markers should vary across the general population. Little research on RI and obsessive-compulsive (OC) symptomatology has been conducted in non-clinical samples, making this criterion difficult to evaluate. Additionally, some studies have failed to find deficits in RI performance in individuals with OCD. A likely explanation for inconsistent findings may be that most studies to date have relied on single measures of RI. RI is composed of multiple domains, which may be differentially related to OCD symptoms. In the current study, we examine associations between multiple domains of RI and OC symptomatology in a non-clinical sample. Two hundred and twenty-two undergraduates came into the lab to complete three separate RI tasks, the motor Stroop task, the go/no-go task, and the stop signal task. Participants also completed self-report questionnaires measuring symptoms of OCD, attention deficit/hyperactivity disorder, behavioral impulsivity, depression, and anxiety. Multiple linear regressions demonstrated that after controlling for symptoms of ADHD, impulsivity, depression, and anxiety, symptoms of OCD significantly predicted action cancellation, the RI domain

captured in the stop signal task. This finding provides support for existence of a unique relationship between OC symptomatology and RI, in an analogue population. OCD symptoms were unrelated to interference control and action restraint, RI domains measured with the motor Stroop and go/no-go tasks, respectively, suggesting that individual domains of RI are not uniformly related to OCD.

Obsessive compulsive disorder (OCD) is a highly disabling clinical condition characterized by recurrent, intrusive, distressing thoughts or images followed by repetitive, time-consuming compulsive behaviors that temporarily reduce distress (APA, 2000). OCD is prevalent (Ruscio, Sten, Chiu, & Kessler, 2010), affecting approximately 2.3% of the population. Neurobiological studies examining structural and functional differences in the brains of individuals with OCD compared to healthy controls have uncovered abnormalities within the fronto-striatal cortex (Saxena & Rauch, 2000), a brain region heavily involved in impulse control and decision making (Lezak, 1995). Based on these findings as well as the intrusive, recurring nature of obsessions and apparent uncontrollability of compulsions experienced by patients with OCD, poor executive functioning has been hypothesized to contribute uniquely to OCD and its maintenance (e.g., Bannon, Gonsalvez, Croft, & Boyce, 2006, Chamberlain, et al., 2008; Menzies et al, 2007; Watkins et al., 2005). It has been posited that response inhibition (RI), the ability to suppress inappropriate or irrelevant responses (Verbruggen & Logan, 2008), is an executive function that may play a particularly significant role in OCD (Chamberlain et al., 2008; Menzies et al., 2007; van Velzen, Vriend, de Wit, & van den Heuvel, 2014; Woolley et al., 2009).

A number of studies have examined RI and its relationship to OCD. Several investigations have found that OCD is associated with increased RI deficits on computerized measures of RI compared with both healthy controls and individuals with other psychopathology (e.g., Bannon et al., 2002; Bersani et al., 2013; Chamberlain et al., 2008; Enright et al., 1995; Gillan et al., 2011; Hartston, 1999; Lei et al., 2017;

McLaughlin et al., 2016; Menzies et al., 2008; Penadés et al., 2007; Zhang et al., 2016). Consequently, deficient RI has been proposed as a candidate endophenotype of OCD (Chamberlain et al., 2005). Additional evidence for this idea comes from work showing first-degree relatives of patients with OCD have impaired RI compared with individuals having no immediate family history of the disorder (Chamberlain et al., 2007; Menzies et al., 2007; Zhang et al., 2015).

However, other studies have failed to identify differences in RI performance between OCD patients and healthy controls (e.g., Bohne, Savage, Deckersbach, Kalanthroff et al., 2008; Boone et al., 1991; Kalanthroff et al., 2016; Krishna et al., 2011). One explanation for these inconsistent findings may be that there are multiple measures researchers have relied on to measure RI, each of which assess different aspects of RI. Like executive functioning, response inhibition itself is not a unitary construct. RI domains can be separated into action restraint, action cancellation, and interference control. Specific computerized tasks capture these different domains. Stroop, Flanker, and Simon tasks measure interference control, the cognitive control needed to prevent interference due to competition of relevant and irrelevant stimuli or stimulus characteristics (Chamberlain & Sahakian, 2007; Nigg, 2000; Sebastian, et al., 2013; van Velzen et al., 2014). The go/no-go task captures action restraint, or the effortful control of a motor response in compliance with changing context cues (Morein-Zamir, Fineberg, Robbins, & Sahakian, 2010; Sebastian, et al., 2013). The stop signal task (SST) measures action cancellation, the inhibition of an ongoing motor response (Logan, 1994; Sebastian, et al., 2013). It has been proposed that interference control, action restraint, and action

cancellation represent early, intermediate, and late processes of RI, respectively (Sebastian et al., 2013).

There is some evidence that these RI domains may be differentially related to OCD symptomatology. One meta-analysis that examined action cancellation across psychiatric disorders identified a medium effect size for a deficit in action cancellation associated with OCD, comparable in magnitude to the action cancellation deficit found in ADHD. On the other hand, a meta-analysis examining action restraint across psychopathology with the use of the go/no-go task found no significant deficit associated with OCD (Wright et al., 2014). Relatedly, a meta-analysis completed by Abramovitch and colleagues (2013) found an overall medium effect size regarding RI deficits in OCD but identified a discrepancy in weighted mean effect sizes across RI domains. A medium weighted mean effect size was found for deficits in Stroop interference (i.e., interference control, $d = -.54$), compared to a small effect size found for commission errors (i.e., action restraint; $d = -.33$). Again, these results suggest that deficits in each RI domain may be more or less relevant to OCD symptomatology. Most studies to date have examined the relationship between OCD symptomatology and RI using a single measure of RI and therefore have been unable to examine deficits according to RI domain. The present study will use three measures of RI – the motor Stroop task, the go/no-go task, and the stop signal task – and will therefore have the ability to examine each RI domain and the possibility that each may be differentially related to OCD symptoms.

Another explanation that has been put forth for the inconsistent findings regarding RI deficits in OCD is the high incidence of comorbidity associated with OCD (Ruscio et

al., 2010). Researchers have argued that RI deficits identified in OCD populations may be explained by co-morbid psychiatric illnesses that also have shown to be associated with other neuropsychological functioning impairments such as ADHD (Boonstra, Oosterlaan, Sergeant, & Buitelaar, 2005), depression and other anxiety disorders (Castaneda, Tuulio-Henriksson, Marttunen, & Suvisaari, 2008). The current study thus examined whether OCD symptoms predicted RI after controlling for symptoms of ADHD, impulsivity, depression, and anxiety.

A recent comprehensive review completed by Abramowitz et al. (2014) emphasized the value of studying analogue samples in OCD research based on evidence that OCD symptoms are dimensional (rather than categorical) and have similar characteristics regardless of diagnostic status. Studying non-clinical samples may be particularly useful in considering the appropriateness of considering RI as an endophenotype for OCD; endophenotypes should vary continuously throughout the general population (Cannon & Keller, 2006). Therefore, if RI is an endophenotype for OCD, RI performance should vary across a non-clinical sample according to the presence of OCD symptomatology.

Very little research has examined the relationship between RI and OC symptomatology in non-clinical samples. Recently, Abramovitch and colleagues (2015) used a standardized version of the go/no-go task to examine RI and its association with OCD symptoms in an undergraduate sample. Investigators found that the high symptom group made more commission errors than the low symptom group but that the high symptom group's performance was in the normative range. To our knowledge, no study

has yet examined the unique relationship between OC symptoms, over and above symptoms of frequently co-morbid psychopathology, and multiple RI domains in a non-clinical sample.

To address this gap, the present study was designed to examine the association between OC symptomatology and three RI domains (interference control, action restraint, and action cancellation) within a non-clinical undergraduate sample. Based on the aforementioned literature showing more consistent findings in regard to OCD and impaired performance on Stroop and stop signal tasks as compared with go/no-go tasks, we hypothesized that OC symptoms would predict poorer interference control and action cancellation over and above symptoms of ADHD, impulsivity, depression, and anxiety but would not significantly predict action restraint.

Method

Participants

Participants were 222 undergraduate college students (68.1% female; $M_{\text{age}} = 19.63$, $SD = 1.46$) enrolled in introductory psychology courses at the University of Pennsylvania. Participants received course credit for their participation in this study. The study was approved by the Institutional Review Board at the University of Pennsylvania.

Measures

Clinical measures. The *Obsessive-compulsive inventory – revised* (OCI-R; Foa et al., 2002) was used to assess the severity of obsessive-compulsive symptoms. The OCI-R is made up of 18 OCD-related symptoms. Participants rate the extent to which they are bothered by these symptoms on a four-point Likert scale, ranging from 0 (not at all) to 4

(extremely bothered). The OCI-R has been shown to have very good test-retest reliability and internal consistency in clinical and non-clinical samples (Foa et al., 2002; Hajcak, Huppert, Simons, & Foa, 2004). The current sample demonstrated good internal consistency ($\alpha = .90$). We used the *Beck Depression Inventory II* (BDI-II; Beck Steer, & Brown, 1996) to assess severity of depressive symptoms. The BDI-II is made up of 21 items that are rated between 0 and 3, with higher scores indicating greater symptom severity. In our sample, the BDI-II demonstrated good internal consistency ($\alpha = .88$), consistent with previous demonstrations of acceptable reliability and validity across clinical and non-clinical samples (Beck et al., 1996). The 20-item scale of the *State-Trait Anxiety Inventory* (STAI; Spielberger & Sydeman, 1994) was used to assess state anxiety. The current sample demonstrated good internal consistency ($\alpha = .95$), in line with previous research showing good psychometric properties (Barns, Harp, & Jung, 2002). To assess self-reported behavioral impulsivity, we used the *Barrat Impulsiveness Scale* (BIS-11; Patton et al., 1995), a 30-item instrument designed to assess the behavioral and personality construct of impulsiveness. The BIS-11 has demonstrated good internal consistency and test-retest reliability (Stanford et al., 2009) and showed good internal consistency in our sample ($\alpha = .81$). Finally, the 18-item *Adult ADHD Self-Report Scale* was used to assess symptoms of ADHD (Kessler, Adler, Ames, & Demler, 2005) and demonstrated good internal consistency ($\alpha = .82$),

Response inhibition tasks. Participants completed three computer tasks (motor Stroop task, go/no-go task, and the stop signal task) that measure different aspects of response inhibition (interference control, action restraint, and action cancellation

respectively). The *motor Stroop task* asks participants to quickly indicate the direction (left vs. right) of an arrow that is presented on either side of the screen. RI performance is indexed by the difference in reaction times from congruent (arrow is presented on the same side of the screen it is pointing toward) vs. incongruent trials (arrow is presented on the opposite side of the screen it is pointing toward). The *go/no-go task* presents letters that compose go trials and no-go trials. Participants are instructed to press the response key promptly when the target figure appears on the screen (i.e., go trial), while refraining from responding to the distracter figure (i.e., no-go trial). The RI outcome variable from this task is number of commission errors (i.e., how often the button is pressed following a no-go trial). Overall, it measures the ability to inhibit pre-potent response (i.e. a response that has not yet been initiated; Lee, Yost, & Telch, 2009). The *stop signal task* presents go trials in which participants are asked to quickly respond by indicating the direction of an arrow presented in the center of the screen. During some trials, however, the target stimuli are presented with a stop signal (a beep sound during the trial). Participants are instructed to cease the response to the target stimulus when a stop signal occurs. This task measures the ability to inhibit ongoing response (i.e. a response that has already been initiated). As the task goes on, an automatic tracking algorithm adjusts how quickly the stop signal is displayed during a go task according to how well the individual is performing. This allows the individual to be successful on stop-signal trials at 50% (Chamberlain et al., 2006; Morein-Zamir, et al., 2010). The main outcome variable of the SST is stop-signal reaction time (SSRT; Lipszyc & Schachar, 2010). SSRT provides an estimate of the latency of the inhibitory process, or how long it takes the participant to

appropriately inhibit a response. The SSRT is inferred from the distribution of reaction times following go-signals and proportion of successful stops (Lijffijt, Kenemans, Verbaten, & van Engeland, 2005).

Procedure

Participants came into the lab to complete response inhibition tasks. Tasks were completed individually, in a quiet room, on a desktop computer. Tasks were run using Inquisit 4 Web software (Inquisit, 2014). Completion of all three tasks took approximately 25 minutes. Participants were then given instructions to complete self-report questionnaires online. Data from three participants were removed from the dataset due to SSRTs under 50ms, indicating deliberate slowing of responses and thus invalidated results (Congdon et al., 2012). Due to computer malfunction, two participants were unable to complete the stop signal task and an additional participant was unable to complete the Stroop task. Complete data was thus available for 216 participants.

Data Analysis

Prior to statistical analysis, each outcome measure was examined for significant outliers and to determine whether assumptions of normality, linearity, and homoscedasticity were met. Variables that were not normally distributed were transformed using square-root transformation.

Hierarchical regression analyses were conducted to determine whether OCD symptomatology explained a significant amount of the variance in performance on each RI task (Stroop, go/no-go, and stop signal tasks) after accounting for symptoms of ADHD, impulsivity, anxiety, and depression. Given that response inhibition is believed

to be a primary deficit in ADHD (Barkley, 1997; Quay, 1997; Wodka et al., 2007), ADHD symptom severity was entered in the first block. Self-rated behavioral impulsivity as measured by the BIS-II, has been shown to account for a significant proportion of the variance on multiple measures of executive functioning (see Stanford et al., 2009 for review) and therefore was entered in the second block. General distress variables (STAI; BDI) were entered in the third block. Finally, OCD symptoms (OCI-R) were entered in the fourth block.

Results

Table 1 shows means and standard deviations for each clinical measure and RI variable as well as correlations between measures and RI variables. OCI-R, BDI, STAI, and BIS-II means and standard deviations were approximately consistent with data from similar, non-clinical samples (e.g., Siev, Huppert, & Chambless, 2010; Stanford et al., 2009).

Tables 2, 3, 4 depict the results of the hierarchical regression analyses predicting the Stroop interference effect in the Motor Stroop task, commission errors in the Go/No-go task; and stop signal reaction time in SST. Regression models did not predict a significant amount of the variance in performance on the Motor stroop task, $F(5, 214) = .70, p = .63, R^2 = .02$, or the go/no-go task, $F(5, 215) = .21, p = .64, R^2 = .01$.

In the case of the SST, the final model predicted a significant amount of the variance in stop signal reaction time, $F(5, 214) = 2.51, p = .03, R^2 = .06$ (see Table 4). In Block 1, ADHD was a significant predictor of SSRT, $F(1, 214) = 5.65, p = .02, R^2 = .03$. In Blocks 2 and 3, impulsivity and distress variables (anxiety and depression) did not add

predictive power to the model; i.e., self-reported impulsivity, depression, and anxiety symptoms did not predict stop signal reaction time over and above ADHD symptoms. However, when OCD symptoms were added to the model, predictive capacity increased significantly. Examination of beta weights in the final model indicated that OCD was a significant independent predictor of stop signal reaction time (see Table 4), $\beta = .17$, $t = 2.33$, $p = .02$.

Discussion

The aim of this study was to examine the relationship between OC symptomatology and individual domains of RI (i.e., interference control, action restraint, and action cancellation) in a nonclinical sample. Results showed that OC symptomatology was associated with poorer action cancellation but not interference control or action restraint. The significant relationship between OC symptoms and action cancellation is in line with previous research documenting longer stop signal reaction times in the stop signal task in patients with OCD as compared to healthy controls (Bersani et al., 2013; Chamberlain et al., 2006; Chamberlain et al., 2007; Lei et al., 2017; McLaughlin et al., 2016; Menzies et al., 2007; Zhang et al., 2016). The lack of significant findings with regard to interference control is somewhat surprising, given previous studies showing an association between the Stroop interference effect and OCD (Bannon et al., 2002; Enright et al., 1995; Nabeyama et al., 2008; Nakeo et al., 2009; Penadés et al., 2007; Schlosser et al., 2010, Zhang et al., 2016). In the case of action restraint, however, null findings were expected, as most previous RI studies have failed to find a

significant difference in the number of errors committed by OCD patients compared to controls (Abramovitch et al., 2013).

A unique aspect of the current study was its use of multiple measures of RI. Within much of the literature examining RI in OCD, RI is treated as a unitary construct that can be assessed using a single measure. However, neuroimaging studies have shown that individual domains of RI depend on overlapping, yet distinct, brain areas (van Velzen, Vriend, de Wit, & van den Heuvel et al., 2014) and thus are likely differentially implicated in specific psychological disorders (Schachar, Logan, Robaey, Ickowicz, & Barr, 2007). The current findings provide support for the idea that individual domains of RI are not uniformly related to OCD and that action cancellation specifically may be a particularly relevant RI domain when examining RI deficits in OCD.

Indeed, studies using the SST to measure RI in OCD have most consistently identified significant deficits as compared with studies using other measures (Lipszyc & Schachar, 2010). This may be due to the specific neuroanatomical and neurochemical correlates associated with action cancellation that the SST requires. Supporting this possibility is research showing that OCD patients exhibit hyperactivity within the presupplementary motor area of the brain during the stop signal task (de Wit et al., 2012), an area known to be important for action cancellation (Aron, 2011; Chao, Luo, Chang, & Chiang-shan, 2009).

Another explanation could be the increased difficulty of the SST as compared with tasks that measure other domains of RI such as the go/no-go and Stroop tasks. It has been proposed that the SST elicits the highest inhibitory load as compared with other RI

tasks (Schachar et al., 2007). There is some evidence from research in other areas of neuropsychological functioning in OCD that differences between OCD and control groups only emerge when difficulty is increased (Rasmussen et al., 2016). Specifically, multiple studies using the N-back task, a measure of working memory, have reported deficient performance in OCD samples on more difficult trials (e.g., 3-back) but not easier trials (e.g., 1-back; deVries et al., 2014; Kashyap, Kumar, Kandavel & Reddy, 2013; van der Wee et al., 2003). Perhaps RI deficits relate to OCD symptoms only past a particular inhibitory load threshold. This may explain inconsistent findings even across studies that use the same type of RI task. For example, although the basic structure and goals of a motor Stroop task would conceivably remain consistent across studies, the parameters may change (e.g., number and order of trials, type of stimuli, amount of time stimuli are presented) and thus lead to different levels of inhibitory load. This possibility highlights the need for the use of standardized measures of RI, such as those used in by Abramovitch et al. (2015; Neurotrax, 2003) to study action restraint in an analogue OCD sample.

Some researchers have argued that studies showing a significant relationship between OCD and any type of neuropsychological impairment, including RI, may be due to anxiety and distress associated with obsessions and compulsions rather than processes specific to OCD (e.g., Abramovitch & Abramowitz, 2003). Thus, another aim of the current study was to examine the relative specificity of an association between RI deficits and OC symptomatology. The finding that OC symptomatology was a unique predictor of action cancellation over and above symptomatology of other psychopathology with

well-established RI deficits (i.e., ADHD) as well as the relative lack of prediction by anxiety and depression symptoms lends support to the argument that RI impairment identified in OCD populations is related to OCD-specific processes.

There are multiple possible explanations for why studies have shown RI impairments related to OCD. One is that RI is an endophenotype (i.e., an intermediate marker of brain dysfunction that represents a genetic vulnerability for a disorder; Gottesman and Gould, 2003) for OCD. The current study's finding that action cancellation (a domain of RI) varied according to OC symptomatology in a non-clinical sample suggests that this relationship may exist in the general population, a characteristic necessary for a trait to be considered an endophenotype and thus lends support to the endophenotype hypothesis. Other explanations have not been ruled out, however, including the possibility that RI performance is a state-related mechanism, negatively affected by levels of OC symptoms (Abramovitch, et al., 2011; Moritz, Hottenrott, Jelinek, Brooks, & Scheurich, 2012) or that a dual state-trait mechanism exists (Abramovitch et al., 2015). For example, it may be that although the psychophysiological response during RI is trait-dependent and thus does not change with symptom reduction, the behavioral performance on RI tasks is malleable and is associated with symptom status.

Understanding the relationship between RI and OC symptomatology is important because of the implications for treatment. Should changes in RI be directly related to changes in symptom severity, there would be promise for targeting and strengthening RI specifically as a means of decreasing OCD severity. Future work could then examine the

value of having patients with OCD engage in response inhibition training (RIT) using computer programs that allow them to practice tasks similar to those performed during measures of RI. Should subsequent RI strengthening be associated with OCD improvement, RIT would have the potential to be used as an adjunctive or even alternative tool for treating the disorder. Given the dearth of CBT practitioners trained in ERP (Marques et al., 2010) as well as the fact that a significant proportion of patients with OCD treated with ERP and medication still experience clinically significant residual symptoms (e.g., Pediatric O.C.D., 2004), an easily disseminated tool that targets a different aspect of OCD than is addressed in current treatments (either CBT or pharmacotherapy with an SSRI) would be of great value to OCD sufferers and those who want to help them. Relatedly, researchers have begun testing the use of Transcranial Direct Current Stimulation (tDCS) as a means of enhancing inhibitory control within areas of the brain that have shown abnormal functioning in individuals with OCD with the goal of symptom improvement and have reported promising results in the context of case studies (Narayanaswamy, Chhabra, Agarwal, & Shrinivasa, 2015). Interventions such as this that could be used for treatment-refractory patients are sorely needed. Additional research that investigates domain-specific RI performance and elucidates its relation to OC symptomatology across the whole spectrum of severity will be important steps in that direction.

The current study had limitations that should be considered, including its reliance on self-report measures as well as lack of structured clinical screening. It is possible that some participants may have met criteria for OCD or other disorders. Additionally, the

sample was composed entirely of undergraduates at a competitive university and thus results may not necessarily generalize to a population with more heterogeneity with regard to characteristics such as age and education.

A major strength of the current study was its use of multiple measures of RI, which allowed us to examine the relationship between individual RI domains and OC symptoms. An additional strength was the use of a non-clinical sample, as demonstrations of significant relationships between symptomatology and RI in non-clinical samples are needed to determine whether RI should be considered an endophenotype of OCD.

In summary, the results of this study support the growing literature indicating that OC symptomatology is related to abnormalities in action cancellation, a specific RI domain. The explanation for why this relationship exists is not yet clear. Future studies that examine multiple domains of RI and OC symptoms in heterogeneous non-clinical samples across the lifespan and clinical samples over the course of treatment may help to elucidate this question.

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Table 1
Correlational analyses of self-report questionnaires and RI variables.

Measures	<i>M (SD)</i>	1	2	3	4	5	6	7
ADHD-SRS	48.89 (8.68)	--	--	--	--	--	--	--
BIS	60.28 (9.04)	.51**	--	--	--	--	--	--
BDI	11.06 (9.34)	.30**	.20**	--	--	--	--	--
STAI	2.12 (.60)	.38**	.11	.64**	--	--	--	--
OCI-R	16.35 (11.44)	.36**	.15*	.32**	.33**	--	--	--
Stroop Int. ¹	51.74 (48.88)	.00	.06	-.03	.00	-.10	--	--
Comm. Err. ²	6.66 (4.22)	.03	.07	-.02	.05	-.04	.02	--
SSRT ³	232.50 (40.47)	.16*	.10	.10	.10	.18**	.24**	.19**

Note: ADHD = Adult ADHD Self-Report Scale; BDI = Beck Depression Inventory II; BIS = Barrat Impulsiveness Scale; OCI-R = Obsessive-compulsive inventory – revised; STAI-State = State-Trait Anxiety Inventory.

¹Stroop interference effect on motor Stroop task (in milliseconds)

²Total commission errors on go/no-go task

³Stop signal reaction time on stop signal task (in milliseconds)

* $p < 0.05$; ** $p < 0.01$

Table 2
Results of hierarchical linear regression predicting Stroop interference on motor Stroop task.

Block	Predictor	β	<i>t</i>	R^2	R^2 change
1	ADHD	-.12	-.17	.00	.00
2	BIS	.09	1.07	.01	.02
3	BDI	-.06	-.61	.01	.00
	STAI	.07	.69		
4	OCI-R	-.12	-1.35	.02	.01

Note: ADHD = Adult ADHD Self-Report Scale; BDI = Beck Depression Inventory II; BIS = Barrat Impulsiveness Scale; OCI-R = Obsessive-compulsive inventory – revised; STAI-State = State-Trait Anxiety Inventory.

β = standardized coefficient in the final model.

Table 3

Results of hierarchical linear regression predicting commission errors on go/no-go task.

Block	Predictor	β	t	R^2	R^2 change
1	ADHD	-.01	-.16	.00	.00
2	BIS	.08	1.03	.01	.00
3	BDI	-.06	-.64	.01	.01
	STAI	.10	1.05		
4	OCI-R	-.04	-.58	.01	.00

Note: ADHD = Adult ADHD Self-Report Scale; BDI = Beck Depression Inventory II; BIS = Barrat Impulsiveness Scale; OCI-R = Obsessive-compulsive inventory – revised; STAI-State = State-Trait Anxiety Inventory.

β = standardized coefficient in the final model.

Table 4

Results of hierarchical linear regression predicting stop signal reaction time on stop signal task.

Block	Predictor	β	t	R^2	R^2 change
1	ADHD	.06	.73	.03	.03*
2	BIS	.05	.61	.03	.00
3	BDI	-.06	.64	.03	.01
	STAI	-.03	-.31		
4	OCI-R	.17*	2.33*	.06	.02*

Note: ADHD = Adult ADHD Self-Report Scale; BDI = Beck Depression Inventory II; BIS = Barrat Impulsiveness Scale; OCI-R = Obsessive-compulsive inventory – revised; STAI-State = State-Trait Anxiety Inventory.

β = standardized coefficient in the final model.

* $p < 0.05$

Chapter 2: Response Inhibition, Processing Speed and Depressive Symptomatology in a Non-clinical Sample

Abstract

Deficits in executive functioning have been posited to play a key role in the etiology of depressive disorders. Based on this premise, response inhibition (RI), a specific type of executive function referring to the ability to suppress irrelevant or inappropriate responses, has been assumed to be impaired in patients with depression. This assumption has been supported in several studies in clinical samples, however, despite the multi-faceted nature of RI, much of this research relied on a single RI measure, the color-word Stroop task. Furthermore, these studies failed to account for other executive functioning deficits, such as cognitive processing speed, that have clearly been shown to be impaired in depressed populations, potentially confounding results. It is thus unclear whether depressive symptomatology is truly related to RI impairment and if so, whether this impairment exists across RI domains. In the current study, we examine associations between multiple domains of RI and depressive symptomatology, controlling for cognitive processing speed, in a non-clinical sample. Two hundred and twenty-two undergraduates came into the lab to complete three separate RI tasks, the motor Stroop task, the go/no-go task, and the stop signal task. A subset of the sample, ninety-nine participants, also completed a set of inspection time tasks, a measure of cognitive processing speed. All participants completed self-report questionnaires measuring symptoms of depression. Results showed that RI domains, as well as cognitive processing speed, were unrelated to depressive symptomatology, suggesting that neither RI nor

cognitive processing speed are trait-based deficits underlying depressive disorders. Cognitive processing speed was associated with performance on the Stroop task, supporting the idea that deficits in cognitive processing speed in clinical samples may have confounded results in previous studies examining RI in depressed patients. More research in non-clinical and clinical samples that utilizes multiple measures of RI as well as methods that control for other cognitive functions related to depression is needed.

Deficits in cognitive and emotional control processes have been increasingly examined in an effort to determine the etiology of a range of psychiatric disorders as well as the relationships between them (Lyche, Jonassen, Stiles, Ullberg, & Landro, 2010; Ochsner and Gross, 2005). Executive function (EF) impairment has been posited to be particularly relevant in several illnesses including depression (for review, see Snyder, 2013). Despite a relatively robust literature base in this area, it is yet unclear exactly how, why, and to what extent EF may be implicated in the disorder. Some researchers have concluded that depression is associated with a global impairment in EF (e.g., Rogers et al., 2004; Snyder, 2013). However, given the multi-dimensional nature of EF (e.g., Miyake & Friedman, 2012), others have argued that discrete EF processes should be studied in association with depression in order to better understand the etiology of the disorder (e.g., Gualtieri, Johnson, Benedict, 2006; Levin, Heller, Mohanty, Herrington, & Miller, 2007). Response inhibition (also referred to as inhibitory control in the literature) is one aspect of EF that has been hypothesized to be impaired in depressed individuals (e.g., Aker, Bo, Harmer, Stiles, & Landro, 2015). It has been proposed that poor inhibitory control may play a role in depression, leading depressed individuals to have difficulty inhibiting attention to negative stimuli, thus causing increased processing of such stimuli and the induction and maintenance of negative emotion (Joormann & D'Avanzato, 2010).

Response inhibition (RI) and its relationship to depression is of particular interest to researchers focused on identifying biomarkers of underlying genetic risks of mental illness. For example, RI has been proposed as a candidate endophenotype of obsessive

compulsive disorder (OCD; Chamberlain et al., 2005). Many studies have shown impairments in RI associated with OCD (Bannon, Gonsalvez, Croft, & Boyce, 2002; Bersani, Quartini, Ratti, Pagliuca, & Gallo, 2013; Chamberlain et al., 2008; Enright, Beech, & Claridge, 1995; Gillan et al., 2011; Hartston and Swerdlow, 1999; Lei, Fan, Zhou, Dong, & Zhu, 2017; McLaughlin et al., 2016; Menzies et al., 2008; Penades et al., 2007; Zhang et al., 2015), however there is still considerable debate regarding whether an RI deficit specific to OCD exists and what the nature of this deficit may be. Given the high rates of co-morbidity between OCD and depression (in an epidemiological study, 40.7% of individuals with OCD also met criteria for major depressive disorder; Ruscio, Stein, Chiu, & Kessler, 2010) some researchers have argued that RI impairment reported in OCD populations is driven by the presence of depressive symptomatology (Basso, Bornstein, Carona, & Morton, 2001; Rasmussen, Siev, Abramovitch, & Wilhelm, 2016). Further, others have argued that an RI deficit associated with depression shows that RI impairment is not uniquely associated with OCD and therefore is not an endophenotype of OCD (Abramovitch & Abramowitz, 2014). Additional research into the relationship between RI and depressive symptomatology can thus aid in furthering our understanding of potential underlying mechanisms of not only depression but also frequently co-occurring mental illnesses such as OCD.

The majority of previous studies of RI in depression have relied on a single measure of RI, the color-word Stroop task (see Bora et al., 2013 and Snyder, 2013 for reviews). Stroop tasks provide a measure of the RI domain known as interference control – the cognitive control needed to prevent interference due to competition of irrelevant

stimuli or stimulus characteristics (Chamberlain & Sahakian, 2007; Nigg, 2000; Sebastian, et al., 2012; van Velzen, Vriend, de Wit, & van den Heuvel, 2014). Although some studies have failed to identify a relationship between Stroop performance and depression (e.g., Aker et al., 2016; Degl'Innocenti, Ågren, & Bäckman, 1998; Wagner, Sinsel, et al., 2006) a meta-analysis completed by Snyder (2013) showed a medium weighted mean effect size for Stroop interference, the main outcome variable of the Stroop task. The reliance on this single measure, however, limits conclusions that can or should be drawn from this literature.

Few studies have examined the association between depression and performance on the go/no-go task or the stop signal task, the two most utilized RI tasks in the field of clinical neuroscience (Criaud & Boulinguez, 2013). Each of these tasks measures a different domain of RI (Verbruggen and Logan, 2008). The go/no-go task is a measure of action restraint (i.e., the effortful control of a motor response in compliance with changing cues; Morein-Zamir, Fineberg, Robbins, & Sahakian, 2010; Sebastian, et al., 2012) while the stop signal task (SST) is a measure of action cancellation (i.e., the inhibition of an ongoing motor response; Logan, 1994; Sebastian, et al., 2012). One study found that individuals with remitted depression showed slower inhibitory processing on the SST compared to never-depressed participants (Aker et al., 2016). Another study found that poorer performance on the SST was related to current but not past depressive symptoms (Bredemeier, Warren, Berenbaum, Miller, & Heller, 2016) suggesting that this deficit may be secondary to depressive symptoms rather than a causal mechanism. On the other hand, two other studies found that depressed patients and healthy controls did not

show significant differences in performance on the SST (Halari et al., 2009; Lyche et al., 2010). Similarly, two studies in individuals with remitted depression reported no differences in performance on the go/no-go task compared to healthy controls (Nixon, Liddle, Worwood, Liotti, & Nixon, 2013; Westheide et al., 2007). Based on this limited literature, it is plausible that impaired Stroop task performance in depressed groups may not be due to an overall RI deficit but perhaps a deficit specific to the interference control domain. The current study examined this possibility by including multiple measures, the motor Stroop task, the go/no-go task, and the stop signal task, in order to capture each RI domain (i.e., interference control, action restraint, and action cancellation).

It has also been posited that poor performance on the Stroop task displayed by depressed populations may be due to impairments in cognitive functions other than RI (Snyder, 2013). Cognitive processing speed is a particular cognitive function that may contribute to performance on the Stroop task (Kertzman et al., 2010; Snyder, 2013). Impaired cognitive processing speed has been consistently shown in individuals with depression (e.g., den Hartog, Derix, van Bommel, Kremer, & Jolles, 2003; Kertzman et al., 2010; Nebes et al., 2000; Payne & Thompson, 2015) and thus may drive findings from the Stroop task in this area. Using only the Stroop task, it is impossible to determine whether a larger “Stroop interference effect” is due to an inability to cognitively process information at an adequate speed, rather than a true RI deficit. Due to this lack of clarity, researchers have called for future studies that examine RI and depressive symptomatology to include control tasks that measure cognitive functions such as processing speed (Snyder, 2013). The current study thus included a set of inspection time

tasks, a measure of processing speed.

Inspection time (IT) has been defined as “the stimulus exposure duration required by a subject to make a simple perceptual judgment” (Anderson & Miller, 1998). IT paradigms have been described as measures of cognitive processing speed or information processing efficiency (Barbeau, Soulieres, Dawson, Zeffiro, & Mottron, 2012; Deary et al., 2004; Waiter et al., 2008). Classic IT paradigms require participants to discriminate between two stimuli displayed for very brief durations (Vickers et al., 1979). A recent study on IT used a set of IT tasks that included paradigms that measured detection and identification of a single stimulus in addition to discrimination between two stimuli, arguing that increased variation in IT measures will provide a wider and more complete measure of processing speed (Payne and Thompson, 2015). The current study thus included an IT task that measures all three types of processing (i.e., detection, identification, and discrimination).

The current study examined depression symptoms in a non-clinical sample, rather than a clinical sample of patients diagnosed with depression. The decision to use a non-clinical sample was based on several factors. First, little research examining RI or processing speed and the association with depression in non-clinical samples has been undertaken (Snyder, 2013). Such research has the potential to shed light on whether potential deficits in RI and processing speed are trait-based and thus related to depressive symptoms regardless of severity rather than being present only when symptoms are expressed at high severity levels. This has implications for the usefulness of these processes in predicting future morbidity as well as considering them as transdiagnostic

markers with the potential to illuminate links between depression and other mental illnesses. Should these deficits emerge only in high levels of severity, it would suggest that they are by-products or effects of depression symptoms rather than permanent cognitive functioning characteristics that are markers of the disorder.

Next, there is evidence that depression symptomatology may be more accurately represented on a continuum rather than categorically (Angst and Merikangas, 2001; Andrews et al., 2007; Bjelland et al., 2009; Gonda et al., 2005; Judd et al., 1998; Ruscio & Ruscio, 2002). Studies examining the latent structure of depression using Meehl's (1995) taxometric procedures have suggested that depression is a dimensional, rather than categorical, construct (Hankin et al., 2005; Ruscio & Ruscio, 2002). Relatedly, researchers have found that depressive symptoms that do not qualify for a diagnosis of major depressive disorder are nevertheless associated with functional impairment (e.g., Angst, Merikangas, & Preisig, 1997; Backenstrass, Frank, Joest, Hingmann, Mundt, Kronmuller, 2006) as well as increased likelihood of experiencing a future major depressive episode (Horwath, Johnson, Klerman, & Weissman, 1992). Furthermore, researchers have shown that across levels of depressive severity (i.e., both subclinical depressive symptoms and major depressive disorder) the number, severity, and duration of depressive symptoms are associated with linear increases in impairment and comorbidity (Kendler and Gardner, 1998; Kessler, Zhao, Blazer, & Swartz, 1997). In college students, even mild to moderate depressive symptoms are associated with a significantly increased risk of suicidal ideation as compared to minimal depressive symptoms (Cukrowicz et al., 2011). Taken together, this evidence suggests that many

clinically significant correlates and outcomes associated with symptoms of depression are relevant across the diagnostic boundary. It is yet unknown whether executive functioning impairments associated with depressive symptoms in clinical populations are relevant across the depressive continuum.

Finally, by using a non-clinical sample of college students, we aimed to broaden the range of severity in our sample and avoid the truncated range of severity scores that would exist in a sample of clinically severe participants. Previous studies have reported that depression symptomatology is common on college campuses, with prevalence rates of students reporting mild to severe depression symptoms ranging from approximately 20-50% (e.g., Bredemeier et al., 2016; Cukrowicz et al., 2011; Eisenberg, Gollust, Golberstein, & Hefner, 2007; Payne & Thompson, 2015). We thus predicted that we would be able to capture symptoms at both ends of the severity spectrum (i.e., minimal to severe) and that despite it being a non-clinical sample, the sample would include a sizable group of individuals with elevated levels of depressive symptomatology.

The primary aims of this study were to investigate whether performance across RI domains would be related to depressive symptomatology in a non-clinical sample and whether this relationship would be mediated by processing speed. Based on previous findings showing that performance on the color and word Stroop task has been consistently associated with depression, we predicted that performance on the motor Stroop task would be related to depression severity. However, based on research demonstrating slower processing speed in depression as well as findings suggesting that processing speed may drive performance on the Stroop task, we predicted that processing

speed would mediate the relationship between depression and performance on the Stroop task. We predicted that the performance on other RI domains as measured by the go/no-go and stop signal tasks would not be related to depressive symptomatology and therefore would not support the theory that a general RI deficit underlies depression.

Finally, a secondary aim of this study was to explore the utility of measuring multiple IT variables (i.e., detection, recognition, and discrimination) within an IT task. Based on previous findings (Payne & Thompson, 2015), it was hypothesized that accuracy rates would differ significantly between IT subtasks, with accuracy rates being highest on detection and lowest on discrimination.

Method

Participants

The full sample consisted of 222 participants (68.1% female; $M_{\text{age}} = 19.63$, $SD = 1.46$) enrolled in introductory psychology courses at the University of Pennsylvania. Participants received course credit for their participation in this study. The study was approved by the Institutional Review Board at the University of Pennsylvania.

Measures

Clinical measures.

We used the *Beck Depression Inventory II* (BDI-II; Beck, Steer, & Brown, 1996) to assess severity of depressive symptoms. The BDI-II is made up of 21-items that are rated between 0 and 3, with higher scores indicating greater symptom severity. In our sample, the BDI-II demonstrated good internal consistency ($\alpha = .88$), consistent with previous demonstrations of acceptable reliability and validity across clinical and non-

clinical samples (Beck et al., 1996).

Response inhibition tasks.

Participants completed three computerized RI tasks including the motor Stroop task, go/no-go task, and the stop signal task.

The *Motor Stroop task* asks participants to quickly indicate the direction (left vs. right) of an arrow that is presented on either side of the screen. Performance is indexed by the difference in reaction times from congruent (arrow is presented on the same side of the screen it is pointing toward) vs. incongruent trials (arrow is presented on the opposite side of the screen it is pointing toward). Stroop tasks are meant to measure interference control, the cognition ability to prevent interference due to competition of relevant and irrelevant stimuli or stimulus characteristics (Chamberlain & Sahakian, 2007; Nigg, 2000; Sebastian, et al., 2013; van Velzen et al., 2014). The motor Stroop task avoids confounds with reading difficulties that can influence performance on the color-word Stroop task (Rubia et al., 2007). It also allows the task to be more comparable in methodology to other motor inhibition tasks used in this study and in most other RI studies in the literature.

The *Go/No-Go task* presents letters that compose go trials and no-go trials. Participants are instructed to press the response key promptly when the target figure appears on the screen (i.e., go trial; any letter with the exception of “X”), while refraining from responding to the distracter figure (i.e., no-go trial; the letter “X”). The main RI outcome on this task is total commission errors (i.e., how often the button is pressed

following a no-go trial). Overall, it measures action restraint, the ability to inhibit pre-potent response (i.e. a response that has not yet been initiated; Lee, Yost, & Telch, 2009).

The *Stop Signal Task* (SST) presents go trials in which participants are asked to quickly respond by indicating the direction of an arrow presented in the center of the screen. During some of the trials, however, the target stimuli are presented with a stop signal (a beep sound during the trial). Participants are instructed to cease the response to the target stimulus when a stop signal occurs. As the task goes on, an automatic tracking algorithm adjusts how quickly the stop signal is displayed during a go task according to how well the individual is performing. This allows the individual to be successful on stop signal trials at 50% (Chamberlain et al., 2006; Morein-Zamir, et al., 2010). The main outcome variable of the SST is stop signal reaction time (SSRT; Lipszyc and Schachar, 2010). SSRT provides an estimate of the latency of the inhibitory process, or how long it takes the participant to appropriately inhibit a response. The SSRT is inferred from the distribution of reaction times following go-signals and proportion of successful stops (Linguist and Thorell, 2009). The SST measures action cancellation, the ability to inhibit ongoing response (i.e. a response that has already been initiated).

Inspection time tasks.

The *Letter Detection and Identification task* (Payne and Thompson, 2015) is a computerized IT task that measures the visual inspection time needed to detect and needed to identify a letter flashed briefly on the screen. This task measures two variables: accuracy for detection of briefly presented letters and accuracy for the identification of the letters presented. Letters appear in the center of the computer screen for varying

amounts of exposure or “inspection time”, with the durations decreasing with each trial block. There are a total of 5 blocks, each composed of 15 trials. For each block, 10 trials contain a target letter and 5 trials are “blank” trials in which no letter appears. Each target letter is presented twice within a block of trials, with the target letters including X, Z, H, K, and E, in size 18 font. Letters are presented in a random order and participants are not told which letters might be presented. Prior to actual test blocks the participant is provided with practice trials to demonstrate, with a 500 ms inspection time. After practice, inspection time for the target letters in Blocks 1, 2, 3, 4, and 5 is 80ms, 64ms, 48ms, 32ms, and 16ms, respectively. The participant is instructed to pay close attention to the stimuli presented and respond as accurately as possible. They are told that the speed of their responses does not matter and that they should not rush their responses. For each trial a “Ready” screen appears with a prompt for the participant to self-initiate the trial sequence by pressing the space bar. Once a trial is initiated there is a refractory period of 500ms during which the screen remains blank. Next, a forward visual mask, a “#” sign, is displayed for 300 ms in the center of the screen, followed by either a letter or a blank screen for either 80ms, 64ms, 48ms, 32ms, and 16ms, depending on the block. Blank trials are presented at random during each block. A backward visual mask (another “#” sign presented in the middle of the screen for 300ms) follows the presentation of the target letter or blank screen. The participant is then prompted to respond and indicate whether a letter was presented. Responses for letter detection are indicated by a key press on a computer keyboard, with designated keys marked (“1” for yes or “3” for no). If participants indicate a letter is detected (by pressing “1”) the next instruction is to attempt

to identify the letter by choosing it on the keyboard. The participant has as long as needed to respond. The general goal of this task is to decide if a letter was present between the first “#” and second “#” (Payne & Thompson, 2015). The current task also has participants go one step farther and once the participant indicates that that a letter was present, the task asks them to identify the target letter that was presented.

This task provides measurements of accuracy for both detection (indicating that a letter was or was not presented) and identification (identifying which letter was presented) for each presentation duration block (80-16 ms). Higher rates of accuracy suggest faster cognitive processing speed.

The *Letter Discrimination Task* (Payne and Thompson, 2015) is a computerized task for visual inspection used to assess speeded discrimination. This task measures accuracy for discrimination of briefly presented letter pairs. Specifically, it requires the participant to decide whether letter pairs, appearing in the center of the computer screen for varying amounts of inspection time, are comprised of same or different letters.

Like the previous task, there are a total of 5 blocks, each composed of 15 trials. Each trial presents one target letter pair. The target letter pairs are XX, KX, EH, ZZ, or XK and are presented in size 18 font. Each letter pair is presented 3 times and the pairs are presented in a random order. The participant is not told which letters will be presented. A “#” is used as a forward and backward visual mask in the middle of the screen during each trial. Due to the larger area of the target stimuli (two letters rather than one), the “#” is larger (36 font) than in the previous trial, in order to adequately mask the stimuli.

Prior to actual test blocks the participant is provided with practice trials to demonstrate, with a 500 ms inspection time. After practice, inspection time for the target letter pairs in Blocks 1, 2, 3, 4, and 5 is 80ms, 64ms, 48ms, 32ms, and 16ms, respectively. The participant is instructed to pay close attention to the stimuli presented and respond as accurately as possible. They are told that the speed of their responses does not matter and that they should not rush their responses.

For each trial a “Ready” screen appears with a prompt for the participant to self-initial the trial sequence by pressing the space bar. Once a trial is initiated there is a refractory period of 500 ms during which the screen remains blank. Next, the forward visual mask (“#”) is displayed for 300 ms, followed by a letter pair for either 80ms, 64ms, 48ms, 32ms, and 16ms, depending on the block. The backward visual mask (“#”) is then presented for 300 ms. The participant is then prompted to indicate whether the letter pair was comprised of two of the same letters or two different letters. They indicate a decision by pressing either “1” for same or “3” for different. The participant has as long as needed to respond.

This task provides measurements of accuracy for discriminating whether letter pairs were the same or different for each presentation duration block (80-16 ms). Higher rates of accuracy suggest greater cognitive processing speed.

Procedure

Participants came into the lab to complete computer tasks. All participants (N=222) completed RI tasks. Data from three participants were removed from the dataset due to SSRTs under 50ms, indicating deliberate slowing of responses which invalidated

results (Congdon et al., 2012). An additional participant was unable to complete the stop signal and Stroop tasks due to computer malfunction. The inspection time tasks were added to the study protocol midway through the study and thus only a subset of participants (n=99) completed IT tasks in addition to RI tasks. Each participant completed RI tasks in a random order. Participants who completed IT tasks did so following completion of RI tasks in order to keep RI conditions constant across all participants. Tasks were completed individually, in a quiet room, on a desktop computer. Tasks were run using Inquisit 4 Web software (Inquisit, 2014). Completion of all three RI tasks took approximately 25 minutes. IT tasks took approximately 10 minutes to complete. Participants were then given instructions to complete self-report questionnaires, including the BDI-II, online. The same sample was used in another study (Morris, Lee, and Franklin, *in preparation*), but the questions addressed and analyses reported in that paper are distinct from those addressed in this one.

Data Analysis

Simple regressions were conducted to examine the relationship between depressive symptomatology and each RI outcome variable (i.e., Stroop interference effect, go commission errors, and stop signal reaction time) within the full sample. Data from the subsample of participants that completed IT tasks was then used to assess whether cognitive processing speed mediated the relationship between depressive symptomatology and RI performance on each task. Mediation analyses were conducted using bootstrapping, a nonparametric resampling procedure, via the macro PROCESS for SPSS (Hayes, 2013). Bootstrapping is advantageous because it does not impose the

assumption of normality of the sampling distribution, a common concern in small samples, and is considered the most powerful approach to detecting statistical mediation (Preacher and Hayes, 2008). The indirect effect was defined as the product of the effect of the independent variable on the mediator (a), and the effect of the mediator on the dependent variable (b), while controlling for the direct effect of the independent variable (c^1) (Preacher and Hayes, 2004, 2008). Bootstrapping estimated the indirect effects and associated 95% confidence intervals (CI) based on the mean of 5000 bootstrapped samples. Indirect effects were deemed statistically significant when the 95% CI did not include zero while mediation hypotheses were rejected when 95% CI did included zero (Preacher & Hayes, 2004, 2008).

A factorial repeated measures analysis of variance (ANOVA) was used to determine whether accuracy differed as a function of inspection time (80, 64, 48, 32, 16ms) and IT task type (detection, recognition, and discrimination).

Results

Table 1 presents descriptive characteristics. Mean BDI scores were $M=11.06$ ($SD=9.34$) and $M=10.32$ ($SD=9.39$) for the full and subsample, respectively. For the full sample, 67% of participants scored in the minimal range (0-13) of depression symptomatology on the BDI, 19% fell in the mild range (14-19), 9% fell in the moderate range (20-28), and 5% fell in the severe range (29-63). The subsample showed a similar distribution of depressive severity (69% in the minimal range; 15% in the mild range; 11% in the moderate range; and 5% in the severe range).

Within the full sample, continuous depression symptomatology was not a significant predictor of performance on the motor Stroop task ($\beta = -.03, t = -.38, p = .71, R^2 = .00$), go/no-go task ($\beta = -.02, t = -.26, p = .80, R^2 = .00$), or the stop signal task ($\beta = .09, t = 1.33, p = .19, R^2 = .01$).

Figures 1, 2, and 3 depict the results of mediation analyses testing whether processing speed mediated the relationship between depressive symptomatology and each measure of RI, within the subsample. The total effects of depression on each measure of RI were not statistically significant nor were indirect effects of depression on RI via processing speed (see Figures 1, 2, 3). Cognitive processing speed was significantly related to Stroop performance, $b = -175.53, SE = 68.81, \text{BootLLCI} = -.312.31, \text{BootULCI} = -38.76$, as well as SST performance, $b = -185.12, SE = 84.82, \text{BootLLCI} = -353.71, \text{BootULCI} = -16.52$.

For IT performance, there was a significant main effect of task type on accuracy, $F(2, 180) = 173.89, p = .00$. Contrasts revealed accuracy on the discrimination task was significantly lower compared to the detection task, $F(1, 90) = 147.36, p = .00$, and significantly higher compared to the identification task, $F(1, 90) = 23.76, p = .00$. Put simply, the detection task was associated with highest rates of accuracy, followed by the discrimination task, and then the identification task. Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of inspection time duration, $\chi(9) = 185.07, p = .00$. Therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity correction ($\epsilon = .51$). There was a significant main effect of inspection time on accuracy, $F(2.06, 185.51) = 480.74, p = .00$, such that

as inspection time decreased, accuracy decreased as well. Again, Mauchly's test indicated that the assumption of sphericity had been violated for the interaction between task type and inspection time. Therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity correction ($\epsilon = .47$). There was a significant interaction between task type and inspection time, $F(3.74, 336.42) = 119.36, p = .00$, such that the effect of task type on accuracy varied according to inspection time. To break down this interaction, contrasts were performed comparing accuracy on the discrimination task to the detection and identification tasks and all inspection durations to the next lowest inspection duration (e.g., 80ms to 64ms, 64ms to 48ms, 48ms to 32ms, and 32ms to 16ms). These revealed significant interactions when comparing accuracy on the detection task to the discrimination task for 64ms compared to 32ms, $F(1, 90) = 4.62, p = .00$, and for 32ms compared to 16ms $F(1, 90) = 17.50, p = .00$. There were also significant interactions when comparing accuracy on the identification task to the discrimination task for 48ms compared to 32ms, $F(1, 90) = 8.99, p = .00$, and for 32ms compared to 16ms, $F(1, 90) = 145.44, p = .00$. The interaction graph (see Figure 4) shows that the discrimination task was associated with the lowest accuracy of the three tasks at 80, 64, and 48ms. At 32ms, the identification and discrimination task accuracies are not significantly different, while the detection task is associated with higher accuracy. Accuracy decreases more sharply on the identification task between 32 and 16ms compared to the other two tasks. At 16 ms, the identification task is associated with the least amount of accuracy, followed by the discrimination task and then the detection task.

Discussion

The primary aim of the present study was to examine the relationship between depressive symptomatology and multiple domains of RI in a non-clinical sample of undergraduates. Contrary to our first hypothesis, there was no relationship between depression symptoms and interference control, as measured by the motor Stroop task. We expected to replicate previous findings showing a larger “Stroop interference effect” in the color-word Stroop task associated with depression. There are several possible explanations for why this result was not replicated in the current sample.

First, interference control may be a state-dependent impairment and thus our use of a non-clinical sample would explain these results. As expected, our sample reported a wide range of depressive severity, with approximately one third of our sample endorsing current depressive symptoms. This positively skewed distribution is typical of a non-clinical, college-aged sample (e.g., Bredemeier et al., 2016; Cukrowicz et al., 2011; Payne & Thompson, 2015). Previous studies have not examined the relationship between performance on the Stroop task and symptoms of depression in non-clinical samples such as ours, but one study examined this relationship in a sample of adults with remitted depression and found no relationship between Stroop performance and history of depression (Aker et al., 2015). Taken together, these findings suggest that this specific RI domain is unlikely to be a trait-marker of depression and that depression symptomatology is not associated with a general executive functioning or response inhibition deficit.

Another possibility is that poor processing speed was responsible for impaired performance on the Stroop task in previous research. In line with hypotheses, processing

speed was a significant, unique predictor of the Stroop interference effect in the current study, however, contrary to hypotheses it was unrelated to depressive symptomatology. Due to the consistency with which the relationship between processing speed and depression has been demonstrated in the literature (see Trivedi and Greer, 2014 for review), this result was unexpected. There is some evidence that processing speed impairments in depression may be state dependent; previous findings suggested that processing speed performance does not predict future depressive symptoms (Simons et al., 2009), suggesting that this deficit may be a byproduct of depression symptoms rather than a causal or underlying contributor. Little published research has addressed this question. Nevertheless, if it is the case that processing speed drives performance on the Stroop task and that processing speed is affected only in individuals meeting diagnostic criteria for depression (as opposed to individuals with minimal or mild symptoms), it would explain why a relationship between Stroop performance and depression did not emerge in our non-clinical sample.

Finally, similar to the explanation that processing speed drove results in previous studies in this area, other confounding variables could have been at play. We used a slightly different version of the Stroop task compared to the color-word version used in previous research. The motor Stroop task avoids confounds with verbal processing that can influence performance on the color-word Stroop task (Rubia et al., 2007). It is possible that previous results were driven by verbal processing impairments rather than deficits in interference control. Support from this possibility comes from studies showing impairments in verbal working memory and verbal fluency related to depression

symptomatology (for review, see Snyder, 2013). It is possible that the motor Stroop task captures different cognitive processes than the color-word Stroop task and therefore use of the motor Stroop task did not replicate findings from the color-word task.

In line with expectations, depressive symptomatology was not related to commission errors on the go/no-go task or stop signal reaction time on the SST. As with the Stroop task, the go/no-go task and SST have not been used to examine RI in non-clinical depression samples. However, our findings are in line with studies examining performance in remitted individuals which did not find that increased commission errors on the go/no-go task was related to previous depressive diagnostic status (Georgiadi, Liotti, Nixon, & Liddle, 2011; Nixon et al., 2013; Westheide et al., 2007). Thus, there continues to be a lack of evidence that action restraint and action cancellation, two domains of RI, are related to depressive symptomatology.

Our findings from the IT tasks supported the use of multiple IT measurements. Mean accuracy on each task was significantly different, suggesting these tasks were each measuring slightly different aspects of processing speed or had different levels of difficulty. There thus seems to be utility in capturing detection and identification processes in addition to the classic discrimination task in future IT/cognitive processing studies. Generally, the current study highlights the importance of examining specific processes rather than relying on single cognitive, executive function, or response inhibition measures to draw conclusions about broad deficits. Although null findings with regard to RI performance and depression symptomatology were consistent across RI

measures, we identified a relationship between cognitive processing and RI in the Stroop and stop signal tasks but not the go/no-go task.

The results of the current study cannot rule out the possibility that RI plays a role in the maintenance of depression or that impaired RI is related to depression, but they do suggest that RI is not a marker of vulnerability for depression or an endophenotype. This has implications for our understanding of other mental illnesses, particularly those for which RI has been considered as an endophenotype, such as OCD. RI impairment in depression has been referred to as evidence that an RI deficit is not unique to OCD and thus is not a useful process to study as a means of improving understanding of OCD's underlying mechanisms and increasing the effectiveness of treatment (e.g., Abramovitch and Abramowitz, 2014; Harsanyi et al., 2014). We would argue that the presence of an RI deficit has not been established in relation to depression and that the findings of the current study cast additional doubt onto the existence of this hypothesized relationship. More research in non-clinical and clinical samples that utilizes multiple measures of RI as well as measures that control for other cognitive functions that may be related to depression are needed.

Limitations of the current study should be considered. Measurement of depressive symptomatology relied on self-report, rather than structured clinical screening. It was therefore not possible to determine diagnostic status of participants with respect to depression or other psychopathology. Another limitation was that the sample was composed entirely of undergraduates at a competitive university. Processing speed, as measured by inspection time, is correlated with intelligence (e.g., Grudnik & Kranzler,

2001), making it likely that our sample possessed higher than average rates of processing speed. It is possible that the expected relationships between processing speed and depression as well as interference control and depression would have emerged in a more heterogeneous sample.

Strengths of our study included the use of multiple RI tasks as well as a measure of processing speed. This diversity of measures allowed us to examine individual RI domains with respect to depression symptomatology while controlling for processing speed, a potential confound in previous studies. Additionally, the examination of these variables in a non-clinical sample was novel and allowed for further consideration of whether RI and processing speed are state-independent or trait-based impairments in depression.

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Table 1

Means, Standard Deviations, Minimum and Maximum values for RI outcome variables.

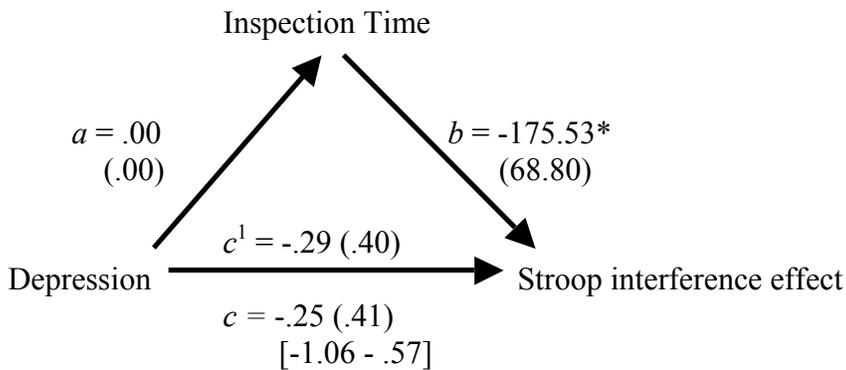
RI outcome variable	Mean (SD)	Min.	Max.
Stroop interference effect ¹	51.75 (48.89)	-355.33	275.25
Commission errors ²	6.66 (4.22)	0	22
SSRT ³	232.50 (40.47)	126.64	395.17

¹Stroop interference effect on motor Stroop task (in milliseconds)

²Total commission errors on go/no-go task

³Stop signal reaction time on stop signal task (in milliseconds)

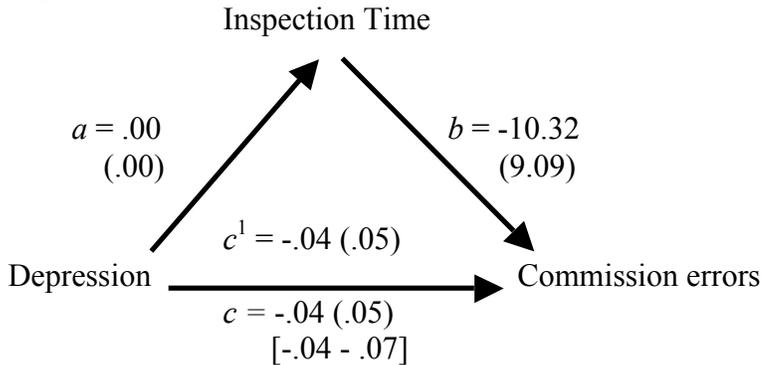
Figure 1



Mediation analyses for Stroop task. There was no significant indirect effect of depression on Stroop interference ($b = .05$, $SE = .13$, BootLLCI = $-.11$, Boot ULCI = $.41$).

* $p < .05$

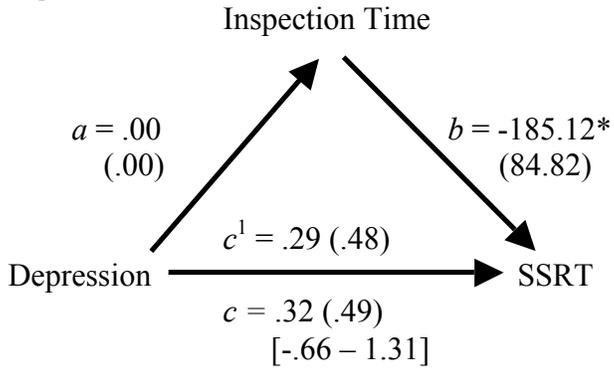
Figure 2



Mediation analyses for Go/No-go task. There was no significant indirect effect of depression on commission errors ($b = .00$, $SE = .05$, BootLLCI = $-.14$, Boot ULCI = $.07$).

* $p < .05$

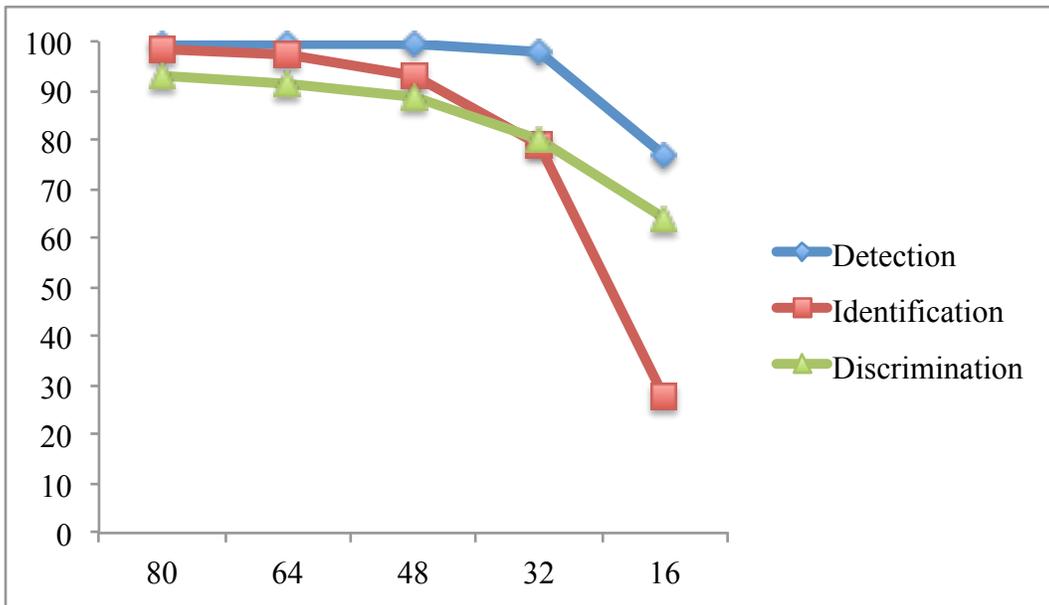
Figure 3



Mediation analyses for SST task. There was no significant indirect effect of depression on SSRT ($b = .04$, $SE = .11$, BootLLCI = $-.20$, Boot ULCI = $.27$).

Figure 4

Inspection time task accuracy across inspection durations.



Chapter 3: Response Inhibition in Youth with OCD compared to Youth with Anxiety Disorders

Abstract

Deficits in response inhibition (RI), a neuropsychological process necessary to suppress inappropriate or irrelevant responses or actions, have been found in studies of adults with obsessive compulsive disorder (OCD). The few studies that have examined RI capabilities in youth with OCD have employed varying methods for measuring RI and relied on small samples. This research has yielded mixed findings, leaving an incomplete picture of RI functioning in pediatric OCD. In the present study, 28 treatment-seeking youth with OCD were compared with 27 treatment-seeking youth with anxiety disorders on three response inhibition domains. No significant differences emerged between groups across RI domains. RI was unrelated to OCD, anxiety, or depression severity but was positively correlated with age. Results do not provide supporting evidence for an RI deficit in youth with OCD and are inconsistent with findings in adults with OCD. Possible explanations for this inconsistency related to neurodevelopmental processes are discussed.

Obsessive compulsive disorder (OCD) is a debilitating, chronic condition that affects up to 3% of children and adolescents (Zohar, 1999). It is associated with significant impairment in social, academic, and family functioning (Piacentini, Bergman, Keller & McCracken, 2003) and often persists into adulthood (Flament et al., 1990; Rasmussen and Eisen, 1990). Fortunately, significant advances have been made over the past twenty years in the development of treatments for this disorder. Both exposure and response prevention (ERP), a type of cognitive behavioral therapy (CBT), and pharmacotherapy with a serotonin reuptake inhibitor (SSRI), have proved efficacious in the treatment of pediatric OCD (March, Frances, Carpenter, & Kahn, 1997; March & Leonard, 1996; Jordan, Reid, Mariaskin, Augusto, & Sulkowski, 2012; Wastson & Rees, 2008; Stein, Ipser, Baldwin, & Badelow, 2007). Although many children and adolescents with OCD have benefited substantially from these interventions, there are a significant number who either do not respond or still have residual symptoms after completing empirically supported treatments (Franklin and Foa, 2011).

Examining underlying neurobiological mechanisms implicated in the etiology and maintenance of OCD constitutes an important next step toward increasing treatment success rates. One line of research aiding in this pursuit is the further study of putative neuropsychological dysfunction in individuals with OCD using computerized tasks that measure basic cognitive functions. Performance on such tasks can potentially serve as a link between underlying neurobiology and observable symptoms and behavior. Although it has become clearer that OCD is not associated with a global deficit in cognitive functioning, identifying the specific neurocognitive abilities impaired in individuals with

OCD and understanding how they relate to symptom expression is a subject of ongoing inquiry (Greisberg & McKay, 2003; Grisham et al., 2009; Grisham & Williams, 2013; Kuelz, Hohagen, & Voderholzer, 2004; Olley, Malhi, & Sachdev, 2007).

Based on the intrusive, recurring nature of obsessions and subjective uncontrollability of compulsions experienced by patients with OCD, poor response inhibition (RI), the ability to suppress inappropriate or irrelevant responses (Verbruggen & Logan, 2008), has been hypothesized to be a neurocognitive function that contributes uniquely to OCD and its maintenance (Bannon, Gonsalvez, Croft, & Boyce, 2006; Chamberlain et al., 2008; Menzies et al., 2007; Watkins et al., 2005; van Velzen, Vriend, de Wit, van den Heuvel, 2014; Woolley et al., 2008). For example, a patient with OCD who has concerns regarding the safety of loved ones in her home may spend hours each evening repeatedly checking that doors are locked and the stove is turned off before going to bed despite knowing rationally that the doors and stove are secure. Compulsions such as these checking behaviors are unique to OCD. A patient with generalized anxiety disorder, for instance, may also worry about the safety of loved ones but is not compelled to respond to these worries with circumscribed, repetitive actions. Additional evidence that RI deficits may be related to OCD comes from neurobiological studies in OCD patients showing atypical neural activation patterns as well as structural brain abnormalities corresponding to areas known to be involved in RI processes including the fronto-striatal network (e.g., Saxena & Rauch, 2000).

A number of studies have examined RI in adults with OCD and shown impaired RI associated with OCD (Bannon et al., 2002; Chamberlain et al., 2007; Chamberlain et

al., 2008; Enright et al., 1995; Gillan et al., 2011; Hartson & Swerdlow, 1999; Lei et al., 2017; McLaughlin et al., 2016; Menzies et al., 2008; Nabeyama et al., 2008; Nigg, 2000; Penades et al., 2007; Schlosser et al., 2010; Zhang et al., 2016). The majority of these compared OCD samples to healthy control groups, leading to an important question of whether this apparent deficit is specific to OCD rather than being reflective of a more general trait or state associated with mental illness (e.g., Abramovitch et al., 2013). It is possible that though RI deficits are not unique to OCD, examining the conditions that do and do not share this impairment can provide clues to transdiagnostic relationships. For example, RI deficits have been found consistently in groups of patients with ADHD (Lipszyc & Schachar, van Velzen et al., 2014) and in some studies of patients with Tourette's Disorder and trichotillomania (van Velzen et al., 2014) but not anxiety disorders (Bannon et al., 2002; Enright et al., 1995; Lipszyc & Schachar, 2010; Wright et al., 2014). These findings support the relatively recent change in the conceptualization of OCD as being diagnostically separate from the group of anxiety disorders it was historically considered to be a part of (APA, 1994; APA 2013) and potentially more accurately thought of as falling within a spectrum of impulsive-compulsive disorders (van Velzen et al., 2014). Relatedly, researchers have encouraged future studies to focus on a more rigorous approach to determining whether RI deficits are specific to underlying OCD pathology, by using one or more clinical comparison groups (e.g., Abramovitch et al., 2013).

RI can be separated into three domains, including interference control, action restraint, and action cancellation. Interference control refers to the ability to resolve a

conflict in which competing response tendencies are co-activated to due to incongruent stimulus dimensions (Chamberlain & Sahakian, 2007; Sebastian, et al., 2013). Action restraint is the effortful control of a response in compliance with changing context cues (Morein-Zamir, Fineberg, Robbins, & Sahakian, 2010; Sebastian, et al., 2013). Finally, action cancellation is the inhibition of an ongoing motor response (Logan, 1994; Sebastian et al., 2013). These domains are considered to be early, intermediate, and late phases of the RI process respectively (Sebastian et al., 2013). Different computerized measures capture specific domains of RI. Stroop and flanker tasks measure interference control, the go/no-go task captures action restraint, and the stop signal task (SST) measures action cancellation.

It may be the case that each RI domain is differentially related to OCD symptomatology. Meta-analyses have suggested that deficits in action restraint, as measured with the go/no-go task, are less consistently and robustly associated with OCD in adults as compared with interference control and action cancellation (Abramovitch et al., 2013; Wright, Lipszyc, Dupuis, Thayapararajah & Schachar, 2014). Unfortunately, the majority of studies in this area have relied on single measures of RI, and have been inconsistent in which measure is utilized, making it difficult to make direct comparisons across RI domains. This inconsistency likely explains why, despite the majority of findings indicating RI impairment related to OCD, some studies have failed to find RI deficits in OCD populations (e.g., Bohne, Savage, Deckersbach, Keuthen, & Wilhelm, 2008; Boone et al., 1991; Kalanthroff et al., 2016; Krishna et al., 2011). Experts have

thus called for future RI studies to include multiple measures of RI (e.g., Abramovitch et al., 2015).

Another area of RI/OCD research that is sorely lacking is in pediatric populations. Few studies have examined RI in pediatric OCD patients, and those that have had limitations that prevent firm conclusions regarding the presence, extent, and nature of RI impairment in pediatric OCD. One such limitation has been the use of RI measures different from those that have consistently shown RI deficits in adults. Children with OCD showed impaired RI in oculomotor tasks which used eye tracking devices (Rosenberg, Dick, O'Hearn, & Sweeney, 1997), in a computerized “emotional” go/no-go task (Waters & Farrell, 2014) as well as in non-computerized Stroop tasks (McGuire et al., 2014; Taner, Bakar, & Oner, 2011) but did not have deficient RI capabilities compared with healthy controls in a non-computerized go/no-go task (Beers et al., 1999).

Four studies did employ computerized tasks that mirrored those used with adults – one employed the SST and Flanker tasks (Hybel et al., 2017); another utilized the SST and Stroop tasks (Woolley et al., 2008); a third used the SST (Ornstein et al., 2010); and a fourth utilized the Simon task, a Stroop-like task (Hajcak, Franklin, Foa, & Simons, 2008). Differences in RI performance between patients with OCD and healthy controls were not identified in these studies. However, three out of four of these studies had small sample sizes (OCD groups of 10-18 participants; Hajcak et al., 2008; Ornstein et al., 2010; Woolley et al., 2008), leading to underpowered analyses and thus limiting conclusions that could be drawn. Despite the use of a well-sized sample (OCD group of n=50) in the study conducted by Hybel and colleagues (2017), the OCD group was

composed of 70% females and excluded patients with tic and depressive disorders (Hybel et al., 2017). Given the preponderance of males as well as the high rates of tic and mood disorders associated with pediatric OCD (Geller, 2006; Kalra & Swedo, 2009), this sample may not be generalizable to pediatric OCD broadly. There have been no studies, to date, that have examined RI performance in well-sized, representative sample of pediatric OCD patients with RI measures across all three domains. It is thus unknown whether an RI deficit exists in pediatric OCD.

Identifying such a deficit in youth would suggest that RI is dysfunctional from the outset of the disorder rather than weakens over the course of a lifetime with OCD. This would further support the claim that RI is a neuropsychological mechanism underlying the disorder and a basic dimension of functioning worthy of study as a means of furthering our understanding of the disorder and its relationship with other psychopathology. It is also essential to determine whether RI deficits are specific to OCD rather than being a general characteristic of psychopathology and thus present in disorders without behavioral signs (i.e., compulsivity or impulsivity) of impaired RI. Rather than relying on healthy control groups, use of comparison groups with psychopathology that should not theoretically present with an RI deficit is imperative to determining whether RI may be a path to potentially tailoring and improving treatment for OCD.

The current study aimed to address this topic by comparing performance in three RI domains between youth with OCD and youth with other anxiety disorders. Based on findings in the adult literature consistently showing impaired RI on Stroop and stop

signal tasks but inconsistent findings with regard to the go/no-go task, we hypothesized that the OCD group would show poorer interference control and action cancellation compared with the anxiety group but that action restraint would not differ across groups.

Method

Participants

Participants were 55 children and adolescents (age range: 7-17 years) receiving clinical care at the Child and Adolescent OCD, Tic, Trichotillomania, and Anxiety Group (COTTAGE), a research center and treatment clinic that specializes in the diagnosis and cognitive behavioral treatment of pediatric OC-spectrum and anxiety disorders at the University of Pennsylvania. Patients from the ages of 7 to 17 who were diagnosed with OCD or with an anxiety disorder (generalized anxiety disorder, social anxiety disorder, separation anxiety disorder, specific phobia, panic disorder, other specified anxiety disorder, unspecified anxiety disorder, or avoidant/restrictive food intake disorder) during an initial evaluation at COTTAGE's open clinic and provided consent to be contacted for research studies were invited to participate in the current study. Those diagnosed with OCD made up the OCD group (n=28) and those diagnosed with an anxiety disorder made up the comparison group (n=27).

Consistent with previous RI studies in adults and children (Bannon et al., 2002; Hajcak et al., 2008; Penades et al., 2007), participants on a stable dose of psychotropic medication were eligible. Although this relationship has not been examined in pediatric samples, research in adult samples have not found differences in performance on RI tasks based on medication status (e.g., Kalanthroff et al., 2016).

Patients who had a diagnosis of attention deficit hyperactivity disorder (ADHD), either historically or provided during the evaluation at COTTAGE, were not eligible to participate in either group, given research showing this patient population possesses an RI deficit, thus confounding the results (Iaboni, Douglas, & Baker, 1995; Oosterlaan, Logan, & Sergeant, 1998).

Patients who had co-morbid diagnoses of Tourette's Disorder, persistent motor or vocal tic disorders, hair pulling disorder, or skin picking disorder were ineligible to participate in the comparison (anxiety) group, given the potential that these disorders may share underlying mechanisms, such as an RI deficit, with OCD (e.g., Brennan and Flessner, 2015).

Additional exclusion criteria included a) being activity psychotic; b) having visual impairments that would prevent participation in computer tasks; c) presenting with developmental disabilities and/or low overall IQ estimated to be below average (equal to or below 79); d) presenting with past/current substance abuse/dependence problems; e) speaking a primary language other than English that would make it difficult to understand instructions in computer tasks.

Measures

Clinical measures.

The *Anxiety Disorders Interview Schedule – Parent Version* (ADIS; Silverman & Nelles, 1988) is a semi-structured interview for assessing DSM-IV anxiety disorders as well as other psychological disorders. The ADIS provides a detailed assessment of anxiety symptoms as well as a more general screening for other psychological disorders.

It was used to establish a diagnosis of OCD (for the OCD group) or an anxiety disorder (for the comparison group) as well as provide information about co-morbid internalizing and externalizing disorders.

The *Children's Yale Brown Obsessive Compulsive Scale* (CYBOCS; Goodman et al., 1989) is a clinician-rated instrument that assesses obsessions and compulsions separately on time consumed, distress, interference, degree of resistance, and control. It is made up of a symptom checklist as well as obsession and compulsion severity scales. Obsession and compulsion severity are rated on five-point Likert scales pertaining to distress, frequency, interference, resistance, and symptom control. The CY-BOCS provides three scores: the obsessions severity score (range = 0-20), the compulsions severity score (range = 0-20), and a total score, which is the sum of all items (range = 0-40; subclinical: 0-7; mild: 8-15; moderate: 16-23; severe: 24-31; extreme: 32-40; Storch et al., 2006). The CYBOCS total score established the level of severity of OCD in the OCD group.

The *Obsessive Compulsive Inventory-Child Version* (OCI-CV; Foa et al., 2010) is a child self-report measure of obsessive-compulsive symptomatology. The OCI-CV has been shown to be internally consistent and have strong test-retest reliability (Foa et al., 2010). Higher scores indicate greater symptomatology. The OCI-CV was used in the current study to establish extent of OC symptomatology in both the OCD and anxious comparison groups.

The *Multidimensional Anxiety Scale for Children* (MASC; March et al., 1997) is a child self-report measure of anxiety. The MASC shows excellent test-retest reliability in

clinical and school samples as well as strong convergent/divergent validity (March, 1998; March, Sullivan & Parker, 1999) The MASC was used in the current study to establish the severity of anxiety in both the OCD and anxious comparison groups.

The *Children's Depression Inventory* (CDI; Kovacs, 1981). The CDI is a self-report scale that inventories cognitive, affective, behavioral, and interpersonal symptoms of depression and has demonstrated adequate psychometric properties (Kovacs, 1985). It is one of the most widely used self-report measures of depression in children and adolescent populations (Lee, Krishnan, & Park, 2012). While the proposed study mainly focuses on how OCD relates to response inhibition capabilities, depression often co-occurs with OCD. Therefore, it is important to have information regarding the presence and severity of depression in study participants.

The *Conners Parent Rating Scale-Revised (CPRS-R)* measures parental ratings of their child's internalizing and externalizing symptoms (Conners et al., 1998). It is a comprehensive, reliable, and valid instrument utilized in many previous research studies of pediatric psychopathology. The CPRS-R yields scores on factors covering both externalizing and internalizing domains including Oppositional, Cognitive Problems, Hyperactivity-Impulsivity, Anxious/Shy, Perfectionism, Social Problems, and Psychosomatic. The CPRS-R provided additional information regarding the clinical presentation of participants in both groups.

Response inhibition tasks.

Participants completed three computer tasks (motor Stroop task, go/no-go task, and the stop signal task) that measure different aspects of response inhibition

(interference control, action restraint, and action cancellation respectively). The *motor Stroop task* asks participants to quickly indicate the direction (left vs. right) of an arrow that is presented on either side of the screen. The main RI outcome variable from the Stroop task is known as the “Stroop interference effect” and is indexed by calculating the difference in reaction times from congruent (arrow is presented on the same side of the screen it is pointing toward) vs. incongruent trials (arrow is presented on the opposite side of the screen it is pointing toward). The *go/no-go task* presents letters that compose go trials and no-go trials. Participants are instructed to press the response key promptly when the target figure appears on the screen (i.e., go trial), while refraining from responding to the distracter figure (i.e., no-go trial). The RI outcome variable from this task is number of commission errors (i.e., how often the button is pressed following a no-go trial). Overall, it measures the ability to inhibit pre-potent response (i.e. a response that has not yet been initiated; Lee, Yost, & Telch, 2009). The *stop signal task* presents go trials in which participants are asked to quickly respond by indicating the direction of an arrow presented in the center of the screen. During some of the trials, however, the target stimuli are presented with a stop signal (e.g., a beep sound during the trial). Participants are instructed to cease the response to the target stimulus when a stop signal occurs. This task measures the ability to inhibit ongoing response (i.e. a response that has already been initiated). As the task goes on, an automatic tracking algorithm adjusts how quickly the stop signal is displayed during a go task according to how well the individual is performing. This allows the individual to be successful on stop-signal trials at 50%, as the goal of this task is to ensure that the “go” response is initiated prior to the need to “stop”

the response (Chamberlain et al., 2006; Morein-Zamir, et al., 2010). The main outcome variable of the SST is stop-signal reaction time (SSRT; Lipszyc & Schachar, 2010). SSRT provides an estimate of the latency of the inhibitory process, or how long it takes the participant to appropriately inhibit a response. The SSRT is inferred from the distribution of reaction times following go-signals and proportion of successful stops (Lijffijt, Kenemans, Verbaten, & van Engeland, 2005).

Procedure

In order to reduce participant burden and in the interest of efficiency, results from the ADIS, CYBOCS, and relevant self-report measures conducted during the participant's initial evaluation at COTTAGE's open clinic were used as diagnostic variables for all participants. In some cases, self-report measures were not completed in their entirety by families as part of this process and thus self-report data is not available for all participants. Similarly, four participants in the OCD group were not administered the CYBOCS during their initial evaluation (despite receiving an OCD diagnosis) and therefore CYBOCS data is not available for the complete group. These numbers are reflected in reporting of results.

RI was measured in participants immediately following the initial evaluation at COTTAGE or within the first three sessions of treatment at COTTAGE. The three computerized RI tasks were completed individually, in a quiet room, on a desktop computer in the clinic. The tasks were delivered in a random order. It took approximately 30 minutes for each participant to complete all three measures. The measures were run

using Inquisit 4 Web software (Inquisit 4). All participants were paid \$10 for their participation in the study.

These procedures were approved by the institutional review board of the University of Pennsylvania.

Data Analyses

Prior to statistical analysis, each outcome measure was examined for significant outliers and to determine whether assumptions of normality were met.

Demographic characteristics of the OCD group and anxious comparison group were compared using χ^2 tests or independent sample t-tests. Correlation coefficients were carried out to examine the relationship between age and RI performance as well as relationships between RI performance and clinical characteristics including OCD, anxiety, and depressive severity. Finally, univariate analyses of covariance (ANCOVA) were utilized to test for differences between groups on each RI measure, controlling for age.

Results

The mean age of the overall sample was 11.8 ($SD = 2.9$, range 7-17). Mean age did not differ significantly across groups (OCD $M = 12.5$, $SD = 2.9$; Anxiety $M = 11.1$, $SD = 2.8$), $t(53) = 1.85$, $p = .07$. Gender was approximately evenly split in the total sample and percentage of males and females did not differ significantly across groups, $\chi(1) = .46$, $p = .50$ (see Table 1). The OCD group had scores within the moderate-severe range on the CYBOCS (see Table 2). The OCD group had significantly higher OCI-CV

scores compared to the anxiety group (see Table 2). The groups did not differ significantly on CDI, MASC, or CPRS scores (see Table 2).

In the OCD group, 64% of participants had comorbid diagnoses including Tourette's disorder or persistent motor or vocal tic disorder (28.6%); generalized anxiety disorder (GAD; 25.0%), social anxiety disorder (21.4%), and major depressive disorder (14.3%). In the anxiety group, 59% of participants had multiple diagnoses. The most common diagnoses included GAD (55.6%), social anxiety disorder (33.3%), separation anxiety disorder (18.5%), and specific phobia (14.8%). Table 3 shows the occurrence of all diagnoses in the sample.

Frequency of psychotropic medication use differed significantly across groups, $\chi(1) = 4.15, p = .04$, with 39.2% of participants in the OCD group and 14.8% of participants in the anxiety group reporting SSRI, SNRI, or tricyclic use (see Table 4).

Based on previous research showing that RI performance on tasks such as the ones used in the current study tends to improve between childhood and adolescence (e.g., Tamm, Menon, & Reiss, 2002), we examined the relationship between age and performance on each RI task. Age was significantly related to the Stroop interference effect on the Stroop task ($r = -.31, p = .02$), total commission errors on the go/no-go task ($r = -.37, p < .01$), and SSRT on the stop signal task ($r = -.38, p < .01$). Based on these findings, analyses investigating group differences in RI performance controlled for age.

For participants in the OCD group, OCD severity, as measured by the CYBOCS, was unrelated to RI performance across tasks (see Table 5). Similarly, across both groups, anxiety, depression, and obsessive-compulsive symptomatology, as measured by

the MASC, CDI, and OCI-CV respectively, were each unrelated to performance on all three RI tasks (see Table 5).

Finally, univariate ANCOVAs controlling for age revealed no significant differences between groups in the Stroop interference effect on the Stroop task, $F(1, 55) = .20, p = .66, \text{partial } \eta^2 = .00$, total commission errors on the go/no-go task, $F(1, 55) = .19, p = .67, \text{partial } \eta^2 = .00$, and the SSRT on the stop signal task, $F(1, 54) = .32, p = .57, \text{partial } \eta^2 = .01$ (See Table 6).¹

Discussion

The purpose of the present study was to examine RI in pediatric OCD. We report that youth with OCD did not show differences in RI performance as compared to youth with other anxiety disorders. This lack of significant differences was consistent across three RI tasks – the motor Stroop task, the go/no-go task, and the stop signal task, which each captured a different domain of RI – interference control, action restraint, and action cancellation, respectively. These null findings are in line with the majority of previous RI studies with pediatric OCD samples (Hajcak et al., 2008; Ornstein et al., 2010; Woolley et al., 2009), which did not find differences in interference control or action cancellation between youth with OCD as compared to healthy controls. They are inconsistent with previous research in the adult literature, however. Several studies have shown impaired RI in OCD samples, particularly in the domains of interference control (Bannon et al., 2002; Enright et al., 1995; Nabeyama et al., 2008; Nakeo et al., 2009; Penadés et al., 2007; Schlosser et al., 2010; Zhang et al., 2016) and action cancellation (Bersani et al.,

¹ Findings were unchanged when groups were compared on RI variables without controlling for age.

2013; Chamberlain et al., 2006; Chamberlain et al., 2007; Lei et al., 2017; McLaughlin et al., 2016; Menzies et al., 2007; Zhang et al., 2015).

Due to limitations in previous RI studies on pediatric OCD, such as use of small samples, samples with remitted or clinically insignificant symptom severity, and use of single RI measures, researchers were cautious to conclude that null findings were truly indicative of a lack of RI impairment associated with pediatric OCD. For example, both Woolley et al. (2007) and Ornstein et al. (2010) reported trends toward impairment on the Stroop task associated with OCD and noted that group differences might have emerged with larger sample sizes. As such, these null findings were treated as preliminary.

The current study improved upon many of these limitations. First, the current study included tasks measuring the full array of RI domains making it less likely that an RI deficit was missed in this sample simply because the domain in which the deficit lies was not measured. Interestingly, there were no significant correlations between task performances in the current sample. Within the general RI literature, correlations between different tasks have tended to be low (Wager et al., 2005), which has led to different explanations. Low correlations among behavioral performances may simply reflect the fact that distinct neural correlates are involved in each RI process (Sebastian et al., 2013) but also raise concern regarding the “purity” of these tasks and whether idiosyncrasies between them lead to individual differences unrelated to RI capability (McNab et al., 2008). Results from the current study cannot speak to either explanation but add strength to the argument that including measures spanning all three domains should, as a rule, be included in studies in this research area.

Another improvement in methodology undertaken in the current study as compared to previous studies is the inclusion of a heterogeneous patient group. The characteristics of the study's sample, in which the OCD group had a moderate to severe level of severity as well as commonly co-occurring disorders including tic disorders and depressive disorders, made it more representative of typical OCD patient samples compared to previous pediatric RI/OCD studies. Finally, the current study used a larger sample than most previous studies. Despite this increase in sample, however, the current study was underpowered to detect small to medium effect sizes. Thus, the lack of significant differences in RI performance across groups should be considered with caution. The current findings do not provide support for the existence of an RI impairment in pediatric OCD but also do not provide sufficient evidence to undermine this possibility.

Although the absence of an RI impairment in this population has not been proven, it is important to consider explanations for the possibility of divergence in findings within pediatric studies from the adult literature. One explanation may be that that deficient RI emerges during development in a way that mirrors normal frontal-striatal circuitry maturation. Functional and structural neuroimaging studies have shown that the emergence of childhood OCD symptoms parallels the period of development in which brain regions thought to be directly involved in RI (e.g., orbitofrontostriatal pathways; Woolley et al., 2008) are going through rapid developmental changes (Abramovitch, Mittelman, Henin, & Geller, 2012). Research with typically developing children, adolescents, and young adults has shown that during RI task completion, younger

participants show more extensive brain activation in broad regions of the prefrontal cortex, whereas older participants show increasingly focal activations in specific regions of the prefrontal cortex (inferior frontal gyrus, insula, and orbitofrontal gyrus) that are thought to play a more specialized role in RI (Casey et al., 1997; Rubia et al., 2000; Tamm, Menon, & Reiss, 2002).

This focalization is thought to increase processing efficiency, and is likely what permits improved task performance through childhood and into late adolescence and early adulthood, a pattern demonstrated in the current study in which performance on all three RI domains were correlated with age. It has thus been suggested that due to this unstable neurodevelopmental period, neuropsychological deficits related to OCD may not fully materialize, or may be too subtle to capture on neuropsychological measures, until prefrontal systems have more fully matured in late adolescence or early adulthood (Abramovitch et al., 2012).

Another possible explanation for inconsistent findings across adult and pediatric samples is that poor RI reflects a neurodegenerative process caused by obsessive-compulsive symptoms, leading RI to weaken significantly over the course of a lifetime of OCD. However, evidence against this possibility comes from studies showing that later age of OCD onset is either unrelated to executive functioning performance (e.g., Abramovitch, Abramowitz, & Mittleman, 2013) or related to worse executive functioning (e.g., Roth et al., 2005). Little research has examined age of onset in relation to RI specifically but Lei and colleagues (2017) found no differences in SSRT between “early-onset” and “late-onset” groups of OCD patients (SSRT was significantly longer in both

OCD groups as compared to the control group), arguing against the presence of a neurodegenerative process in OCD.

Regardless of the potential contributing factors for the possible lack of RI impairment specific to pediatric OCD, this study does not provide supporting evidence for RI performance to be considered a valid indicator of genotypic or phenotypic OCD status in children and adolescents. Based on relatively consistent findings of impaired interference control and action cancelation in adults with OCD, studies in the adult OCD literature have pointed to RI as a potential target for the development of novel treatment techniques for treatment-refractory patients (e.g., McLaughlin et al., 2016). The current study does not preclude this potential path, particularly in adult populations, but it does suggest that researchers and treatment providers should be cautious about assuming such interventions would be relevant in pediatric populations, even if they prove fruitful in adults.

The current study had limitations that should be considered. First, due to the clinical context in which this study was carried out, completion rates of self-report measures did not include the whole sample. Although rates of incompleteness did not differ significantly across groups, demographic variables and rates of anxiety and depression symptomatology severity were not captured for the whole sample. Next, the wide age range of the study sample must be considered. The time- and energy-intensive aspects of neurocognitive studies as well as the high rates of comorbidity in pediatric OCD make it difficult to obtain large sample sizes, which led to our decision to increase the inclusiveness of the age range in the current study. However, as a result, the specificity of

findings to young children or adolescents is unknown. Future studies in this area should consider multi-site studies in order to obtain well-powered samples as well as adequate sample sizes of specific age groups.

Additionally, the exclusion of participants with co-morbid ADHD may limit the generalizability of these findings. Given the elevated rates of co-morbidity between pediatric OCD and ADHD, with recently reported prevalence rates of ADHD in treatment seeking OCD samples between 17% and 25% (Masi et al., 2006, 2010), the sample in the current study may not be representative of a significant proportion of pediatric cases of OCD. It will be important for future research to examine RI in specific subgroups of patients with both OCD and ADHD, as it may be the case that RI is particularly impaired in these types of patients, leading them to benefit most substantially from RI-targeted interventions.

Finally, the current study did not collect information regarding family psychiatric history. Given the possibility that impaired RI is an endophenotype of OCD and thus may be present in first-degree family members of OCD patients (e.g., Chamberlain et al., 2007) we cannot rule out the possibility that RI may have been affected in members of the comparison group. Although assessing this information accurately can be difficult, it may be worth doing so if increasing evidence supports the hypothesis that impaired RI is an endophenotype of OCD.

In conclusion, the current study adds to the small literature examining neurocognition and RI in pediatric OCD. The divergence in findings from adult studies highlights the necessity of the pursuit of research specific to child psychopathology.

Future research in this area should examine the longitudinal process of the development of RI in OCD samples as they move from childhood, through adolescence, and into adulthood. It would be illuminating to identify the correlates of the developmental age at which an RI impairment becomes apparent in OCD. For example, is it related to time since symptom onset, the consolidation of brain activation patterns during tasks of RI, the presence of co-occurring psychopathology, the extent to which pediatric OCD is treated, or the likelihood of the disorder persisting into adulthood? Answers to these questions could shed light on whether RI would be best utilized as a marker of vulnerability for OCD or co-morbid disorders, prognosis for the course of the illness, a target for treatment, or whether efforts should be shifted away from RI to other neurocognitive and neurobiological processes in the quest for increased understanding of OCD across the developmental spectrum.

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Table 1
Sample demographics.

Demographic	% OCD group (N=28)	% Anxiety group (N=27)	% Total sample (N=55)
Gender			
Female	48.3	53.8	50.9
Male	51.7	46.2	49.1
Racial background			
Caucasian	69.0	69.2	69.1
African American	3.4	0	1.8
Asian American	6.9	0	3.6
Did not report	21.7	31.8	25.5
Ethnicity			
Hispanic/Latino	0	0	0
Non Hispanic/Latino	79.3	69.2	74.5
Did not report	21.7	21.7	25.5

Table 2
Clinical Characteristics.

Measure	OCD group (N=28)			Anxiety group (N=27)			<i>t</i> (df)	Sig.
	n	<i>M</i>	<i>SD</i>	n	<i>M</i>	<i>SD</i>		
CYBOCS	24	22.6	5.7	NA	NA	NA		
MASC	21	91.7	29.1	19	97.0	26.4	-.61 (38)	.56
OCI	20	42.4	7.2	19	34.7	6.5	3.5 (37)	.001
CDI	18	41.9	9.1	16	41.6	10.8	.11 (32)	.92
CPRS	21	71.4	33.5	20	59.8	31.7	1.1 (39)	.26
<i>CPRS Domains</i>								
Oppositional		23.2	7.78		21.48	9.29	.69 (39)	.50
Cog. Problems		22.95	6.52		21.20	7.31	.81(39)	.42
Hyperact/Imp.		13.90	3.73		12.15	3.34	1.58 (39)	.12
Anxious/Shy		16.00	6.32		17.80	6.45	-.90 (39)	.37
Perfectionism		16.76	6.20		13.35	4.50	2.01(39)	.05
Social Problems		7.57	2.69		8.15	3.23	-.62(39)	.54
Psychosomatic		10.23	4.19		10.40	2.96	-.14(39)	.89

Note. CDI = Children's Depression Inventory; CPRS = Conners Parent Rating Scale-Revised; CYBOCS = Children's Yale Brown Obsessive Compulsive Scale
MASC = Multidimensional Anxiety Scale for Children; OCI = Obsessive Compulsive Inventory-Child Version.

Table 3
OC spectrum, anxiety, and mood diagnoses across groups.

	% OCD group	% Anxiety group
Tourette's/Persistent Tic Disorder	28.6	NA
Generalized Anxiety Disorder	25.0	55.6
Social Anxiety Disorder	21.4	33.3
Major Depressive Disorder	14.3	7.4
Panic w/Agoraphobia	3.6	3.7
Avoidant restrictive food intake disorder	3.6	11.1
Unspecified Anxiety Disorder	3.6	11.1
Selective Mutism	3.6	3.7
Hair Pulling Disorder	3.6	NA
Separation Anxiety Disorder	0	18.5
Specific Phobia	0	14.8
Provisional Tic Disorder	0	7.4

Table 4
Medication Use.

	OCD group (N=28)	Anxiety group (N=27)
<i>Selective Serotonin Reuptake Inhibitors</i>		
Sertraline	3	0
Fluoxetine	5	1
Escitalopram	1	2
<i>Serotonin-norepinephrine Reuptake Inhibitors</i>		
Duloxetine	1	1
<i>Tricyclics</i>		
Clomipramine	1	0

Table 5
Correlational analyses of clinical measures and RI variables.

Measures	1	2	3	4	5	6
CYBOCS	--	--	--	--	--	--
OCI-CV	.12	--	--	--	--	--
MASC	-.09	.47**	--	--	--	--
CDI	.26	.10	.14	--	--	--
Stroop Int. ¹	-.13	-.01	-.06	.08	--	--
Comm. Err. ²	-.17	-.12	.13	.03	.06	--
SSRT ³	-.22	-.03	-.04	-.07	.12	.27

Note: CDI = Children's Depression Inventory; OCI-CV = Obsessive-compulsive inventory – Child Version; MASC = Multidimensional Anxiety Scale for Children

¹Stroop interference effect on motor Stroop task (in milliseconds)

²Total commission errors on go/no-go task

³Stop signal reaction time on stop signal task (in milliseconds)

** $p < 0.01$

Table 6
RI performance across groups.

Variable	OCD group		Anxiety group		<i>F</i>	Sig	<i>partial</i> η^2
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>			
Interference effect ¹	55.27	47.78	68.68	53.69	.20	.66	.00
Commission errors ²	7.89	5.53	9.44	5.29	.19	.67	.00
SSRT ³	263.92	67.74	269.35	94.93	.33	.57	.01

¹Stroop interference effect on motor Stroop task (in milliseconds)

²Total commission errors on go/no-go task

³Stop signal reaction time on stop signal task (in milliseconds)

CONCLUSION

Response inhibition (RI) is a basic neurocognitive process that has been shown to be impaired in adult patients with obsessive compulsive disorder (OCD; Bannon et al., 2002; Bersani et al., 2013; Chamberlain et al., 2008; Enright et al., 1995; Gillan et al., 2011; Hartston, 1999; Lei et al., 2017; McLaughlin et al., 2016; Menzies et al., 2008; Penadés et al., 2007; Zhang et al., 2016). More research is needed, however, to determine the nature and specificity of the relationship between RI and OCD. To aid in this pursuit, three studies were undertaken in the context of this dissertation with the goal of addressing the following overarching questions: 1) Is there a response inhibition deficit related to obsessive compulsive symptomatology regardless of diagnostic status?; 2) Is RI impairment specific to OCD?; and 3) Is there an RI deficit in OCD that is present throughout development?

Answers to these questions have important implications for how the field may be able to improve outcomes for patients with OCD. Despite the development of treatments that help many patients reduce the severity of their OCD symptoms, a significant number of patients do not fully respond to these interventions (Franklin & Foa, 2011). In order to improve these treatment outcomes, the possible underlying mechanisms of the disorder, such as RI, need to be better understood. Better understanding regarding the nature and specificity of an RI deficit associated with OCD can provide information regarding the usefulness of testing RI as either a precursor to symptom development, a new treatment target, or a predictor of treatment response. Using RI in these ways could potentially lead

to new methods of prevention, early intervention, novel targeted or adjunctive treatments, or personalized intervention selection thus leading to fewer people suffering from OCD.

The studies in this dissertation used varied approaches to address the goal of increased understanding of the nature of a potential RI deficit associated with OCD. One method that all three studies employed was the use of three RI tasks, measuring all three RI domains (i.e., action restraint, interference control, and action cancellation). Most previous studies in the RI/OCD literature have failed to include multiple measures that capture each domain of RI. More attention must be given to the possibility that each RI domain may be differentially related to OCD. RI performance across tasks included in these studies confirm the theory that RI is not a unitary construct and that individual domains should be considered and measured consistently in studies that aim to investigate the role of RI in OCD. Correlations among the three different RI measures were significant but small in among the non-clinical undergraduate sample used in Chapters 1 and 2 and were not significant in the pediatric sample of patients with OCD or anxiety disorders, highlighting the likelihood that each task was capturing a unique process. Based on results from Chapter 1, which showed a significant relationship between OC symptomatology and action cancellation (as measured with the stop signal task) but not with action restraint or interference control, it is possible that action cancellation may be a particularly relevant RI domain when examining RI deficits in OCD. In line with this possibility, studies using the stop signal task have most consistently identified RI impairment associated with OCD as compared with studies using other measures (Lipszyc & Schachar, 2010). It is therefore recommended that the

stop signal task, in particular, be consistently included in studies in this area in order to capture an OCD/RI relationship.

In order to investigate the potential trait-based nature of RI impairment related to OCD, Chapter 1 examined the relationship between RI and obsessive compulsive (OC) symptomatology in a non-clinical sample. Results showed that OC symptomatology was a unique predictor of one domain of RI, action cancellation, over and above other symptomatology. This study thus provides support for the possibility that RI impairment (in at least one RI domain) is an endophenotype or trait-based marker for OCD specifically. It therefore encourages future research to move closer to examining RI as a potential precursor to symptom development. Should this relationship be established, RI in individuals with other risk factors for OCD could conceivably be measured and those with impaired performance could be provided with preventative measures or early interventions.

Evidence regarding the specificity of an RI impairment to OCD relative to other psychiatric illnesses that should not theoretically be associated with deficient RI, such as depression, is essential in determining whether RI is playing a unique role in the etiology or maintenance of OCD. It has been common practice in the RI/OCD literature to either exclude patients with depressive disorders or control for depressive symptoms based on the premise that executive functioning deficits are associated with depression. However, limited evidence supports the assumption that RI impairment specifically is associated with depressive symptomatology. Chapter 2, therefore, examined associations between RI and depressive symptomatology in a non-clinical sample. Findings from Chapter 2, in

which depressive symptomatology was not associated with RI performance in any domain, suggest that future research should take a different approach by being inclusive of depressive symptomatology in studies examining the relationship between OCD and RI. This methodology would lead to more representative OCD samples and increased power to detect an RI deficit associated with OCD symptomatology, therefore allowing a more accurate understanding of this relationship. Establishing the presence of an RI impairment specific to OCD also opens the door for testing RI as a treatment target. Should RI be involved in the maintenance of the disorder, symptoms may be affected by improving RI using computer-based RI training. Given the transportability and ease of implementation of such an intervention, continued pursuit of this line of research could lead to valuable advances in the field.

Although Chapters 1 and 2 support the possibility that an RI impairment is a unique process in OCD, Chapter 3 did not provide evidence that this relationship is present throughout development, prior to early adulthood. There were no significant differences in RI performance, across RI domains, between youth with OCD and youth with anxiety disorders. Given that the study was underpowered to detect small to medium effect sizes, the lack of significant differences must be considered with caution. Future studies should continue with this population in order to establish the presence or absence of RI deficits. It would be particularly illuminating to conduct studies with increasingly specific age ranges to determine whether there is a point in development at which an RI impairment becomes apparent following a period of no evident abnormality.

Evidence from Chapters 1 and 2 of this dissertation supporting the possible trait-based nature of an RI deficit in OCD as well as the specificity of this relationship suggest that consideration of RI as an underlying mechanism of OCD should continue. Chapter 3 leads to the cautious consideration of the possibility that youth may not exhibit the same relationship between OCD and RI as adults and pushes us to continue related studies with increased sample sizes. It also encourages the generation of testable hypotheses to explain a possible divergence in the OCD/RI relationship in youth and adults.

In addition to examining the potential role of development in the presence of this relationship, it is also suggested that future research investigate the possibility that deficits in RI are most pronounced or relevant to a subset of OCD patients, such as those with certain co-morbidities or types of OCD symptoms. For example, given the high rates of co-morbidity between OCD, attentive deficit hyperactivity disorder, and tic disorders, the involvement of the cortico-striato-thalamocortico circuits in all three disorders (e.g., Lebowitz et al., 2012), as well as the shared phenomenology regarding difficulty with some type of inhibition, it is possible that OCD patients with co-morbid ADHD and/or tic disorders are particularly affected by impaired RI. Ideally, studies would compare RI in patient groups with and without each of these disorders as well as comparison groups with patients with anxiety disorders. These types of clinical comparisons would allow for a better understanding of whether deficient RI is a transdiagnostic mechanism that may connect these disorders. They could also reveal whether an RI deficit is more relevant to certain OCD subgroups and therefore might be more likely to benefit from RI targeted interventions.

Similarly, it is possible that specific types of OCD symptoms are more or less related to RI deficits. For example, some have posited that perfectionism or “incompleteness” symptoms in OCD, which cause an individual to perseverate and repeat an action again and again in an effort to feel “complete,” may be the phenomenological manifestation of a faulty “stop signal” mechanism whereas those patients whose symptoms surround fears of harm coming to self or others are driven by an overreaction to threat or uncertainty (e.g., Zor, Szechtman, Hermesh, Fineberg, & Eilam, 2011). Studies that compare RI in patient groups based on primary “incompleteness” versus “harm avoidance” symptomatology could test this theory. If an RI impairment is found to be more pronounced in “incompleteness” OCD patients, adjunctive RI interventions could be tested for these individuals specifically.

Taken together, findings from the studies that compose this dissertation suggest that investigation of RI as a possible underlying mechanism of OCD should continue but that many important questions remain unanswered. These include (but are not limited to) RI’s role in the etiology and maintenance of the disorder, the presence and/or extent of impairment across different types of OCD patients, and the malleability of this neurocognitive process. Answers to these questions will be crucial in gauging the value of continued research on RI in the service of reducing the number of people who suffer from OCD and minimizing the suffering of those that do.

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