Developmental risk factors and outcomes associated with impulsive reactions to emotions

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Lauren Demers

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Advisors: Kathleen M. Thomas, Ph.D., Bonnie Klimes-Dougan, Ph.D.

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Dedication

To my parents, for always believing in me and helping me get here.

Abstract

Deficits in emotion regulation, such as impulsive reactions to emotional experiences, often follows early adversity and appear across many forms of psychopathology. However, there is limited research on factors that may contribute to differences in emotion regulation and on the potential protective effects of emotion regulation. Data on both developmental risk factors and outcomes associated with impulsive reactions to emotional experiences are needed to develop effective and targeted intervention programs. The current dissertation utilized questionnaire, behavioral, and neuroimaging data to examine early experiences that have been theorized to contribute to impulsive reactions to emotions, and also whether better regulation reduces risk for negative impacts of early adversity. Study 1 compared the performance and neural underpinnings of inhibitory control in the context of emotional distraction of 38 healthy adults with childhood maltreatment histories and 34 non-maltreated healthy adults. Results indicated that resilience to psychopathology after childhood maltreatment is associated with better inhibitory control and more efficient neural activity in the context negative emotional distraction. Results also showed greater adaptive functioning in everyday contexts was associated with better inhibitory control and greater activation in an action-monitoring brain region during negative emotional distraction. Study 2 examined differences in psychopathology and self-reported, performance-based, and neuroimaging measures of impulsive reactions to emotional experiences in 50 adolescent girls with histories of self-harm and 21 comparison adolescent girls. As expected, the adolescents who engaged in self-harm behaviors reported more impulsive reactions to negative emotional experiences. However, rather than showing a specific deficit in the context of negative emotions, as expected, they showed relatively worse regulation and less efficient neural activity across both emotional and non-emotional conditions. Across all adolescents, internalizing and externalizing symptoms related to worse inhibitory control in negative contexts. Study 3 sought to determine whether the relationship between childhood maltreatment and self-harm in a sample of 50 adolescent girls was moderated by impulsive reactions to emotions and associated neural activation. Unexpectedly, maltreatment history was not related to self-harm frequency in this sample and therefore analyses examining moderation were not run. Overall, the current project addresses gaps in our understanding about impulsive reactions to emotional experiences.

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Chapter 1: General Introduction

Developmental risk factors and outcomes associated with impulsive reactions to emotions

Emotion dysregulation is broadly defined as the disruption of goal-directed behavior by emotional experience or expression (Beauchaine & Cicchetti, 2019). Goal-directed behaviors may be thwarted by thought and/or action during states of heightened emotions and high arousal as inadequate control over emotions often manifests as impulsive thought or action (Johnson, Carver, & Joormann, 2013). Deficits in emotion regulation are seen across many forms of psychopathology; therefore, emotion dysregulation is considered a transdiagnostic construct (Aldao, Nolen-Hoeksema, & Schweizer, 2010; Beauchaine & Cicchetti, 2019; Southam-Gerow & Kendall, 2002). While there is extensive and transdiagnostic research examining risk factors for poor emotion regulation generally (e.g., Morris, Silk, Steinberg, Myers, & Robinson, 2007; Rothbart, Posner, & Kieras, 2006), there is less research addressing the impact of emotional context on behavior regulation, such as cognitive control or impulsive responding. More information on neural underpinnings and developmental risk factors contributing to impulsive reactions to emotions may support the development of effective early intervention programs for psychopathology.

The behavioral or cognitive manifestations of emotion dysregulation differ across individuals. Take for example three individuals who are all temperamentally highly emotionally reactive and experience intense and long-lasting emotions but differ on other traits or experiences. In an individual who has these tendencies and also shows sensation-seeking and high sensitivity to incentives, emotion dysregulation may manifest as antisocial impulses. In contrast, for an individual with similar tendencies who was also raised in an invalidating environment and finds it very hard to restrain impulsive behaviors, emotion dysregulation may manifest in non-suicidal self-injury (NSSI; intentional damage to one's body tissue without suicidal intent, including cutting and carving skin). Yet, another individual with these traits and also threat-avoidant tendencies may experience overwhelming anxious thoughts. Although the behavior manifestations differ, deficits in emotion regulation are observed across many forms of psychopathology (Aldao et al., 2010; Beauchaine & Cicchetti, 2019; Southam-Gerow & Kendall, 2002).

For the past 25 years, psychologists have studied emotion regulation at multiple levels of analysis, including neurohormonal, electrophysiological, cardiovascular, and neurobiological (Beauchaine & Cicchetti, 2019). In the neuroimaging literature, it is generally maintained that goal-directed action or cognitive control is considered the primary function of the prefrontal cortex (PFC; Miller & Cohen, 2001). The PFC, including the dorsolateral prefrontal cortex (dlPFC), dorsomedial prefrontal cortex (dmPFC), ventromedial prefrontal cortex (vmPFC), and ventrolateral prefrontal cortex (vlPFC), enables focus on goal-relevant information and attention away from goal-irrelevant information (Ochsner & Gross, 2005). In instances when goal-directed attention and behavior are in competition with emotional content, the PFC is critically involved in cognitive regulation of emotion (Davidson, 2002). However, for some individuals, vigilance towards threat, mediated by amygdala hyperresponsivity, may be overwhelmingly strong while signals from the PFC are too weak to facilitate goal-directed action. This pattern may result in increased attention to task-irrelevant emotional information (e.g., Bishop, 2008; Fales, Barch, Rundle, Mintun, Snyder, Cohen, … & Sheline, 2008). Weaker connectivity between the amygdala and regions within the prefrontal cortex has been related to the presence of elevated anxiety symptoms (e.g., Pagliaccio, Luby, Bogdan, Agrawal, Gaffrey, Belden, … & Barch, 2015). More broadly, functional neuroimaging studies have shown that frontal, as well as cingulate, parietal, and insular regions are involved in diverse cognitive processing demands and their functioning is perturbed across disorders (i.e., transdiagnostically; McTeague, Goodkind, & Etkin, 2016).

There is recent evidence that poor control over impulsive reactions to emotions is a core vulnerability to both externalizing and internalizing problems (Johnson et al., 2013). A large body of literature indicates that impulsive reactions to emotions are associated with increased externalizing problems, such as violence, sensation seeking, and substance abuse (e.g., Berg, Latzman, Bliwise, & Lilenfeld, 2015; Cyders, Flory, Rainer, & Smith, 2009; Dick, Smith, Olausson, Mitchell, Leeman, O'Malley, & Sher, 2010; Whiteside & Lynam, 2003). While the extant literature has focused less on the relationship between impulsive reactions to emotions and internalizing problems, one meta-analysis identified a moderate effect size between depressive symptoms and impulsive reactions to negative emotions (i.e., negative urgency; Berg et al., 2015). Together, this literature highlights the importance of continued research on impulsive reactions to emotions. More work is needed to understand how this vulnerability factor translates into impulsive actions across diagnostic categories. It seems that vulnerability for poor inhibitory control, as well as the precise form of impulsive thought or action that emerges, is determined in part by factors such as a person's past experiences and personality.

To date, there is negligible research on developmental risk factors contributing to impulsive reactions to emotions. This lack of literature makes it difficult to develop effective early intervention programs targeted for at-risk populations. In particular, a greater understanding of the early experiences and personality traits that may contribute to impulsive reactions to emotions is necessary to identify at-risk groups. Further, research on individual differences in impulsive reactions to emotions has the potential to provide insight into whether skill in this domain could serve as a protection factor against the known negative risks of early adversity (e.g., psychopathology, NSSI, low educational attainment, less stable or skilled employment). Continued investigation into both developmental risk factors and outcomes associated with impulsive reactions to emotions may ultimately reduce the mental health burden of early adversity.

Risk factors for impulsive reactions to emotions

Child maltreatment

Child maltreatment (CM) is one early experience that may contribute to a greater likelihood of emotion dysregulation manifesting as impulsive reactions to emotions. CM is known to affect one's ability to detect threat (Pollak, Vardi, Putzer Bechner, & Curtin, 2005) and inhibit responses (DePrince, Weinzierl, & Combs, 2009; Mezzacappa, Kindlon, & Earls, 2001; Navalta, Polcari, Webster, Boghossian, & Teicher, 2006). The biological effects of CM include excessively high levels of stress hormones that directly affect neural systems responsible for stress reactivity, self-regulation, inhibitory control, and planning behavior (Hart & Rubia, 2012; Teicher, Samson, Anderson, & Ohashi, 2016). As such, early experiences of CM may disrupt the development of inhibitory control capacities.

In addition to the evidence supporting difficulty with inhibitory control in adults who were maltreated as children, there is also documented emotion dysregulation (for review see, Pechtel & Pizzagalli, 2011). However, there is limited research examining the intersection of inhibitory control and emotion in the context of CM history. Data from longitudinal studies suggests that certain personality traits representing mastery over impulses (i.e., ego resilience) and the ability to modify impulse control in response to environmental stressors (i.e., ego control) may act as protective factors following CM (Cicchetti & Rogosch, 1997; Kim, Cicchetti, Rogosch, & Manley, 2009). The extant literature on behavioral measures of conflict monitoring in emotional contexts following CM relies primarily on tasks like the emotional Stroop, which indexes interference of attentional processing by emotional (i.e., emotional interference). While a recent meta-analysis based on over 50 separate studies revealed large Stroop interference effect by trauma-related words in individuals with PTSD compared to healthy control groups (Joyal, Wensing, Levasseur-Moreau, Leblond, Sack, & Fecteau, 2019), there has been limited research on emotional interference in CM in particular.

Two studies examining emotional interference in individuals with history of CM are suggestive of greater attentional distraction by emotional stimuli in CM groups compared to healthy controls (Caldwell, Krug, Carter, & Minzenberg, 2014; Mackiewicz Seghete, DePrince, Banich, 2018). Emotional Stroop tasks have also been used in two recent, comparably smaller functional MRI studies investigating the effects of emotional interference on neural activation in brain regions associated with cognitive control (e.g., Herzog, Niedtfeld, Rausch, Thome, Mueller-Engelmann, Steil, ... & Schmahl, 2017; Mackiewicz Seghete, Kaiser, DePrince, Banich, 2017). While both studies found CM history related to neural activation during cognitive control in the context of emotional content, the direction of findings was mixed. Further, because emotional stimuli are central to emotional Stroop tasks rather than included as background distractions, performance reflects a variety of cognitive (i.e., regulation of attention, inhibitory control) and emotional processes (i.e., recognition and interpretation of emotional stimuli) simultaneously. Therefore, measures of interest on these tasks do not necessarily represent individual differences in disruption of goal-directed behavior by emotional distraction. Further, accurate performance on emotional Stroop tasks is not believed to index response inhibition per-se, but is commonly thought to be achieved by selective inhibition dampening the fast, automatic activation associated with word-reading, so the slower deliberate route associated with facial affect recognition may be completed. As such, while preliminary evidence suggests CM may put one at risk for elevated impulsive reactions to emotions, this question has not yet been tested directly.

Personality factors

Personality traits also may contribute risk for elevated impulsive reactions to emotions. Alexithymia, the impaired ability to attend to and verbally label emotions via ongoing introspection (Sifneos, 1973), is a transdiagnostic vulnerability factor for various psychosomatic and mental disorders (Rufer, Albrecht, Zaum, Schnyder, Mueller-Pfeiffer, Hand, & Schmidt, 2010; Steinweg, Dallas, & Rea, 2011; Nowakowski, McFarlane, & Cassin, 2013). Individuals with limited ability to identify, describe, and consider feelings may act rashly in response to negative affect when they are unable to effectively regulate feelings that they cannot fully identify or understand. Previous research has shown that levels of alexithymia positively correlate with the self-reported tendency to react impulsively to negative emotions (Fink, Anestis, Selby, & Joiner, 2010; Gaher, Arens, & Shishido, 2013). Alexithymia has also been identified as a risk factor for behavioral impulse control problems including pathological gambling (Noël, Saeremans, Kornreich, Bechara, Jaafari, & Fantini-Hauwel, 2018), alcohol dependence (Cruise & Becerra, 2018), binge eating (Pinaquy, Chabrol, Simon, Louvet, & Barbe, 2012), and non-suicidal self-injury (Hasking & Claes, 2020; Swannell, Martin, Page, Hasking, Hazell, Taylor, & Protani, 2012). At the behavioral and neurobiological levels, alexithymia has been related to deficits in automatic processing of emotional stimuli (for review, see Donges & Suslow, 2017). While prior findings indicate that alexithymia may be a risk factor for increased vigilance to emotionally negative information (Demers, Westlund Schreiner, Hunt, Mueller, Klimes-Dougan, Thomas, & Cullen, 2019), it remains largely unclear whether alexithymia is also related to altered impulsive reactions to emotions.

Importantly, the relationship between alexithymia and dysregulated behaviors has been found to be statistically mediated by a distinct but related personality trait, termed negative urgency (Fink et al., 2010). Negative urgency is the tendency to engage in impulsive behavior under conditions of negative affect (Whiteside, Lynam, Miller, & Reynolds, 2005). In terms of clinical outcomes, negative urgency is a strong predictor for problematic behavior, including drug and alcohol abuse (Cyders & Smith, 2007, 2008; Smith & Cyders, 2016; Fischer & Smith, 2008; Menary, Corbin, Leeman, Fucito, Toll, DeMartini, & O'Malley, 2015; Whiteside et al., 2005) and the onset of NSSI (Riley, Combs, Jordan, & Smith, 2015). Cognitive research indicates that negative urgency is related to impaired inhibitory control at multiple stages, including difficulty withholding prepotent responses to infrequently presented negative stimuli and decreased ability to terminate already-initiated responses to negative stimuli (Allen & Hooley, 2019). However, it is unclear how these behavioral disruptions relate to alexithymia and negative urgency. Elucidation of the cognitive processing disturbances related to the negative urgency trait has the potential to bolster construct validity. A better understanding of personality traits related to the tendency to make impulsive reactions to emotions may inform treatment programs designed for individuals who engage in risky behaviors such as NSSI. For instance, findings suggestive of a positive relationship between alexithymia or negative urgency and impulsive reactions to emotions may indicate that individuals high on these personality traits should be explicitly targeted by intervention programs and taught impulse control and planning skills in the context of negative emotions.

Resistance to impulsive reactions to emotions as a potential buffer against adversity

Individual variability in impulsive reactions to emotions may partially explain the multifinality, or variance in outcomes, observed in high-risk samples. Numerous retrospective studies from community and clinical samples have reported strong associations between CM and psychopathology (Norman, Byambaa, De, Butchart, Scott, & Vos, 2012), suicidal behavior (for review, see Miller, Esposito-Smythers, Weismoore, & Renshaw, 2013) and non-suicidal self-injury (NSSI; Yates, Carlson, & Egeland, 2008; Ystgaard, Hestetun, Loeb, & Mehlum, 2004). Still, many individuals demonstrate the capacity for resilient outcomes in one or more domains despite the presence of chronic and severe adversity (Cicchetti, Rogosch, Lynch, & Holt, 1993).

It is possible that inhibitory control capacities, particularly in the context of negative emotion, allow individuals to act in accordance with their long-term goals rather than acting rashly out of emotional arousal. A growing body of research shows altered neural processing of threat-related information following childhood trauma (for review, see Hein & Monk, 2016), and more recent work indicates that individual differences in such processing act as a transdiagnostic mechanism contributing to the emergence of psychopathology (Weissman, Jenness, Colich, Bryant Miller, Sambrook, Sheridan, & McLaughlin, 2019). Furthermore, greater recruitment of PFC control regions and stronger modulation of amygdala reactivity during emotional viewing and reappraisal have recently been shown to be protective against psychopathology across a 2-year period in maltreated youth (e.g., Rodman, Jenness, Weissman, Pine, & McLaughlin, 2019). Other forms of resilient outcomes, including educational attainment, job status and work performance, and strength of interpersonal relationships, are also linked to altered modulation of amygdala reactivity during an emotion-matching task for high-risk adults regardless of CM history (Demers, Jedd McKenzie, Hunt, Cicchetti, Cowell, Rogosch, … & Thomas, 2017). However, it is unknown whether resistance to impulsive reactions to emotions may moderate the relationship between CM and maladaptive developmental outcomes. It is possible that better inhibitory control abilities during emotional situations or contexts can mitigate or reduce the relationship between CM and negative outcomes (e.g., psychopathology symptoms), and support more adaptive behavioral outcomes in adulthood (i.e., resilience).

One negative outcome that has been robustly related to self-reported impulsivity is non-suicidal self-injury (NSSI; intentional damage to one's body tissue without suicidal intent, including cutting and carving skin; Claes, Vandereycken, & Vertommen, 2003; Hasking, Coric, Swannell, Martin, Thompson, & Frost, 2010; Janis & Nock, 2009; MacLaren & Best, 2010). Individuals raised in invalidating caregiving environments and exposed to traumatic events are at increased risk of using self-injury (McKenzie & Gross, 2014; Yates et al., 2008). They have been shown to demonstrate weaknesses in impulse control and emotion processing (Domínguez-Baleón, Gutiérrez-Mondragón, Campos-

González, & Rentería, 2018; Groschwitz & Plener, 2012; Schmaal, van Harmelen, Chatzi, Lippard, Toenders, …, & Blumberg, 2019). This profile may make it more challenging for individuals to utilize adaptive coping strategies while experiencing stress, and therefore resort to use of NSSI, a relatively fast and easily accessible form of emotion regulation (Bentley, Nock, & Barlow, 2014).

There is limited neuroimaging data in this population, and while it seems to corroborate self- and parent-report of elevated impulsivity, the behavioral measures of impulsive behavior do not align. Self-injurers are not distinguished from non-injurers on measures of inhibitory control derived behavioral tasks including the stop-signal task, the continuous performance test, the Iowa gambling task, or delayed discounting tasks (Glenn & Klonsky, 2010; Janis & Nock, 2009). Of note, these tasks do not provide an affective context, that is, they assess inhibitory control in a neutral emotional context. It is possible that studies of inhibitory control in these samples have not revealed group differences because negative affect provides the context for impulsive behaviors in self-injurers. More recent investigations have begun to explore impulsivity within the context of emotion in NSSI samples, and results have been mixed (Allen & Hooley, 2015, 2017, 2019; Lengel, DeShong, & Mullins-Sweatt, 2016). Additional studies with larger samples are needed to clarify whether those who engage in NSSI demonstrate impaired inhibitory control generally, in the context of negative emotion, or not at all on laboratory measures. Further research is also needed to determine whether better inhibitory control abilities during emotional situations or contexts mitigate, or reduce, the relationship between CM and NSSI frequency.

The Current Project

In my dissertation, I address these gaps in the literature by examining developmental risk factors and outcomes associated with impulsive reactions to emotions. I also investigate whether resistance to impulsive reactions to emotions reduces risk for negative impacts of early adversity. I address these research questions using data from two study samples, and index impulsive reactions in the context of emotional distraction using both behavioral and brain measures. The following chapters describe the results from these studies, as well as my interpretations of the findings. Finally, the dissertation includes a general discussion of the results and how they fit within the broader literature on early adversity and emotion dysregulation.

Chapter 2

Impact of childhood maltreatment and resilience on behavioral and neural patterns of inhibitory control during emotional distraction.

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Child maltreatment (CM) represents one of the most adverse and stressful challenges that a child may experience (Cicchetti & Lynch, 1995) and has complex and multifaceted long-term sequelae. There is a clear link between CM and heightened risk for long-lasting problems in domains associated with poor emotion regulation and impulse control (Aldao, Nolen-Hoeksema, & Schweizer, 2010) including poor physical and mental health, drug and alcohol misuse, and criminal and other risky behaviors (Gilbert, Widom, Browne, Fergusson, Webb & Janson, 2009; Pechtel & Pizzagalli, 2011). However, there has been limited research examining the intersection of inhibitory control and emotion in the context of CM history. It is plausible that inhibitory control, the ability to prevent a response or stop an ongoing response (Nigg, 2017), is particularly disturbed during emotionally negative contexts for individuals who experienced maltreatment. For instance, when individuals with a history of CM encounter fearful stimuli in their environment, they might have trouble regulating their emotions while simultaneously avoiding distractions and engaging in goal-directed behavior. In fact, previous work has linked childhood abuse with deficits in emotional conflict regulation (Marusak, Martin, & Etkin & Thomason, 2015; Powers, Etkin, Gyurak, Bradley, & Jovanovic, 2015). Nonetheless, multifinality, or variance in outcomes has been observed in high-risk samples, including maltreated individuals (Cicchetti, Rogosch, Lynch, & Holt, 1993). Recent research provides preliminary evidence that resilient adults show an improved ability to regulate emotions, dampen threat processing, and habituate stress responses (for review, see Moreno-López, Ioannidis, Dahl Askelund, Smith, Shueler, & van Harmelen, 2019), whereas adults with long-lasting negative effects of trauma exposure (e.g., experiencing post-traumatic stress disorder; PTSD) demonstrate impaired attentional control in the context of emotional information (Fani, King, Clendinen, Hardy, Surapaneni, Blair, …, & Ressler, 2019). Individual differences in adaptive functioning during adulthood may result from variation in the ability to inhibit impulses in the context of emotional distractions, underpinned by coordination of cognitive-affective brain circuits.

Executive function differences following CM

A growing body of research that compares individuals with and without CM indicates that executive functions (EF) generally, and inhibitory control in particular, are impaired following CM (van der Bij, Op den Kelder, Montagne, & Hagenaars, 2020). Disruptions in EF, including attention shifting, cognitive and behavioral inhibition, working memory maintenance, and self-regulation and self-monitoring, have been identified consistently in both children and adults exposed to trauma. In children, exposure to familial trauma (relative to non-familial or no trauma exposure) has been associated with poorer performance on an EF composite including working memory, inhibitory control, auditory attention, and processing speed tasks (DePrince, Weinzierl, & Combs, 2009) and on specific measures of inhibitory control (Cowell, Cicchetti, Rogosch, & Toth, 2015). Children with substantiated abuse histories show more impaired inhibitory control relative to non-abused children, including non-abused children with psychiatric issues (Mezzacappa, Kindlon, & Earls, 2001). Caregivers also report more EF challenges in children exposed to maltreatment relative to non-maltreated children (Fay-Stammbach & Hawes, 2019). In adults exposed to childhood trauma, diminished inhibitory control been also observed (Daly, Hildenbrand, Turner, Berkowitz, & Tarazi, 2017; Navalta, Polcari, Webster, Boghossian, & Teicher, 2006). Poor executive functioning, and elevated impulsivity in particular, often persists into adulthood in maltreated populations (Pechtel & Pizzagalli, 2011).

Several mutually compatible theories have been proposed to explain the link between CM and impaired EF, and elevated impulsivity in particular. It has been posited that impulsive dispositions and associated behavioral difficulties tax parental resources, resulting in an elevated likelihood of parental abuse, particularly when parents are prone to impulsivity themselves (Liu, 2019). A transactional relationship may exist as parental corporal punishment has been associated with an increased likelihood of children engaging in misbehavior (Gershoff, 2002). In addition, it has been theorized that the maltreating rearing environment, often marked by unpredictability, results in prioritization of short-term goals in the face of long-term uncertainties (Belsky, Schlomer, & Ellis, 2011). Furthermore, maltreated children often are deprived of many of the experiences believed to promote adaptive functioning across the lifespan, rendering them vulnerable to physical and psychosocial maladjustment (Cicchetti & Lynch, 1993; Cicchetti & Toth, 2005; Gilbert, Widom, Browne, Fergusson, Webb, & Janson, 2009). For instance, children in maltreating families are less likely to observe healthy emotion management in parents or to be taught how to cope with their own emotions (Muehlenkamp, Kerr, Bradley, & Larsen, 2010). Finally, elevated impulsivity following childhood maltreatment has been linked to the impacts of early adversity on neural development. CM has the potential to alter brain structure and function via disruption of neurodevelopmental processes that occur during childhood and adolescence including, synaptic remodeling, glial cell proliferation, myelination, dendritic and axonal branching, and programmed cell death (de Graaf-Peters and Hadders-Algra, 2006; Sowell, Peterson, Thompson, Welcome, Henkenius, & Toga, 2003). These alterations may be adaptive for children in maltreating contexts where it is important to be vigilant to threat and ready to flee, which sometimes translates to impulsive behaviors.

Psychobiology and neuroimaging research provide further insights into the link between CM and elevated impulsivity. Emerging evidence suggests that CM is associated with deficits in brain regions that support EF including lateral frontostriatal and parieto-temporal regions (Andersen, Tomada, Vincow, Valente, Polcari, & Teicher, 2008; Bremner, Vermetten, Vythilingam, Afzal, Schmahl, Elzinga, & Charney, 2004; Hanson et al., 2010; Hart & Rubia, 2012; Herzog, Niedtfeld, Rausch, Thome, Mueller-Engelmann, Steil, … & Schmahl, 2017; Mackiewicz Seghete, DePrince, Banich, 2018; Mackiewicz Seghete, Kaiser, DePrince, Banich, 2017). Within the frontal lobe, alteration of right inferior frontal gyrus (IFG) was recently identified as a potential neurodevelopmental consequence of early adversity (Luby, Barch, Whalen, Tillman, & Belden, 2017; Sun, Haswell, Morey, & De Bellis, 2019). This region in particular has been implicated in inhibitory control with functional magnetic resonance imaging (fMRI) studies using paradigms such as the Go/No-Go and Stop Signal tasks (Aron et al., 2004; Bari & Robbins, 2013; Chikazoe et al., 2007). Thus, altered functioning in the right IFG may help explain CM-related impairments in inhibitory control. While these alterations may have supported functioning that was adaptive in a maltreating context, they are not necessarily adaptive as maltreated children grow into adulthood and are in non-maltreating contexts (Rieder & Cicchetti, 1989). At the same time, it is possible that individuals who are more resistant to the negative consequences associated with CM show a unique neural pattern associated with their resilience. Mental health after CM has been shown to be aided by increased or more flexible connectivity between central executive brain regions and emotion-processing limbic regions (for review, see Moreno-López et al., 2020). Little is known about how resilient functioning may relate to differences in the neural systems supporting EF.

Emotion regulation and processing differences following CM

Relative to the small body of work on EF in the context of CM, the findings of altered emotion regulation following CM are quite numerous. It has been shown that the high levels of stress hormones observed in maltreated children can alter neural systems, especially in prefrontal cortical regions involved in emotion regulation (Hart & Rubia, 2012; Pechtel & Pizzagalli, 2011; Teicher, Samson, Anderson, & Oshashi, 2016). The prefrontal brain regions most consistently identified as structurally altered following CM include ventromedial and orbitofrontal cortex (Hanson, Chung, Avants, Shirtcliff, Gee, Davidson, & Pollak, 2010; Hart & Rubia, 2012). These prefrontal regions have been consistently implicated in the regulation of affective signals from subcortical structures including the amygdala (Phillips, Drevets, Rauch, & Lane, 2003). Elevated threat-related activation of the amygdala itself, particularly on the right side, has also been linked to childhood trauma (Grant, Cannistraci, Hollon, Gore, & Shelton, 2011; Nooner, Mennes, Brown, Castellanos, Leventhal, Milham, & Colcombe, 2013; for review, see Hein & Monk, 2016). Furthermore, frontolimbic functional connectivity—the degree to which activity in the prefrontal cortex (PFC) relates to activity in the limbic system —has also been shown to be altered in maltreated individuals during emotion-processing tasks (Fonzo et al., 2013; Jedd et al., 2015). Thus, brain systems crucial to emotion processing and regulation, including prefrontal and limbic regions, as well as the connectivity between these regions, have been shown to be impacted by CM.

It is important to consider, however, that the impact of CM is not uniform; many individuals with maltreatment histories exhibit resilience in various domains of functioning. Thus, when only group differences in childhood trauma are evaluated, the impact of individual differences in adaptation may be masked. More recent research examining individual differences following CM provides preliminary evidence that altered emotion processing and improved emotion regulation may foster resilience. For instance, individual differences in threat-processing have recently been identified as a transdiagnostic mechanism contributing to the emergence of psychopathology (Weissman, Jenness, Colich, Bryant Miller, Sambrook, Sheridan, & McLaughlin, 2019). Further, a recent study indicates that greater recruitment of prefrontal control regions and stronger modulation of amygdala reactivity during emotional viewing and reappraisal are protective against psychopathology (Rodman, Jenness, Weissman, Pine, & McLaughlin, 2019). Previously maltreated adults without clinically significant psychopathology symptoms have been shown to have lower information transmission from the right amygdala to other brain network nodes when compared to maltreated adults with significant symptomatology (Ohashi, Anderson, Bolger, Khan, McGreenery, & Teicher, 2019). Other research has demonstrated stronger amygdala connectivity in frontal and parietal regions during emotional viewing in maltreated adults with greater current adaptive functioning (Demers, Jedd McKenzie, Hunt, Cicchetti, Cowell, …, & Thomas, 2018). Together, these findings suggest that effective emotion regulation, subserved by strong frontolimbic modulation, may support resilience following CM.

Maltreatment-related differences in inhibitory control in the context of emotion

It remains unknown whether individual differences in inhibitory control in the context of negative emotional distractions and associated neural activation are also protective against negative impacts of early adversity. One behavioral study addressed this interface by using two versions of the laboratory Stroop task in a maltreated sample: 1) a non-emotional task, consisting of emotionally neutral male or female faces presented with a congruent or incongruent word (male or female), and 2) an emotional task, consisting of a neutral or fearful face paired with a congruent or incongruent emotion word (neutral or fearful). Participants were instructed to ignore the word and respond based on the face. Results revealed impaired performance on the emotional, but not the non-emotional task in women with more self-reported childhood abuse. These individuals had the most difficulty with incongruent fearful stimuli (Caldwell, Krug, Carter, & Minzenberg, 2014). Emotional Stroop tasks have been used in two recent, comparably smaller fMRI studies investigating the effects of emotional interference on neural activation in brain regions associated with cognitive control (Herzog et al., 2017; Mackiewicz et al., 2017). While both studies found effects of CM history on neural activation to emotional content in brain regions associated with cognitive control, the direction of findings was mixed. Herzog and colleagues used a region of interest approach and showed greater activation in the dorsolateral PFC, ventromedial PFC, dorsal anterior cingulate cortex (dACC) in the context of trauma-related words in female patients with complex PTSD compared to healthy females with and without trauma exposure (Herzog et al., 2017). Their findings suggest current psychological functioning relates to emotional conflict regulation. In Mackiewicz and colleagues' study, adult females exposed to childhood abuse showed greater activation of right IFG and the left cerebellum than the control group and less activation in the left dorsolateral PFC and right dACC compared to the control group during the cognitive control condition across all trial types, and greater activation in the left IFG than the control group during emotional trials in particular (Mackiewicz et al., 2017).

The extant literature on inhibitory control in emotional contexts following CM relies primarily on tasks like the emotional Stroop, where in some cases, the emotional stimuli are task-relevant, and in other cases, effects of word valence may be relatively weak. That is, in the study by Caldwell and colleagues, attention to and processing of the affective face stimuli is necessary for task performance (Caldwell et al., 2014). Therefore, this task likely indexes a variety of cognitive and emotional processes simultaneously, making it difficult to determine whether inhibitory control, separate from recognition or interpretation of emotional stimuli, is disrupted specifically in the context of negative distraction. In the studies by Herzog's and Mackiewicz's groups, which both use emotion color word Stroop tasks, the emotion word is considered task-irrelevant since reading the word is not actually required during the task and the word is a distractor that captures attention (Herzog et al., 2017; Mackiewicz et al., 2017). Yet, previous work has demonstrated that valence effects on PFC activation are more apparent when stimuli are emotional pictures than when they are words (Kensinger & Schacter, 2006). Therefore, a task with background emotional pictorial stimuli that are unrelated to the task goal may more robustly and accurately index the effect of emotional distraction on inhibitory control. As such, while preliminary evidence suggests CM may put one at risk for elevated emotional interference, the effect of negative emotional distraction on inhibitory control in adults with CM history requires further study.

The present study

In the present study, we evaluated the impact of task-irrelevant negative emotional content on inhibitory control and neural activity in a longitudinal sample of adults with documented histories of child maltreatment. Inclusion of a longitudinal non-maltreated comparison group recruited from the same schools and neighborhoods as the CM group allowed us more to clearly isolate effects of maltreatment from high socioeconomic adversity. Additionally, we assessed whether individual differences in current adaptive functioning related to behavioral or brain measures of inhibitory control in emotional contexts.

We predicted that previously maltreated adults would show poorer inhibitory control than non-maltreated comparison adults under negative distraction, as prior work has shown that maltreated children are more vigilant to threat. Therefore, at the level of the brain, during conditions requiring inhibitory control during emotional distraction, we expected a hyperactive right amygdala response in the CM group, which would indicate greater emotional reactivity to negative valence image distractors during the inhibitory control task. We predicted hypoactive prefrontal regulation, as evidenced by less prefrontal activation, due to its protracted development (de Graaf-Peters & Hadders-Algra, 2006; Sowell, Peterson, Thompson, Welcome, Henkenius, & Toga, 2003), its susceptibility to early life stress (Diorio, Vaiu, & Meaney, 1993), and its role in inhibitory control (Arnsten & Rubia, 2012). In particular, we expected the CM group would show greater activation in the right IFG, a region known to play an important role in impulse control and emotion regulation, based on recent findings implicating functional connectivity for this region in risk for externalizing problems following early adversity (Luby et al., 2017). Finally, we predicted that differences in frontal activity would relate to current adaptive functioning of the participants, such that greater adaptive functioning would be associated with greater frontal cortex engagement.

Methods

Participants

Participants included 72 adults (*M* = 30.18; 37 males and 35 females) from a longitudinal sample first recruited when they were 6-12 years old through a research summer camp for low-income, high-risk children. At the initial recruitment, 93% of parents reported a history of receiving public assistance. Thirty-eight participants had a history of CM as documented by Department of Human Services (DHS) records, and 34 participants were classified as non-CM based on a lack of DHS records of maltreatment through age 17. The Maternal Maltreatment Classification Interview (MMCI; Cicchetti, Toth, & Manly, 2003) was used to further verify CM history or the lack thereof. Comprehensive DHS records were coded using the maltreatment classification system to classify the type (i.e., neglect, physical abuse, sexual abuse, emotional abuse) of each report of substantiated maltreatment (Barnett, Manly, & Cicchetti, 1993). The majority (60%) of the CM group experienced more than one type of maltreatment. In adulthood, internalizing and externalizing symptoms were in the broad average range for 90% of the current sample, and not different between groups, suggesting that the present sample is relatively healthy and may represent a resilient subset of maltreated individuals. Relative to participants from the larger longitudinal sample who did not participate in this phase of the study, the current sample had lower rates of adolescent conduct disorder and attention problems and better self-reported attachment to fathers during adolescence, although there were no differences in demographics, maltreatment history, cognitive ability during adolescence, or other psychopathology measures during adolescence. All participants provided informed consent in compliance with the University of Rochester's Institutional Review Board and were compensated for their time. Demographic information for the current subsample is provided in Table 1.

Data from an additional 29 individuals were collected but excluded from the final analysis due to: serious mental illness identified by history of hospitalization (2 CM), structural brain anomalies (4 CM, 5 comparison), excessive head motion (7 CM, 5 comparison), or low response rate on the task (4 CM, 2 comparison). Imaging data were not collected on an additional 13 individuals who returned to the lab for the study but either had metal in the body (1 comparison), claustrophobia (3 CM), or were too large to scan (6 CM, 3 comparison). An additional 57 longitudinal participants were contacted and screened but either declined to participate at the adult time point, or were unable to participate due to incarceration, death, MRI contraindications, or job or personal scheduling conflicts.

Measure of Adult Adaptive Functioning

Adult adaptive functioning, or competence, was assessed by examining each participant's competence or success on several stage-salient developmental tasks. A developmental task has been defined as a task typical to a certain period of life for which successful achievement leads to approval by society as well as competence or future successes (Havighurst, 1956; Schulenberg, Bryant, & O'Malley, 2004). We used a composite (range 0–14) of rank scores based on participants' progress in seven domains of development: education, work, financial autonomy, romantic involvement, peer involvement, family involvement, and substance abuse. All participants completed the Adult Self-Report (ASR; Achenbach & Rescorla, 2003) and a demographics questionnaire. Information from each domain was drawn from these measures. Adaptive functioning was defined in relation to others from similar economic and social backgrounds, given that participants were ranked on each developmental task relative to other study participants. For each domain, rankings were based on cutoffs that approximately divided the participants into thirds (lowest, middle, and highest; see details in the Appendix Material). This approach was based on work by Schulenberg, Bryant, and O'Malley (2004) and has been previously published by our group (Demers et al., 2018; Demers et al., 2019). Further details are included in the Appendix. While ranking based on comparison to others within the sample limits external validity, it increases our ability to observe individual variation within our study population.

Behavioral fMRI Imaging Paradigm

Participants underwent functional magnetic resonance imaging (fMRI) during performance of an IAPS Go/No-Go task (Cohen-Gilbert & Thomas, 2013). The IAPS Go/No-Go measures the ability to inhibit a dominant response in the context of visual distractors. In this task, letters were presented sequentially in a small box at the center of the screen while negative, positive, neutral or scrambled images were displayed in the background. Participants were instructed to ignore the background images and respond as quickly as possible with a button press to the presentation of every letter (Go stimuli), except the letter X (No-Go stimulus). The letters included H, P, R, S, T, and X. Go stimuli made up 73% of all trials such that participants acquired a prepotent tendency to press and needed to actively inhibit responses during No-Go trials.

Images were selected from the International Affective Picture System (IAPS; Lang et al., 2008), a collection of photographs selected to span a wide range of content and emotional valence. One hundred and eighty images were selected for use in this task. One third of the images had negative valence ratings (valence $M = 3.17$, $SD = 0.58$; arousal $M = 5.53$, $SD = 0.83$), one third had positive valence ratings (valence $M = 7.36$, $SD = 0.39$; arousal $M = 5.05$, $SD = 0.82$), one third ratings as close to neutral (5) as possible (valence $M = 5.25$, $SD = 0.50$; arousal $M = 3.34$, $SD = 0.83$). To create an additional emotionally neutral control condition that did not include object information, 120 of the selected IAPS images were also scrambled using a 32 x 32 grid.

The task was presented using E-Prime software (Psychological Software Tools Inc., Sharpsburg, PA) while participants were in the MRI scanner. The task included two runs, with trials blocked by stimulus valence within each run. Each run began and ended with a block of 15 scrambled image Go trials followed by a block of rest (fixation cross). Each run also included eight Go/No-Go blocks (two of each background type: negative, positive, neutral, or scrambled), presented in pseudorandom order. Each Go/No-Go block contained 15 trials, each with a unique IAPS image. Background IAPS images covered the entire screen and appeared for 200ms before a small white box containing a black letter appeared in the center of the image for 500ms. This design, with images presented alone prior to presentation of the letter stimulus, was used to make it more difficult for participants to ignore picture content. An inter-stimulus interval of 540ms followed each trial. Participants' responses (press or no press) and reaction times were recorded using a hand-held button box. Behavioral performance was measured by accuracy on No-Go trials across the emotional background types, and reaction time on accurate Go trials by background type.

fMRI Data Acquisition

Individuals were scanned on a Siemens 3T TIM Trio whole-body scanner using a 32-channel head coil. High-resolution, T1-weighted images were acquired for each participant using an MPRAGE sequence (echo time [TE] = 3.4 ms, repetition time [TR] = 2530 ms, field of view = 256 mm, matrix = 256x256, slice thickness = 1 mm, flip angle = 7°, 192 sagittal slices) for co-registration of functional images. Functional data were acquired using an echo-planar imaging sequence (TE = 30 ms, TR = 2500 ms, field of view = 224 mm, matrix = 64x64, slice thickness = 3.5 mm with a 29% gap, flip angle = 90°, 36 interleaved oblique axial slices). To correct geometric distortion in the functional data, a fieldmap volume was collected immediately prior to the functional data acquisition using the same slice prescription (TE1 = 5.19 ms, TE2 = 7.65 ms, TR = 400 ms, field of view = 224 mm, matrix = 64x64, slice thickness = 3.5 mm with a 29% gap, flip angle = 60°, 36 interleaved oblique axial slices).

fMRI Data Analysis

Preprocessing

Functional imaging data were analyzed using FSL6.0.1 software. Head motion in the scanner was assessed and data points were censored based on the following parameters: 1) absolute motion exceeding one voxel of overall displacement from the first volume in the series and 2) relative motion exceeding one half voxel from one volume to the next. Volumes immediately preceding and following those that meet the relative motion criterion were also excluded. Motion displacement was quantified using the root mean square across the six head motion parameters. Participants with above threshold motion in more than 25% of data points (TRs) were excluded from further analyses, such that the final sample of 72 participants each had at least 171 TRs, or 7 minutes 8 seconds, of usable task data. Additionally, usable structural scans were required for inclusion in the analysis. In addition to fMRI data quality, participants with less than 60% accuracy on Go trials with scrambled background images were deemed to demonstrate poor understanding of the task demands and were excluded from further analyses. fMRI preprocessing steps included motion correction with MCFLIRT, skull stripping using the Brain Extraction Tool, slice time correction, geometric unwarping based on a fieldmap volume, spatial smoothing using a 6-mm full width at half maximum Gaussian kernel, and high-pass temporal filtering with a filter cutoff of 100 sec based on the block design task. Each participant's functional images were registered to the corresponding high-resolution anatomical image (using 6 df), which were in turn registered to the Montreal Neurological Institute standard space (152 individual T1 2-mm template) using 12 df.

Task Analysis

Single-subject data were entered into a general linear model using gamma-convolved predictors for the four image-background conditions (negative valence, positive valence, neutral valence, scrambled images), with rest blocks serving as the unmarked baseline. Additional predictors of noninterest included a predictor for an unused buffer period (short fixation period at the beginning of the task), a predictor for the all-Go trial blocks, six predictors for head motion (three rotation and three linear translation), and a censoring (motion displacement) predictor for each motion-affected TR. The activation contrast of interest was response to negative > response to neutral.

Group Analysis

Whole-brain mixed effects regression analyses were conducted to assess activation differences between the maltreated and comparison groups, with age and gender as centered nuisance variables. We used FSL/FEAT (FLAME 1) to correct for multiple testing across voxels with a voxel-level threshold of $p < .005$ and a cluster threshold (calculated using Gaussian random field theory maximum height thresholding) of $p < .05$.

Statistical Analyses

We first conducted independent t-tests or χ^2 tests on demographic variables to confirm group equivalence, and on psychopathology variables to explore group differences in symptoms. To parallel the imaging contrast of negative vs. neutral valence background conditions, we used 2x2 mixed-model analyses of variance (ANOVA) to test effects of group (CM vs. comparison) and emotional background type (negative vs. neutral) on task performance, with age and gender as covariates. Analyses were run on the main inhibitory measures, No-Go accuracy and Go trial reaction time, and also on Go trial accuracy. Follow-up paired-sample *t*-tests were used to examine significant effects. To examine the relationship between adult adaptive functioning and task performance, another set of ANOVAs was run with this index as a covariate of interest. We used SPSS/ PASW 25.0 (SPSS, Chicago, IL) to conduct behavioral analyses.

Results

Group demographics and psychopathology

There were no group differences in age, gender race, ethnicity, other demographic variables, or psychopathology (see Table 1).

Table 1. *Demographics and sample characteristics for the maltreated and comparison groups*

Sample Characteristics	Maltreated Group (*N*=38)	Comparison Group (*N*=34)	*p*-value
Age (years), *M* (*SD*)	30.89 (3.25)	29.38 (3.70)	.07
Gender, *n*	17 Males, 21 Females	20 Males, 14 Females	.24
Race, *n* [%]			.32
Black	25 [65.8%]	26 [76.5%]	
White	10 [26.3%]	3 [8.8%]	
Other/multiracial	3 [7.9%]	5 [14.7%]	
Current annual family income, *M* (*SD*)	$27.39k ($19.39k)	$33.86k ($24.02k)	.21
Range	$2.30k – $99.90k	$5.20k – $99.90k	
Marital status, *n* [%]			.39
Not married	34 [89.5%]	28 [82.4%]	
Married	4 [10.5%]	6 [17.8%]	
Current work status, *n* [%]			.52
Working full time	16 [42.1%]	17 [50.0%]	

Working part time	6 [15.8%]	8 [23.5%]	
Not working	16 [42.1%]	9 [26.5%]	
Education, *n* [%]			.70
Some high school	9 [23.7%]	4 [11.8%]	
High school diploma or GED	13 [34.2%]	15 [44.1%]	
Tech degree, associate's degree, or some college	12 [31.6%]	14 [41.2%]	
Bachelor's or master's degree	4 [10.5%]	1 [2.9%]	
Number of CM subtypes (1-4), *M* (*SD*)	1.97 (0.91)	0	
Adult adaptive functioning, *M (SD)*	6.53 (3.06)	7.58 (2.80)	.13
ASR Internalizing Symptoms, *M (SD)*	51.66 (10.73)	51.68 (12.64)	.99
ASR Externalizing Symptoms, *M (SD)*	52.023 (10.87)	51.29 (10.94)	.78

Note: Statistical effects were tested by ANOVA or two-tailed *t*-test as appropriate for the number of levels. ASR = Achenbach Adult Self-Report (scores above 60 fall in the borderline clinical range)

IAPS Go/No-Go task performance

A mixed-model ANOVA was conducted to compare the effects of background image valence (neutral or negative), a within-subjects factor, and group (comparison or CM), a between-subjects factor, on No-Go accuracy. There was a statistically significant interaction between image valence and group for No-Go accuracy, $F(1, 68) = 5.8787$, $p = .02$, $\eta^2 = .081$. Simple main effects analyses showed that the comparison group was significantly less accurate on trials with negative compared to neutral background images ($p = .01$, $d = .45$), but there were no accuracy differences by background image valence for the CM group ($p = .30$, $d = .17$). The CM group was more accurate than the comparison group on No-Go trials with negative backgrounds [$t(70) = -1.98$, $p = .050$, $d = .47$; see Figure 1, Table 2], but there was no group difference for No-Go trials with neutral background [$t(70) = 0.12$, $p = .90$].

A second mixed-model ANOVA was conducted to compare the effects of background image valence and group (comparison or CM) on Go trial reaction time. There were no significant interactions or main effects. When Go trial accuracy was inspected, there were no significant effects of image valence, group, and their interaction [$F(68, 1) = 0.07$, $p = .79$], $F(68, 1) = 3.37$, $p = .07$, $F(68, 1) = 0.46$, $p = .50$, respectively].

Finally, analyses were conducted to evaluate the association between adult adaptive functioning and task performance above and beyond the influence of group. There was a significant main effect of adult adaptive functioning on No-Go trial accuracy, $F(1,67) = 3.9595$, $p = .050$, $d = .06$, but not Go trial reaction time ($p = .19$). Greater adaptive functioning was associated with higher No-Go accuracy. There were no significant interactions between CM group and adult adaptive functioning for either accuracy or reaction time (p's $> .68$).).

As a check of our assumptions, we confirmed that when background images were scrambled, reaction time and accuracy did not differ between groups (No-Go trial accuracy, $t(70) = -.33$, $p = .74$; Go trial reaction time, $t(70) = -1.51$, $p = .14$).

Task-Related Brain Activity

An analysis of task-related brain activation in the whole sample (all subjects, negative > neutral contrast) revealed significant activation in multiple brain regions, including visual cortex, PFC, cingulate gyrus, amygdala, and hippocampus. These regions are consistent with those reported in previous studies using Go/No-Go paradigms (e.g., Chester, Lynam, Milich, Powell, Andersen, & DeWall, 2016; Cohen-Gilbert, Nickerson, Sneider, Oot, Seraikas, Rohan, & Silveri, 2017) and emotional tasks (Frank, Dewitt, Hudgens-Haney, Schaeffer, Ball, Schwarz, …, & Sabatinelli, 2014).

Group Differences in Task-Related Brain Activity

Comparison of task-related activity by group revealed that the comparison group recruited prefrontal regions (left frontal pole, right inferior frontal gyrus, right frontal pole; Table 3, Figure 2) more than the CM group when performing the inhibitory control task in the context of negative background images. Follow-up simple effects analyses using percent signal change values extracted from the three significant ROIs showed that the comparison group showed a 0.29%, 0.38%, and 0.15% mean difference signal change for the three ROIs respectively, whereas the CM group showed a 0.05%, 0.09% and .05% mean difference signal change for the three ROIs respectively.

Relationship between Current Adaptive Functioning and Task-Related Activation

We evaluated whether differences in task activation were related to individual differences in current adaptive functioning across the full sample. Correlations were run between percent signal change values extracted from the three significant ROIs and adult adaptive functioning scores, with age and sex as covariates. Adult adaptive functioning was significantly related to task-related activity of the right frontal pole $r(68) = .41$, $p < .001$, but not related to task-related activity of the left frontal pole, $r(68) = .22$, $p = .07$, nor task-related activity of the right inferior frontal gyrus, $r(68) = .01$, $p = .98$. Individuals with greater adult adaptive functioning showed more activity in frontal pole regions when the background images were negative compared to neutral. The relationship between adaptive functioning and right frontal pole activation survived Bonferroni correction for multiple comparisons.

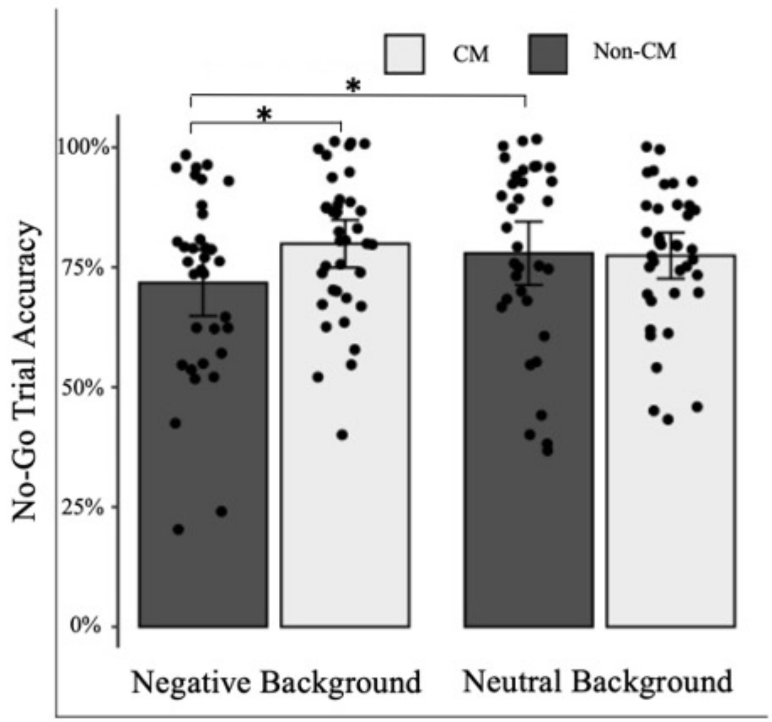

Figure 1. *Accuracy on No-Go trials for maltreated and comparison groups*

Accuracy on No-Go trials was impaired by negative background images relative to neutral backgrounds in the comparison group, but not the maltreated group. Accuracy on No-Go trials with negative background images was lower in the comparison group than the maltreated group. Error bars show 95% confidence intervals. * $p < .05$

Table 2. *IAPS Go/No-Go task performance for the maltreated and comparison groups*

	CM (n = 38)		Comp (n = 34)	
	Negative Background	Neutral Background	Negative Background	Neutral Background
Go Acc.	.95 (.07)	.96 (.07)	.91 (.12)	.91 (.12)
No-Go Acc.	.80 (.15)	.77 (.15)	.72 (.20)	.78 (.19)
Go RT	442 (38)	426 (42)	424 (43)	408 (40)

CM = Childhood maltreatment; Comp = comparison group; Acc. = accuracy; RT = reaction time (in milliseconds). Values are given as mean (standard deviation).

Table 3. *Group differences in task-related brain activity for negative > neutral background image contrast*

Region	Brodmann Area	Volume, mm^3	MNI Coordinates			Z value		
			x	y	z	Max	Mean	SD
Left frontal pole	10	510	-24	38	16	3.81	2.92	0.25
Right inferior frontal gyrus	45	329	50	24	4	3.69	2.90	0.25
Right frontal pole	9	508	8	60	36	4.01	2.98	0.31

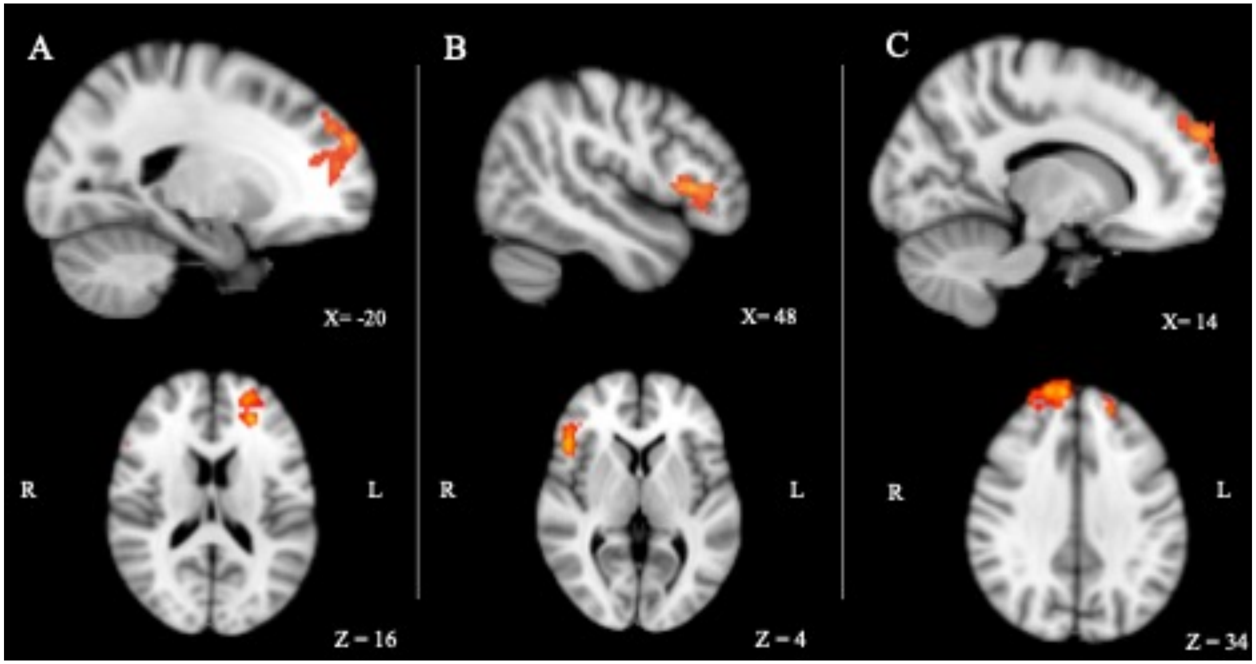

Figure 2. *Neural activation differences for comparison and maltreatment groups*

The comparison group showed greater activity than the maltreated group for Negative > Neutral images in three PFC regions including (A) left frontal pole, (B) right inferior frontal gyrus, (C) right frontal pole ($p < .05$ cluster corrected).

Discussion

This study examined the interface between inhibitory control and emotion and associated neural underpinnings in the context of CM history. Contrary to our predictions, negative emotional images adversely affected inhibitory control in the comparison group, but not the maltreated group. Additionally, relative to the maltreated group, the comparison group showed greater prefrontal activation during conditions when inhibitory control was required and when background images were negative compared to neutral. Better adaptive functioning in everyday contexts was related to this greater prefrontal activation and superior inhibitory control in the context of negative distractors.

In the present study, we did not observe the expected performance deficit in inhibitory control in our CM group. This could be due to the fact that the comparison group was well matched on other dimensions of early risk apart from CM which likely acted as confounds in prior studies. Therefore, our results suggest that CM history in healthy adults does not predict general impulsivity on a laboratory task when compared to peers from similar contexts. This finding is consistent with Liu's (2019) recent meta-analysis which also did not show support for an association with behavioral task performance. Liu (2019) did find an association between CM history and self- and parent-reported impulsivity, although only a small number of behavioral studies were included.

The effects of emotional distraction on behavioral performance differed by group. Accuracy was reduced in the context of negative images only for the comparison group and not the maltreated group. It is possible that adults with a history of maltreatment have learned based on their early experiences to maintain inhibitory control even in negative contexts. A group comparison of accuracy and reaction time for scrambled image backgrounds, which inherently do not require as much attention regulation, allowed us to rule out differences in inhibitory control in non-emotional contexts. Given the lack of more general group differences, it seems that the CM group is showing enhanced attention regulation in the face of negative images, rather than simply allocating more attentional resources to inhibitory control overall. The decreased emotion-related impulsivity seen in the maltreated group relative to the comparison group aligns with prior work reporting that young adults with child abuse histories demonstrated less impulsivity on laboratory-based measures than those without abuse histories (Sujan, Humphreys, Ray, & Lee, 2014). This adaptive strategy may reflect a form of long-term resilience despite early adverse experience.

It is also possible that the negative images used in this study were differentially arousing to the two groups, such that they were not arousing enough to elicit a strong interference response from adults in the maltreated group. It is possible that individuals with a history of CM have been relatively desensitized to negative images through consistent exposure to negative emotional contexts early in life. Previous research has suggested that arousal improves behavioral response inhibition in nonclinical populations (Shields, Sazma, & Yonelinas, 2016). This effect, however, may be moderated by emotion-related impulsivity. In a recent study by Pearlstein, Johnson, Modavi, Peckham, and Carver (2019), individuals who rated themselves as having lower emotion-related impulsivity showed improving response inhibition on a trial-by-trial basis following increased arousal (indexed by pupil dilation), whereas for those rating themselves higher in emotion-related impulsivity, response inhibition declined following higher arousal. However, we did not measure either physiological or self-reported arousal in this study and therefore cannot address this possibility.

The accuracy detriment associated with negative backgrounds in the comparison group was unexpected although in a logical direction. Previous research in normative samples has shown a negligible effect of emotional distraction on task accuracy, whereas effects on reaction time are more typical (e.g., Chester et al., 2016; Cohen-Gilbert & Thomas, 2013; Cohen-Gilbert et al., 2017). However, in prior work with this task, younger adolescents (ages 13-14 years) showed poorer No-Go accuracy when the background image was negative (Cohen-Gilbert & Thomas, 2013). Given that the adults in the current sample have all experienced high levels of stress vis-à-vis poverty, results may suggest that early adversity may lead to immature inhibitory control in the face of negative emotional content. However, without a low-risk control group in the present sample, this possibility cannot be tested. The comparison group's impaired behavioral performance on the task in the context of task-irrelevant negative images was accompanied by increased recruitment of frontal brain regions, including regions associated with inhibitory control (e.g., right IFG; Aron et al., 2004; Chester et al., 2016;

Chikazoe et al., 2007), relative to the CM group. Although this particular executive function domain (i.e., inhibitory control) has not been assessed in previous imaging studies of maltreatment, Schweizer and colleagues found similar evidence of enhanced cognition in the context of strong emotion following early adversity (Schweizer, Walsh, Stretton, Dunn, Goodyet, & Dalgleish, 2016). Their work suggests that the neural underpinnings of emotion regulation in healthy adolescents and young adults exposed to moderate childhood adversities may be operating more efficiently (Schweizer et al., 2016) than in those with low adversity. Specifically, the group with higher childhood adversities showed enhanced emotion regulation over positive and negative affect during a film-based task, which was associated with reduced recruitment of frontal regulatory brain regions and amygdala activation. These findings align with our results of enhanced behavioral performance and reduced recruitment of brain regions associated with inhibitory control in the maltreated relative to comparison group. The sample and task paradigm used in the present study and in Schweizer's differed substantially (i.e., Schweizer's sample had moderate childhood adversity but not maltreatment, and the paradigm involved explicit instructions to regulate one's emotional reaction to film clips). Still, the similarity in results may indicate that generally healthy adults who experienced extreme stress in childhood may develop an enhanced ability to regulate their attention and emotional reactions in the context of task-relevant or -irrelevant emotional stimuli, at least within the controlled laboratory environment.

Others have also found CM history to be associated with differential activation in multiple prefrontal regions during emotionally-charged executive function tasks. For instance, one recent study found CM was associated with reduced activation in the left dorsolateral PFC and right dACC, and increased activation in the IFG (Mackiewicz et al., 2017), while another study found increased activation in dorsolateral PFC, dACC, and ventromedial and ventromedial PFC, and no differences in the right IFG (Herzog et al., 2017). However, in both of these studies, the maltreated groups had significantly higher levels of depression and/or PTSD symptomatology than the comparison groups. Unlike these two samples, the present sample may represent a resilient subset of maltreated individuals, as internalizing and externalizing symptoms were in the broad average range for 90% of the current sample. In this way, our sample is more similar to Schweizer's sample of healthy individuals exposed to moderate childhood adversities. Together, these studies may indicate that, in healthy adults with histories of early adversity and/or abuse, regulatory control is not disrupted by negative contexts, despite less recruitment of neural systems typically implicated in inhibitory control.

Better performance and more efficient neural recruitment of inhibitory control systems when engaged in a laboratory task does not necessarily extend to real-life application of these skills. Our results showed that across the entire sample, greater activation of the frontal pole related to higher levels of current adaptive functioning. Previous research indicates that activation in this brain region is involved in monitoring action outcomes (Koechlin, 2011). The ability to monitor one's behavior and inhibit impulses within aversive contexts is likely critical to success in everyday situations reflected in the adaptive functioning measure. For instance, resisting the urge to use alcohol or other substances when depressed and refraining from hostile behavior when angered, can serve an individual in social relationships as well as educational and occupational progress. Our prior work in this sample has demonstrated that adult adaptive functioning also relates to frontolimbic functional connectivity, an index of efficient emotion regulation (Demers et al., 2018). It is possible that the maltreated group is able to regulate their responding with less recruitment of typical neural systems despite negative distractions in a laboratory-based task, but that adaptive functioning within the real world requires greater activation of neural regions involved in inhibitory control for all participants.

This study makes several important contributions to the existing maltreatment and resilience literatures. First, unlike the previous studies on inhibitory control during emotional contexts in maltreated individuals, this sample includes both a larger total sample and a comparison group that is well-matched longitudinally on socioeconomic characteristics. The two groups also had similar levels of current internalizing and externalizing symptoms and current adaptive functioning. Therefore, we were better able to isolate effects specific to maltreatment without confounding group differences in poverty, general risk, or adult level of functioning. Unlike most studies of maltreatment that only evaluate risk factors, we also investigated promotive factors by examining whether group differences in neural activity related to individual differences in adaptive functioning. Similarly, the sample was assessed prospectively from childhood into adulthood, reducing typical measurement errors inherent in retrospective report. Finally, this study is unique in its focus on brain systems involved in inhibitory control during emotional distraction in the context of maltreatment history. The majority of prior work has used facial viewing tasks that do not tap into executive functioning skills in emotional contexts or have used emotional Stroop tasks that don't include highly arousing stimuli. In contrast, we examined inhibitory control during emotional contexts using a paradigm with task-irrelevant emotional stimuli, thereby allowing us to isolate the impact of negative emotional distraction on executive function. Further, by using this paradigm in the scanner, we were able to evaluate the impact of negative emotional distraction on brain activation during inhibitory control.

Despite important contributions to the extant literature, this study had several limitations. First, the sample size per group limits our ability to confidently draw conclusions due to low statistical power and necessitates replication. Unfortunately, few prospective neuroimaging studies of maltreatment have large enough sample sizes to adequately power complex statistical analyses capable of teasing apart the influences of multiple risk factors for poor adaptive functioning. Although participants were followed longitudinally since childhood, MRI assessment was conducted only at the most recent time point in adulthood. Therefore, we cannot determine the directionality of the relationships between maltreatment, emotion-related inhibitory control, adaptive functioning, and brain circuitry. Also, without a low-risk control sample, we could not determine whether the observed disruptions in inhibitory control by negative stimuli are present only in individuals who have experienced high-risk early environments, including poverty, or would also be evident in low-risk adult populations. Additional work with a low-risk comparison group is needed to determine if relationships between current functioning and neural measures of inhibitory control are specific to adaptation after early adversity or if they can be generalized to adaptive functioning and competence, regardless of early environment. It is also possible that the composition of participants included in our comparison and maltreated groups is not representative of individuals from high-risk, low-income backgrounds. It is probable that current life stressors and factors related to adult adaptive functioning influenced which participants were able to continue in the study. For instance, some individuals had employment conflicts prohibiting research participation, while other individuals from the original sample (maltreated or not) were excluded based on incarceration, bullets or other metal fragments in the body, obesity significant enough to preclude MRI scanning, severe mental illness (e.g., schizophrenia) or cognitive impairment, or an inability to locate the individual for recruitment (e.g., homelessness or high mobility) – conditions that are often exacerbated by a history of chronic poverty, racial discrimination, and various forms of trauma. Consequently, our sample represents a restricted range of developmental outcomes seen in high-risk, low socioeconomic status populations. Replication with a larger sample is warranted. In addition, while adult adaptive functioning may indicate the capacity for resilience, further study of resilient processes throughout development is needed.

Finally, given the inherent constraints of fMRI, we chose to use a block design rather than an event-related design for the IAPS Go/No-Go paradigm. Therefore, we were unable to compare neural activity on Go and No-Go trials or accurate and inaccurate trials. Also due to the block design nature of the task, comparison of neural signal between negative and neutral blocks likely represents contextual monitoring more broadly than just inhibitory control. We also did not have any autonomic measures of arousal, so we were unable to determine if participants had different physiological reactions to the images in the task. As noted above, it is possible that performance by the maltreated group was less disrupted by task-irrelevant negative images because they found the images less arousing, perhaps owing to a systematic desensitization based on past life experiences. Future research should consider level of arousal, as well as level of emotion-related impulsivity (Pearlstein et al., 2019) when evaluating the effect of emotional distraction on inhibitory control.

In conclusion, results suggest that psychiatrically healthy adults who endured childhood maltreatment may have an enhanced ability to regulate their attention and limit impulsive reactions in the context of task-irrelevant emotional stimuli within a laboratory task. This enhancement may reflect learning from earlier experiences such that the negative content in a laboratory setting may be less arousing and therefore less distracting for adults who have experienced CM. Additionally, while early maltreatment experience may train enhanced inhibitory control in the face of negative or threatening stimuli, it is not necessarily synonymous with positive real-world outcomes. Adult adaptive functioning within real world contexts was associated with greater activation of neural regions involved in inhibitory control, suggesting that multiple risk and protective mechanisms may be at work in this sample.

APPENDIX

Description of Adult Adaptive Functioning

The adult adaptive functioning scores ranged from 0 through 14 and were generated through a composite of rank scores (0 through 2) on seven domains of functioning. Participants were ranked in one of three categories for each domain based on their success on the developmental task relative to other participants in the study. This approach was taken to emulate work by Schulenberg et al (2004). Information from each domain was drawn from the Adult Self Report measure (ASR; Achenbach, 2003) and a demographics questionnaire. Thereby, this score includes both objectively verifiable components (e.g., education attainment, annual income) and subjective components (e.g., friendship quality, family involvement).

For the education domain, 25 individuals did not finish high school (however 12 of those received their GED) and were categorized as lower, 16 graduated from high school and were categorized as middle, and 31 pursued further education (18 earned a vocational technical diploma or completed part of a collegiate program, 8 earned an associate's degree, 3 earned a bachelor's degree, and 2 earned a master's degree) and were categorized as upper.

Success in work was based on occupational standing according to the Hauser and Warren Socioeconomic Index (SEI) score that considers earnings, education, and prestige associated
with occupations (1997), and the job satisfaction and confidence scores on the ASR. Scores for the participants' current work and usual work were averaged to create one score. Eighteen were categorized as lower in this domain, including individuals who were

currently unemployed or disabled. Individuals who reported that they were keeping house or in school, or held a job of mediocre occupational standing (e.g., maid, janitor, construction laborer, kitchen worker), or an adaptive functioning job score of < 1.5 (low job satisfaction and confidence) were considered middle rank in this domain. This group contained 36 individuals. Finally, 18 participants who had a relatively high SEI score (e.g., health aide, teacher or teacher's aide, general office clerk, sales worker) and an average ASR job score greater than 1.5 (medium-high job satisfaction and confidence) were considered in the upper rank.

Financial autonomy was based on total family income rank within this sample. The range of family income levels were divided into approximate thirds. Twenty-two individuals were in the lower rank category, which included those earning less than $20k/year. Thirty-one individuals' family income was between $20-40k and were in the middle rank category. Lastly, 19 individuals were in the upper rank category with family earnings of $40-120k. Based on the 2013 Federal Poverty Guidelines, the poverty line is defined as household income of less than $23.5k/year for a family of four (US Department of Health and Human Services, 2013).

Ranking of success in the romantic involvement domain differed from rankings by Schulenberg and colleagues (2004) to reflect the average age of marriage in New York State (28 years of age, as opposed to 26 years, which was used in Schulenberg's ranking). Unmarried and non-cohabiting individuals who were 28 years old or younger were classified as in the middle category. Otherwise, rankings were based on marital status, divorce history, and relationship ratings given on the ASR. To be classified as lower, individuals had to have been divorced more than twice, single and not cohabiting, or in a low-quality marriage (ASR adaptive functioning Spouse/Partner score < 1). This group contained 21 individuals. The middle rank group, which contained 33 individuals, included divorced but remarried participants, unmarried but cohabiting participants, and married but unsatisfied participants (ASR adaptive functioning spouse/partner score = 1-1.5). Eighteen individuals were classified as high rank in the romantic involvement domain, which included individuals who had never been divorced and were currently in a high- quality marriage (ASR average Spouse/Partner satisfaction-related score > 1.5).

For the peer involvement domain, ranking was based on the ASR adaptive functioning friends scale. This scale encompasses quantity of friendships, contact with friends and quality of friendships. Twenty-four participants were low (ASR score < 1.75), 20 participants were middle (score = 1.75 - 2.25), and 28 participants were high (score > 2.25) in this domain.

Family involvement rankings were also based on the ASR report, using the adaptive functioning family scale, which indexes how well one gets along with family members. These scores were averaged across family members that participants reported having contact with (including parents, siblings, and children), as it may actually be adaptive to not have contact with some family members, particularly if maltreatment was perpetrated by a family member. Twenty-seven participants were categorized as low (score < 1.25), while 18 were middle (score = 1.25 - 1.75) and 27 were high (score > 1.75).

The last developmental task domain indexed in this sample was related to substance abuse. Rankings were based on ASR Substance Use Scales for tobacco, alcohol, and drugs. Scores on these three subscales (ranging from 50 to 100) were averaged. The sample was nearly evenly divided into thirds, with 29 individuals ranked as low (score > 66.67), 31 ranked as middle (score = 50 - 66.67), and 28 ranked as high (score = 50).

Chapter 3

General, not emotion-specific, inhibitory control deficits and neural alterations in NSSI

Abstract

Non-suicidal self-injury (NSSI) is often associated with elevated impulsivity. However, findings from behavioral measures of impulsivity are mixed, possibly due to differences in age and NSSI severity across previous studies. Given the role of negative urgency in NSSI etiology, negative mood may be necessary to elicit impulsive behavior in laboratory tasks. Fifty adolescent (M = 15 years) females with a history of NSSI behaviors and 21 comparison adolescents reported on their negative urgency, psychopathology, and NSSI behaviors, and performed a Go/No-Go task in which task-relevant stimuli (letters) were presented at the center of a large task-irrelevant images depicting negative or neutral scenes, while undergoing functional magnetic resonance imaging. The NSSI group reported higher negative urgency, showed poorer performance overall but not specific to emotional condition, and showed greater activation in the dorsal medial prefrontal cortex and the left lingual gyrus when performing the inhibitory control task without emotional distractors. No group differences in brain activation were observed for emotional contrasts on the task. The current study indicates that adolescent girls who engage in NSSI show impaired action restraint, across both emotional and non-emotional conditions, relative to adolescent females who do not engage in NSSI.

Non-suicidal self-injury (NSSI) is the intentional, direct destruction of one's own body tissue without suicidal intent in a manner that is not culturally sanctioned (Nock, 2009), and is included in the DSM-5 "Conditions for Further Study" (American Psychiatric Association, 2013). NSSI is not limited to one class of diagnoses, but occurs among people with a wide range of psychiatric disorders, and in some cases, in those with no disorder (Nock, Joiner, Gordon, Lloyd-Richardson, 2006). NSSI that is categorized as impulsive (as opposed to stereotypic or major/psychosis-related) is characteristically episodic, intermittent, or recurrent self-injury, such as cutting, that is associated with tension release or emotion regulation (Simeon & Favazza, 2001). These behaviors are alarmingly prevalent, with lifetime prevalence of NSSI measured to be about 6%, with about half of those individuals self-injuring five or more times (Klonsky, 2011). Rates in adolescents are higher (i.e., between 13 and 45%; Jacobson & Gould 2007; Lloyd-Richardson, Perrine, Dierker, & Kelley, 2007), with an average age of onset around 16 years old (Klonsky, 2011). Gender differences in rates of NSSI suggest that girls and women are at highest risk (Zetterqvist et al., 2013). Recent research has focused on the characteristics of people who engage in NSSI in an effort to identity potential risk factors.

Nearly four decades ago, "Deliberate Self-Harm Syndrome" was considered an impulse control disorder based on the conceptualization that self-injurers have an inability to resist the impulse, or urge, to injure themselves (Pattison & Kahan, 1983). Impulsivity remains a trait frequently associated with NSSI, and numerous studies utilizing self-report measures have shown a relationship between impulsivity and self-harm. For instance, research has replicated relationships between NSSI and high impulsiveness and low conscientiousness (e.g., Claes, Vandereycken, & Vertommen, 2003; Claes et al., 2010; Hasking, Coric, Swannell, Martin, Thompson, & Frost, 2010; Evans, Platts, Liebenau, 1996; Janis & Nock, 2009; MacLaren & Best, 2010). Repeated self-injury has also been linked to self-reported non-planning impulsivity (Herpertz, Sass, Favazza, 1997), and parent- and self-ratings of lower effortful control (Baetens, Claes, Willem, Muehlenkamp, & Bijttebier, 2011). Overall, this body of literature suggests that individuals who self-injure (and their parents) view themselves as having impaired behavioral control and planning abilities.

A small but growing body of neuroimaging evidence on NSSI and suicidal thoughts and behaviors indicates possible weaknesses in impulse regulation as well as emotion processing (for review, see Domínguez-Baleón, Gutiérrez-Mondragón, Campos-González, & Rentería, 2018; Groschwitz & Plener, 2012; Schmaal, van Harmelen, Chatzi, Lippard, Toenders, …, & Blumberg, 2019). Structural and functional neuroimaging data indicate NSSI and suicidality are associated with alterations in the ventral prefrontal cortex (PFC), dorsal PFC, anterior cingulate cortex, amygdala and insula (Domínguez-Baleón et al., 2018; Groschwitz & Plener, 2012; Schmaal et al., 2019). Further, a few studies have reported that individuals who engage in NSSI exhibit enhanced neural activation in frontal brain regions during emotional, social, and reward processing (Brown et al., 2017; Groschwitz et al., 2016; Osuch, Ford, Wrath, Bartha, & Neufeld, 2014; Plener, Bubalo, Fladung, Ludolph, & Lulé, 2012; Vega, Ripollés, Soto, Torrubia, Ribas, Monreal, …, & Marco-Pallarés, 2018). However, only one prior study has examined brain activation patterns in individuals with NSSI during tasks requiring cognitive control (Dahlgren, Hooley, Best, Sagar, Gonec, & Gruber, 2017). Neural and behavioral measures of interference control (as indexed by the Multi-Source Interference Task) were compared across 15 young adult females with NSSI behaviors and 15 young adult female control participants. Similar to previous research using laboratory tasks designed to assess impulsive behaviors (e.g., Glenn & Klonsky, 2010; Janis & Nock, 2009; McCloskey, Look, Chen, Pajoumand, & Berman, 2012), behavioral results did not corroborate self-reports of elevated impulsivity, as task performance was similar across groups. However, the NSSI group showed increased activation of cingulate cortex and decreased activation of dorsolateral PFC cortex compared to the control group during trials requiring greater cognitive control. The authors interpreted this pattern as indicating that neural compensation may be necessary for those who self-injury in order to complete the task as successfully as healthy controls. The limited neuroimaging data in this population seems to corroborate self- and parent-report of impulsivity, although behavioral measures of impulsive behavior do not align.

There are various factors that could account for the general inconsistency between self-reported and behavioral measures of impulsivity between individuals who do and do not engage in NSSI. First, a large literature demonstrates only a weak relationship between self-report and behavioral measures of impulsivity, perhaps because they tap distinct aspects of the construct (MacKillop, Weafer, Gray, Oshri, Palmar, & de Wit, 2016; Sharma, Markon, & Clark, 2014; Stahl, Voss, Schmitz, Nuszbaum, Tüscher, Lieb, & Klauer, 2014). Self-report measures of impulsivity comprise a heterogenous cluster of lower-level factors, such as impulsivity, sensation seeking, risk taking, novelty seeking, boredom susceptibility, and unorderliness (Depue & Collins, 1999). There are many different measures of impulsivity and they are not highly correlated and do not load onto a single factor (Dick, Smith, Olausson, Mitchell, Leeman, O'Malley, & Sher, 2010). Additionally, when impulsivity is broken down into factors, self-injurers are best distinguished by negative urgency (i.e., the tendency to engage in impulsive behavior under conditions of negative affect; Whiteside, Lynam, Miller, & Reynolds, 2005), as opposed to sensation seeking, low perseverance, or lack of premeditation (Claes & Muehlenkamp, 2013; Davis-Becker, Peterson, & Fischer, 2014; Glenn & Klonsky, 2010; Lynam, Miller, Miller, Bornovalovo, & Lejuez, 2011). A previous study indicated that negative urgency is associated with neural activation in the amygdala and orbital frontal cortex, regions implicated in emotion processing and inhibitory control (Cyders, Dzemidzic, Eiler, Coskunpinar, Karayadi, & Kareken, 2015). Moreover, results from a study that tracked feelings of negative affect, sadness, and guilt as well as urges to engage in NSSI over 14 days revealed that negative urgency and sadness predicted urges to engage in NSSI (Bresin, Carter, & Gordon, 2013). As such, negative mood may be necessary to elicit impulsive behavior in laboratory tasks, given the role of negative urgency in NSSI etiology.

More recent investigations have begun to explore impulsivity within the context of emotion in NSSI samples. Two recent studies used negative mood induction writing procedures in young adult samples to examine the effects of negative mood on performance measures of impulsivity in self-harming individuals (Allen & Hooley, 2017; Lengel, DeShong, & Mullins-Sweatt, 2016). While mood induction increased negative mood in both studies, the NSSI groups did not show impaired task performance in either study (Allen & Hooley, 2017; Lengel et al., 2016). In contrast, individuals who report a history of NSSI showed more difficulty suppressing prepotent responses to images depicting negative content on a modified stop-signal task that uses affective stimuli

(Allen & Hooley, 2015; Allen & Hooley, 2019). In contrast, these same individuals showed no difference in impulsivity during a Go/No-Go task with emotional faces (Allen & Hooley, 2019). Additional studies with larger samples are needed to clarify whether those who engage in NSSI demonstrate impaired inhibitory control generally, in the context of negative emotion, or not at all on laboratory measures. Concurrent neuroimaging measurements may provide insight into potential compensatory brain systems recruited by individuals who engage in NSSI.

The current study aimed to evaluate further whether impulsive reactions are elevated in individuals who engage in NSSI, both generally and in the context of negative emotional distraction. In contrast to the previous work in this area, we focused specifically on adolescents. Also, rather than using task-relevant emotional stimuli that may tap multiple cognitive processes (i.e., regulation of attention, inhibitory control, recognition and interpretation of emotional stimuli) making it difficult to isolate whether inhibitory control is disrupted simply by the presence of emotional content, we measured resistance to impulsive reactions to emotions using a modified Go/No-Go task that incorporates affective picture stimuli as task-irrelevant distractors. Based on prior findings, we expected the NSSI group would report elevated negative urgency, which would relate to more commission errors on trials with negative emotional distractors and elevated orbital frontal and amygdala activation. We predicted that the NSSI group would show no behavioral differences on general inhibitory control, but would show specific deficits in the context of negative emotional stimuli. Further, we predicted that the NSSI group would show increased activation of the anterior cingulate cortex and PFC associated with general inhibitory control, and elevated amygdala activation compared to the control participants during negative emotional distraction.

Methods

Participants

Participants included seventy-one adolescent females ages 12 to 17 years (*M* = 15.08 years, *SD* = 1.16 years) with or without history of NSSI. Overall, 50 participants had engaged in NSSI while 21 participants had never engaged in NSSI. Participants were recruited from clinics and hospital services of the University of Minnesota, Medical Center and Masonic Children's Hospital, by letters and study brochures at local clinics for adolescents with mood disorders, at the Minnesota State Fair Driven to Discover Research Facility, as well as by flyers posted in the community and advertisements posted on Google and social media sites.

All participants provided informed assent, and parents gave consent, in compliance with the University of Minnesota's Institutional Review Board. All participants were compensated for their time. For this study, exclusion criteria included: male sex, being pre-menarche, IQ lower than 80, current or past history of neurological disorders or trauma, known major medical or severe mental illness (i.e., primary psychotic disorder, bipolar spectrum disorder, autism spectrum disorder, current substance use disorder, active suicidality), or MRI contraindications (including pregnancy, claustrophobia, metal in the body, or extreme obesity). Demographic information for the current sample are provided in Table 1.

All participants completed a comprehensive diagnostic assessment conducted by trained clinicians or graduate students under the supervision of a licensed psychologist. Interviews were conducted separately with adolescents and parents for the Kiddie Schedule of Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997). The primary parent/guardian of participants reported perceptions of their child's internalizing and externalizing problems on the Child Behavior Checklist (CBCL; Achenbach, 1991), which includes broad-band psychopathology scales adjusted for age and sex norms. NSSI was measured using the Self-Injurious Thoughts and Behaviors Interview (SITBI; Nock, Holmberg, Photos, & Michel, 2007). The SITBI is a structured clinical interview that assesses the presence and frequency (number of episodes) of NSSI, and has been shown to have strong interrater reliability (average $\kappa = .99$), test–retest reliability across 6 months (average $\kappa =.70$), and convergent validity with respect to other measures of suicide ideation (average $\kappa = .54$) and suicide attempts ($\kappa = .65$; Nock et al., 2007).

Table 1. *Demographics and sample characteristics for adolescents with NSSI and comparison group*

Sample Characteristics	NSSI Group *N* = 50	Comparison Group *N* = 21	*p* Value
Age, *M (SD)*	15.15 (1.09)	14.92 (1.31)	.45
Race, *n* (%)			.71
White	38 (76)	15 (71.4)	
African American	0 (0)	1 (4.8)	
Asian	2 (4)	1 (4.8)	
Native American	2 (4)	0 (0)	
Multiracial	8 (16)	2 (9.5)	
Other	0 (0)	2 (9.5)	
Hispanic, *n* (%)	5 (10)	1 (4.8)	.48
WASI-II IQ, *M* (*SD*)	*N* = 40, 107.85 (8.82)	*N* = 19, 111.89 (8.42)	.10
CBCL Internalizing T-Score, *M* (*SD*)	*N* = 47, 63.96 (9.79)	*N* = 18, 46.67 (8.94)	<.001
CBCL Externalizing T-Score, *M* (*SD*)	*N* = 47, 53.70 (10.92)	*N* = 18, 42.28 (9.49)	<.001

DSM-IV Diagnoses, *n* (%)			
Mood Disorder	Current: 45 (90)	Current: 2 (9.5)	<.001
	Ever: 48 (96)	Ever: 4 (19)	<.001
Anxiety Disorder	Current: 29 (58)	Current: 2 (9.5)	<.001
	Ever: 37 (74)	Ever: 3 (14)	<.001
Attention Deficit/Hyper-	Current: 19 (38)	Current: 2 (9.5)	.02
activity Disorder	Ever: 19 (38)	Ever: 2 (9.5)	.02
Eating Disorder	Current: 7 (14)	Current: 1 (4.8)	.26
	Ever: 8 (16)	Ever: 1 (4.8)	.19
PTSD	Current: 13 (26)	Current: 0 (0)	.04
	Ever: 18 (36)	Ever: 0 (0)	.006
NSSI Frequency			
Past year, range, median, *M* (*SD*)	0 – 300, 5, 18.53 (50.74)		
Lifetime, range, median, *M* (*SD*)	1 – 930, 20, 78.85 (167.76)		
NSSI Method (*N* = 53)			
Cutting, *n* (%)	45 (90)		
Severe scratching, *n* (%)	18 (36)		
Banging/hitting self, *n* (%)	11 (22)		
Interfering with wound , *n* (%)	10 (20)		
Burning, *n* (%)	8 (16)		

Rubbing skin, *n* (%)	7 (14)
Carving, *n* (%)	6 (12)
Pulling hair, *n* (%)	4 (8)
Biting self, *n* (%)	3 (6)
Sticking with needles, *n* (%)	3 (6)
Swallowing substances, *n* (%)	2 (4)
Pinching, *n* (%)	2 (4)

Data from an additional 12 individuals were collected but excluded from the final analysis due to excessive head motion (4 NSSI, 1 comparison), scan failures (2 NSSI, 1 comparison), or missing task data (3 NSSI, 1 comparison). SITBI data were available for 48 participants, and CBCL data were available for 65 participants.

Self-reported impulsivity was measured using the UPPS-P Impulsive Behavior Scale (UPPS-P; Lynam et al., 2006). The UPPS-P is a 59-item inventory to measure of dimensions of impulsivity, with each item rated on a 4-point Likert scale ranging from 1 (strongly agree) to 4 (strongly disagree). Dimensions, or subscales, include negative and positive urgency (i.e., the tendency to engage in impulsive behavior under conditions of negative or positive affect, respectively), (lack of) premeditation (i.e., difficulty thinking and reflecting on the consequences of an act before engaging in the act), (lack of) perseverance (i.e., inability to remain focused on a uninteresting or challenging task), and sensation seeking (i.e., tendency to pursue exciting and potentially dangerous activities). The subscales demonstrate convergent and discriminant validity (Cyders & Smith, 2007; Cyders & Smith, 2008), as well as internal consistency across samples (e.g., Allen & Hooley, 2018; Claes & Muehlenkamp, 2013; Gagnon, Daelman, McDuff, & Kocka, 2013). UPPS-P data were available for 52 participants.

Behavioral fMRI Imaging Paradigm

Participants underwent functional magnetic resonance imaging (fMRI) during performance of an IAPS Go/No-Go task (Cohen-Gilbert & Thomas, 2013). The IAPS Go/No-Go measures the ability to inhibit a dominant response in the context of visual distractors. In this task, letters were presented sequentially in a small box at the center of the screen while negative, positive, neutral or scrambled images were displayed in the background. Participants were instructed to ignore the background images and respond as quickly as possible with a button press to the presentation of every letter (Go stimuli), except the letter X (No-Go stimulus). The letters included H, P, R, S, T, and X. Go stimuli made up 73% of all trials such that participants acquired a prepotent tendency to press and needed to actively inhibit responses during No-Go trials.

Images were selected from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008), a collection of photographs selected to span a wide range of content and emotional valence. One hundred and eighty images were selected for use in this task. One third of the images had highly positive valence ratings, one third had highly negative valence ratings, and one third had neutral ratings near the midpoint of the valence scale. To create an additional emotionally neutral control condition that did not include object information, the selected IAPS images were also scrambled using a 32 x 32 grid.

The task was presented using E-Prime software (Psychological Software Tools Inc., Sharpsburg, PA) while participants were in the MRI scanner. The task included two runs, with trials blocked by stimulus valence within each run. Each run began and ended with a block of 15 scrambled image Go trials followed by a block of rest (fixation cross). Each run also included eight Go/No-Go blocks (two of each background type: negative, positive, neutral, or scrambled), presented in pseudorandom order. Each Go/No-Go block contained 15 trials, each with a unique IAPS image. Background IAPS images covered the entire screen and appeared for 200ms before a small white box containing a black letter appeared in the center of the image for 500ms. This design, with images presented alone prior to presentation of the letter stimulus, was used to make it more difficult for participants to ignore picture content. An inter-stimulus interval of 540ms followed each trial. Participants' responses (press or no press) and reaction times were recorded using a hand-held button box.

Behavioral performance was measured by accuracy on Go and No-Go trials across the four background types, and reaction time on accurate Go trials by background type. An overall measure of behavioral performance was indexed by the sensitivity index, d-prime, by background type. D-prime is the standardized difference between the hit rate (accuracy on Go trials) and false alarm rate (i.e., commission errors on No-Go trials) distributions. Larger values of d-prime indicate that a person has a high hit rate and a low false alarm rate, in other words is performing well on both trial types. To account for situations when participants detect every signal (H = 1.00) and/or make no false alarms (FA = 0.00), we used the loglinear approach (Hautus, 1995) in which we added 0.5 to both the number of hits and the number of false alarms and added 1 to both the number of Go trials and the number of No-Go trials.

fMRI Data Acquisition

Individuals were scanned at the University of Minnesota Center for Magnetic Resonance Research (CMRR) using a Siemens 3 Tesla Prisma scanner (Erlangen, Germany) and a 32- channel radio-frequency (RF) head coil. High-resolution structural data were acquired using the Human Connectome Project (HCP) structural acquisition protocol for each participant using a T_1 weighted multi-echo, MPRAGE sequence (multi echo time [TE] = 1.81, 3.6, 5.39, 7.18 ms, repetition time [TR] = 2500 ms, inversion time [TI] = 1000 ms, flip angle = 8°, , 0.8mm isotropic resolution, 8 minutes) and a T_2 weighted SPACE sequence (TE = 564 ms, TR = 3200 ms, variable flip angle, 0.8mm isotropic resolution, 7 minutes). Two HCP spin echo EPI field map scans (AP and PA phase encode, <1 minute total; (TE = 66 ms, TR = 8000 ms, , flip angle = 90°, 2.0 mm isotropic voxel, 72 interleaved slices) were acquired with voxel parameters matching those of the fMRI task acquisition and were used to correct the fMRI data for the geometric distortion caused by magnetic field inhomogeneity. Functional data were acquired using a multiband echo planar imaging sequence. Whole brain T2*- weighted functional volumes with 2mm isotropic voxel resolution were obtained during the IAPS Go/No-Go task (2 runs, 5 minutes each; TE = 37 ms, TR = 800 ms, multi-band accel. factor = 8, flip angle = 52°, 72 interleaved slices).

fMRI Data Analysis

Preprocessing

We used version 4.01 of the minimal preprocessing pipelines of the Human Connectome Project (HCP) (Glasser, Sotiropoulous, Wilson, Coalson, Tischl, Andersson, …, & Van Essen, 2013) for the structural and functional scans. The HCP minimal processing stream for the structural scans included brain extraction and registration to the Montreal Neurological Institute (MNI) template. The minimal preprocessing pipeline for the functional scans included brain extraction, motion and distortion correction, registration to the subject structural data and the MNI template, and temporal and 2mm of spatial smoothing. Further spatial smoothing using a 4 mm full width at half-maximum Gaussian kernel was then carried in a separate step using the FSL5.0.10 software.

Volumes were censored such that only volumes with absolute head motion less than 1-mm of translation and 1° of rotation between volumes were included in the analysis (Tomasi, Chang, Caparelli, & Ernst, 2007). Participants with motion exceeding threshold in more than 25% of data points (TRs) were excluded from further analyses. Therefore, the final sample of 71 participants each had at least 510 TRs, or 7 minutes 8 seconds, of usable task data.

Task Analysis

Single-subject data were entered into a general linear model using gamma-convolved predictors for the four image-background conditions (negative valence, positive valence, neutral valence, scrambled images), and a predictor for the all-Go trial blocks, with rest blocks serving as the unmarked baseline. An additional predictor of noninterest modeled an unused buffer period (short fixation period at the beginning of the task). Impulsive reactions to negative emotion were indexed via the contrast of negative valence > neutral valence. General inhibitory control without emotional context was indexed via the contrast of scrambled images > all-Go trial blocks.

Group Analysis

Whole-brain mixed effects regression analyses were conducted to assess activation differences between the NSSI and comparison groups, with age as a centered nuisance variable. We used Gaussian random field theory to correct for multiple testing across voxels using a voxel-wise significance threshold of $p < .005$ and a cluster threshold of $p < .05$.

Statistical Analyses

We first conducted independent t-tests or χ^2 tests on demographic variables, general cognitive ability (to confirm group equivalence), and psychopathology (to explore group differences in symptoms). Self-reported impulsivity on the UPPS-P was compared using independent *t*-tests. We also assessed whether negative urgency score related to task performance measures using a repeated measures analyses of variance (ANOVA) with age as a covariate.

Neural activation maps for the Go/No-Go scrambled > All Go scrambled, and for the Go/No-Go negative > Go/No-Go neutral contrasts were probed for group differences using multiple regression in FSL5.0.10 with age as a covariate. Whole-brain mixed effects regression analyses were conducted to assess whether activation was correlated with negative urgency score, including age as a centered nuisance variable. We used Gaussian random field theory to correct for multiple testing across voxels using a voxel-wise significance threshold of $p < .005$ and a cluster threshold of $p < .05$.

Next, we evaluated the performance measures on the IAPS Go/No-Go task. To parallel the imaging contrast of negative vs. neutral valence background conditions, we used 2x2 repeated measures analyses of variance (ANOVA) to test effects of group (NSSI vs. comparison) and emotional background type (negative vs. neutral) on task performance, with age as a covariate. We used SPSS/ PASW 25.0 (SPSS, Chicago, IL) to conduct behavioral analyses.

Results

Group demographics, cognitive ability, and psychopathology

There were no group differences in age, race, ethnicity, or cognitive ability (see Table 1). Age, but not cognitive ability, was positively correlated with sensitivity on the behavioral task (i.e., d-prime) for all background types (*p*'s ranged from .002 to .028) and therefore was included as a covariate in all analyses. As expected, the NSSI group had a significantly higher proportion of members with current or past mood disorders, anxiety disorders, attention deficit/hyperactivity disorder, and post-traumatic stress disorders. There were no group differences for current or past eating disorders. The groups also differed on parent-reported internalizing and externalizing symptoms reported on the CBCL, with the NSSI group having significantly greater levels of symptoms on both dimensions.

Self-reported impulsivity

There were group differences on four of the five subscales on the UPPS-P. The NSSI group reported greater negative urgency [$t(50) = -5.55$, $p < .001$, $M_{\text{NSSI}} = 2.83$,

M_{COMP} = 1.84], positive urgency [$t(50) = -5.15$, $p < .001$, M_{NSSI} = 2.25, M_{COMP} = 1.34], lack of premeditation [$t(50) = -2.45$, $p = .02$, M_{NSSI} = 2.36, M_{COMP} = 1.95], and lack of perseverance [$t(50) = -4.15$, $p < .001$, M_{NSSI} = 2.53, M_{COMP} = 1.91]. Groups did not differ on self-reported sensation seeking ($p > .05$, M_{NSSI} = 2.57, M_{COMP} = 2.55).

IAPS Go/No-Go task performance

The relative effect of background on task performance was similar across the full group; the interaction between background and group was not significant for any measure. There was an overall effect of background valence on d-prime [$F(1,68) = 4.59$, $p = .04$], No-Go performance [$F(1,68) = 5.21$, $p = .03$], and Go RT [$F(1,68) = 12.92$, $p = .001$]. Follow-up analyses indicate that d-prime for the negative background condition was significantly lower than d-prime for neutral backgrounds [$t(70) = -2.37$ $p = .02$]. No-Go accuracy was lower when backgrounds were negative compared to neutral [$t(70) = 2.46$, $p = .02$]. Go trial RT for the negative background condition was significantly longer for negative compared to neutral backgrounds [$t(70) = 3.56$, $p = .001$]. There was a significant main effect of group membership for d-prime [$F(1,68) = 5.63$, $p = .02$], and a marginal effect for No-Go accuracy [$F(1, 68) = 3.17$, $p = .08$]. The comparison group had higher d-prime values (i.e., better overall performance) and marginally greater accuracy for No-Go trials compared to the NSSI group. Group membership did not significantly predict Go reaction times. For averages, see Table 2.

There was no group difference for the effect of negative compared to neutral background on metrics of task performance; that is there were no significant group X background interactions (all *p*'s > .34).

Finally, we examined whether individual differences in negative urgency related to task performance. There was a main effect of negative urgency on Go RT [$F(1,49) = 6.14$, $p = .02$], but not d-prime or No-Go accuracy. The interaction between negative urgency and background valence was not significant [$F(1,49) = 0.86$, $p = .36$].

fMRI task reactivity, group differences, and correlations with negative urgency

To explore neural reactivity in the context of inhibitory control without emotional content, we examined the contrast of scrambled Go/No-Go blocks > allGo trial blocks.

Across the entire sample, this comparison revealed significant activation in multiple brain regions, including the anterior cingulate cortex, bilateral dorsolateral PFC, bilateral inferior parietal regions, dorsal medial cortex, bilateral insula/inferior frontal cortex, bilateral pre-supplementary motor area cortex, intracalcarine cortex, bilateral caudate, and cerebellum. These regions are consistent with meta-analytic findings of fMRI activation associated with Go/No-Go tasks (Simmonds, Pekar, & Mostofsky, 2008).

Group difference analyses indicated greater activation in the dorsal medial PFC and the left lingual gyrus for the NSSI group relative to the comparison group, reflecting differences in inhibitory control (Table 3, Figure 2). There were no other regions that showed significant group differences.

An analysis emotion-related reactivity (negative > neutral background) in the whole sample revealed significant activation in multiple brain regions, including the bilateral amygdala, bilateral inferior frontal gyrus, superior frontal gyrus, medial prefrontal gyrus, bilateral inferior temporal gyrus, precuneus, occipital lobe, and cerebellum (Figure 3). These regions are consistent with those identified in other emotional interference tasks (Hung, Gaillard, Yarmak, & Arsalidou, 2017). There were no group differences in emotion-related reactivity to the task.

Using centered negative urgency score as a continuous predictor, we inspected whether there were any areas of the brain in which task-related activity (NoGo negative > NoGo neutral) related to an individual's level of negative urgency. The left superior parietal lobule (94 voxels, MNI coordinates: -28, -44, 46) showed an interaction with emotion (negative > neutral background) and negative urgency, such that greater activation was observed in those with higher negative urgency scores.

Table 2. *IAPS Go/No-Go task performance for NSSI and comparison groups*

	NSSI Group (n = 50)		Comparison Group (n = 21)	
	Neutral	Negative	Neutral	Negative
D-prime*	2.49 (.76)	2.33 (.88)	2.83 (.56)	2.67 (.53)
Go Acc.	.98 (.04)	.97 (.05)	.99 (.02)	.99 (.01)
No-Go Acc.†	.65 (.21)	.61 (.21)	.72 (.16)	.67 (.16)
Go RT	393 (40)	402 (50)	379 (32)	395 (31)

Acc. = accuracy; RT = reaction time (in milliseconds). Values are given as mean (standard deviation). Main effect of group, * $p < .05$, † $p < .10$.

Table 3. *NSSI and comparison group differences in task-related brain activity for Go/No-Go > all Go (scrambled) image contrast*

Region	Volume, voxels	Z-value max	MNI Coordinates		
			x	y	z
Dorsal medial PFC	164	3.41	0	48	20
Left lingual gyrus	144	3.78	-12	-84	-12

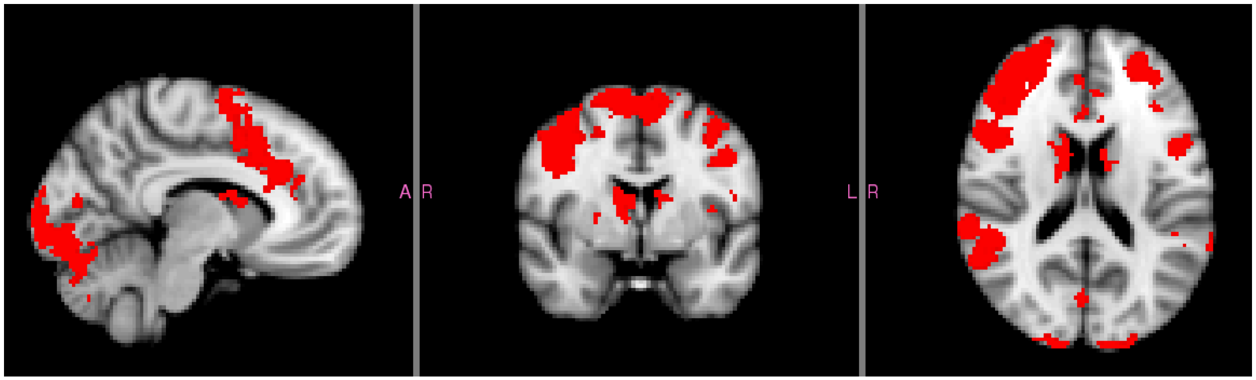

Figure 1. *Neural activation differences for Go/No-Go relative to all Go Scrambled background condition in all adolescents*

Sections show increased activation to Go/No-Go Scrambled background condition relative to all Go Scrambled background condition across the full sample (p <.05 cluster corrected). A, anterior; R, right, L, left.

Figure 2. *NSSI vs. comparison group differences in neural activation for Go/No-Go relative to all Go*

The NSSI group showed greater activity than the comparison group for Go/No-Go > all Go images in two regions (p < .05 cluster corrected).

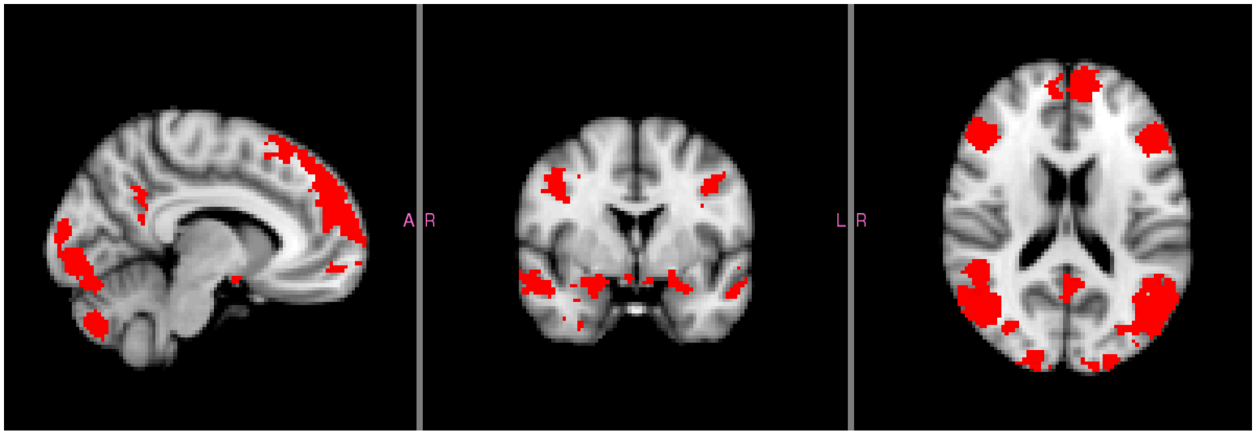

Figure 3. *Neural activation differences Go/No-Go relative to all Go neutral background condition in all adolescents*
Increased activation to Go/No-Go Negative background condition relative to Go/No-Go Neutral background condition across the full sample (p <.05 cluster corrected). A, anterior; R, right, L, left.

Discussion

NSSI has been conceptualized as an impulse control disorder, yet there have been conflicting findings as to whether or not individuals who engage in self-injury demonstrate higher levels of impulsivity in the laboratory, either in general or in the context of negative emotion. Further, this question has been understudied in adolescents, with only two prior behavioral studies of general impulsivity within self-injurers in this developmental stage (Janis & Nock, 2009; Oldershaw, Grima, Jollant, Richards, Simic, …, & Schmidt, 2008), although adolescence is the period with the highest levels of NSSI (Jacobson & Gould 2007; Lloyd-Richardson et al., 2007). The current study indicates that adolescent girls who engage in NSSI report higher levels of impulsivity, demonstrate impaired inhibitory control on a laboratory task, and show altered neural activity while completing the laboratory task relative to adolescent girls who do not engage in NSSI. However, performance on the task was impaired to a similar extent by negative emotional distractor content in adolescent girls who did and did not report engaging in self-harm. The effect of negative emotional interference observed across the full sample was largely consistent with a prior study that used the same behavioral task in a healthy adolescent sample, which reported emotionally negative stimuli impaired No-Go accuracy in girls ages 13 to 14 years, impaired overall performance (i.e., d-prime) in adolescents ages 11 to 14 years, and prolonged RTs on Go trials for 11 to 25 year-olds (Cohen-Gilbert & Thomas, 2013). Results suggest that the NSSI group showed age-typical negative emotional interference, but did not show relatively greater impulsivity within the context of emotion compared to the non-NSSI group nor differences in neural activity in the context of negative relative to neutral content.

The existing literature consistently reports elevated self-reported impulsivity in individuals who engage in NSSI, but prior findings on behavioral measures of impulsivity are more mixed (e.g., Glenn & Klonsky, 2010; Janis & Nock, 2009). Therefore, results from our self-report data were unsurprising and consistent with prior findings of elevated self-reported impulsivity in individuals who engage in NSSI, with specific elevations in urgency, lack of premeditation, and lack of perseverance (Claes & Muehlenkamp, 2013; Glenn & Klonsky, 2010). However, the observed group difference for impulsivity as measured by overall performance on the inhibitory control task is novel.

In fact, prior studies using laboratory tasks designed to assess impulsive behaviors have not corroborated self-reports of elevated impulsivity in NSSI populations. No group differences were found for performance on either response inhibition (i.e., a stop-signal task; Glenn & Klonsky, 2010; continuous performance test; Janis & Nock, 2009; go/no-go task; McCloskey et al., 2012) or risky decision making tasks (i.e., Iowa and Bechara gambling tasks; Janis & Nock, 2009; McCloskey et al., 2012). Further, in the aforementioned studies, self-reported impulsivity did not correlate with behavioral impulsivity measures (Glenn & Klonsky, 2010; Janis & Nock, 2009; McCloskey et al., 2012). Importantly, laboratory tasks used to assess impulsive behavior may not tap into equivalent cognitive mechanisms. The Go/No-Go task which has been shown to measure action restraint and the stop-signal task which has been shown to measure action cancellation recruit widely different neural dynamics (Raud, Westerhausen, Dooley, & Huster, 2020). While McCloskey and colleagues' study was similar to ours in that it used a Go/No-Go task, they financially rewarded superior performance, which may have resulted in confounding effort effects in addition to simultaneous engagement of reward systems of the brain (2012). Therefore, the current study is unique in its assessment of action restraint without reward incentive. As such, results from the current study should be interpreted as indicating that adolescent females who engage in NSSI show impaired action restraint relative to adolescent females who do not engage in NSSI.

Evidence of impulsive behavior in NSSI has been reported in a minority of studies. For example, after accounting for age, Janis and Nock (2009) and Oldershaw and colleagues both found that adolescents who had reported recently engaging in self-harm made more impulsive choices on a decision-making task (Oldershaw et al., 2008). Developmental effects on impulse control may obscure group contrasts when age is not considered statistically. In our sample, age did positively correlate with overall task performance across all emotional background conditions. It is also possible that group differences in impulsive behaviors on laboratory tasks are only observed in adolescents, while previous studies with null effects of group have examined adult samples (Dahlgren et al., 2017; Glenn & Klonsky, 2010; McCloskey et al., 2012).

Of note, NSSI symptoms in the current sample may also be relatively more severe than those in prior samples. Ninety percent of participants had a current mood disorder compared to previous studies examining impulsivity in NSSI samples which report the presence of any psychiatric diagnosis ranging from 34% to 80% (Allen & Hooley, 2015, 2017, 2019, Dahlgren et al., 2017; Glen & Klonsky, 2010; Janis & Nock, 2009; McCloskey et al., 2012). Seventy-five percent of the current NSSI sample reported self-injury in the past year, whereas in previous studies the proportion of adult participants with NSSI episodes in the past year ranged from 17% to 60% (Allen & Hooley, 2015, 2017, 2019, Glen & Klonsky, 2010; Lengel et al., 2016) and the proportion of adolescent participants with NSSI episodes in the past month ranged from 55% to 70% (Janis & Nock, 2009; Oldershaw et al., 2009). Therefore, it is possible that differences in impulsivity are only detectable when NSSI samples report high levels of recent NSSI and have high levels of psychiatric complexity.

As hypothesized, the NSSI group demonstrated increased dorsal medial PFC activation during the cognitive control task relative to comparison participants. These findings are consistent with findings from previous NSSI neuroimaging studies reporting elevated frontal neural activation during emotional processing tasks (Brown & Plener, 2017; Groschwitz, Plener, Groen, Bonenberger, & Abler, 2016; Osuch et al., 2014; Plener et al., 2012). Neuroimaging evidence suggests that the dorsal medial PFC is active during (Buhle, Silvers, Wager, Lopez, Onyemekwu, Kober, & Ochsner, 2013; Rive, Rooijen, Veltman, Mary, Schene, & Ruhé, 2013), mentalizing (Andrews-Hanna, Smallwood, & Spreng, 2014; Wagner, Haxby, & Heatherton, 2012), and self-referential thinking (Meyer & Lieberman, 2018; Northoff, Heinzel, de Greck, Bermpohl, Dobrowolny, & Panksepp, 2006). The elevated activation identified in the dorsal medial PFC had partial overlap with the anterior cingulate cortex, which has been shown to be involved in conflict monitoring (Yeung, 2014) and emotional processing and regulation (Etkin, Egner, & Kalisch, 2011; Ichikawa, Siegle, Jones, Kamishima, Thompson, Gross, & Ohira, 2011). It is possible that the participants with NSSI histories recruited more neural resources for conflict monitoring and were reflecting on their relatively poor performance more than the comparison group while completing the task, and therefore engaging in more self-referential thinking and emotion regulation. Further, a recent study of neural correlates of cognitive control found greater anterior cingulate activation in an NSSI group relative to a control group (Dahlgren et al., 2017).

The NSSI group also activated the lingual gyrus more than the comparison group on the inhibitory control task. The lingual gyrus is involved in identification and recognition of visual stimuli, especially letters (Mechelli, Humphreys, Mayall, Olson, & Price, 2000). Given the target stimuli were letters for this task, it is possible that the NSSI group had to dedicate more neural resources to attend to and track the targets on the inhibitory control task relative to the comparison group. This possibility may further support the conceptualization of NSSI as an impulse control disorder.

Contrary to our predictions, the impact of negative emotional backgrounds during the inhibitory control task did not differ between groups. There were no behavioral or neural differences for the negative > neutral contrast. Our findings are consistent with prior reports of a lack of group differences in performance on an affective Go/No-Go task (Allen & Hooley, 2019). A possible explanation of the lack of group differences may be that self-injurers are only impulsive in certain contexts. People who engage in NSSI typically report doing so as a form of emotion regulation in response to extreme emotional distress (Bentley, Nock, & Barlow, 2014). The negative emotional stimuli used in this task, in addition to the negative mood induction writing procedures used in prior research (Allen & Hooley, 2017; Lengel, DeShong, & Mullins-Sweatt, 2016), may not have been experienced as sufficiently distressing by those in the NSSI group.

Support for this possibility comes from our finding that higher self-reported negative urgency did not relate to more inhibitory control errors in the context of negative emotional distractors, as we had expected it to. Instead, negative urgency was related to overall longer RT on Go trials. Longer reaction times on Go trials have been implicated in impaired vigilance, slowing to compensate for perceived or actual inhibitory deficit, and poor executive control (Wright, Lipszyc, Dupuis, Waran Thayapararajah, & Schachar, 2014). Yet, the relationship between negative urgency and Go RT was not specific to background valence. Therefore, the task may not be sensitive enough to detect individual differences in negative urgency via impaired inhibitory control specifically in the context of the negative emotional distractors. The task-based neural correlates of negative urgency observed suggest that those with elevated negative urgency may have used a compensatory mechanism while performing the task. Adolescents with higher levels of negative urgency showed more activation in the left superior parietal lobule, a region of the brain implicated in attentional control (Scolari, Seidl-Rathkopf, & Kastner, 2016), when employing inhibitory control in the context of emotionally negative distractors. Therefore, perhaps those with elevated negative urgency were able to use additional attentional resources when background images were negative in order to maintain adequate inhibitory control. Prior research has demonstrated similar patterns of compensation in adults with attention-deficit disorders, whom show elevated activity in the parietal cortex alongside typical task performance (Dillo, Göke, Prox-Vagedes, Szycik, Roy, Donnerstag,... & Ohlmeier, 2010). In other contexts outside the laboratory when distractions are more salient and require more emotion regulation and attentional control, these compensatory mechanisms may not be effective. Therefore, laboratory-based behavioral measures may fail to capture the impulsiveness that self-injurers demonstrate in other contexts.

This study makes several important contributions to the existing NSSI literature. First, it is one of only a few studies of impulsivity in adolescents who engage in self-injury, despite adolescence being the period of highest risk for NSSI behaviors. This is the second study to examine neural correlates of impulsivity, and the first to examine the effects of emotional distraction on impulsivity in this population. The sample size and degree of NSSI and psychopathology severity is also unique for a neuroimaging study of this kind. In addition, given the task employed, we were able to examine inhibitory control with and without emotional contexts using a paradigm with task-irrelevant emotional stimuli. This allowed us to examine general inhibitory control as well as the impact of negative emotional distraction on inhibitory control in the same sample.

Despite important contributions to the extant literature, this study has several limitations. While our comparison group is not a healthy control group completely free of psychiatric diagnosis, there were significant group differences in current parent-reported internalizing and externalizing symptoms and diagnoses. Therefore, we cannot conclude that differences in inhibitory control are related solely to NSSI, and not more general psychopathology. In addition, given the inherent constraints of fMRI, we chose to use a block design rather than an event-related design for the IAPS Go/No-Go paradigm.

Therefore, we were unable to compare neural activity on Go and No-Go trials or accurate and inaccurate trials. We also did not assess autonomic arousal, so we were unable to examine individual differences in physiological reactions to the images in the task. As noted above, it is possible that the adolescents in this study did not have strong physiological reactions to the stimuli. Future research should consider level of arousal when studying impulsivity in the context of emotional distractors (Pearlstein, Johnson, Modavi, Peckman, & Carver, 2019) when evaluating the effect of emotional distraction on inhibitory control.

Altogether, our results suggest that adolescent females who engage in NSSI behaviors show impaired action restraint as well as elevated dorsal medial PFC activation relative to adolescent females who do not engage in NSSI. This finding corroborates previously and widely reported differences in impulsivity observed in those who self-injure. However, contrary to our expectations, elevated emotion-related impulsivity in the NSSI group was not observed in behavior or in brain activation. Further research examining emotional contexts that are more clearly arousing or distressing to self-injurers is warranted.

The current study offers clinical implications for NSSI treatment. The NSSI group relative deficit in action restraint, which reflects both processes of attentional control and inhibitory processing, is commonly addressed in evidence-based treatments. Cognitive behavioral therapy and associated treatments (e.g., dialectical behavioral therapy) teach patients to flexibly restructure their thoughts and behaviors away from their automatic maladaptive response to instead represent more adaptive, realistic, or helpful thoughts and behaviors (Mennin & Fresco, 2014). Learning this skill may be particularly difficult for an individual with poor attentional control and inhibitory processing, suggesting that treatment providers need to take extra care to provide patients with ample opportunities to practice this skill. Further, patients should be taught skills to understand and effectively manage emotions and tolerate distress. Interventions should also focus on instilling individuals with confidence in their coping skills (Hasking, Whitlock, Voon, & Rose, 2017). It will be important for intervention programs to specifically target impulse control and planning skills in the context of negative emotions, as negative urgency is a consistent predictor for risky, maladaptive coping, including NSSI.

Chapter 4

Child maltreatment as a risk factor for self-harm: The role of impulsive reactions to emotions

Introduction

Between 13 and 45% of adolescents report engaging in non-suicidal self-injury (NSSI) behaviors (Jacobson and Gould 2007; Lloyd-Richardson, Perrine, Dierker, & Kelley, 2007), including cutting the skin, burning, self-hitting, or ingesting potentially hazardous material (Black & Mildred, 2016). History of childhood maltreatment (CM; e.g., abuse or neglect) has been related to risk for NSSI, with up to 79% of adult self-injurers reporting a history of CM (Gratz et al., 2002; Low, Jones, MacLeod, Power, & Duggan, 2000; van der Kolk et al., 1991; Wiederman et al., 1999). Further, multiple retrospective studies from community and clinical samples have reported strong associations between CM and suicidal behavior (for review, see Miller, Esposito-Smythers, Weismoore, & Renshaw, 2013) and non-suicidal self-injury, especially in females (NSSI; e.g., Boudewyn & Liem, 1995; Lipschitz, Winegar, Hartnick, Foote, & Southwick, 1999). The association between CM and NSSI has been shown to persist even above and beyond the effects of other risk factors for self-injury, including child cognitive ability, socioeconomic status, maternal life stress, parental loss, familial disruption, and childhood exposure to partner violence (Yates, Carlson, & Egeland, 2008; Ystgaard, Hestetun, Loeb, & Mehlum, 2004).

Self-injurers report an elevated tendency to engage in impulsive behavior, especially under conditions of negative affect (Bresin, Carter, & Gordon, 2013; Claes & Muehlenkamp, 2013; Davis-Becker, Peterson, & Fischer, 2014; Glenn & Klonsky, 2010; Lynam, Miller, Miller, Bornovalovo, & Lejuez, 2011). This profile may make it more challenging for individuals to utilize adaptive coping strategies, and therefore resort to use of NSSI, a relatively fast and easily accessible form of emotion regulation (Bentley et al., 2014). It is plausible that the elevated rates of NSSI in CM populations may be due in part to the long-lasting effects of early trauma on emotionality and impulsivity (Braquehais, Oquendo, Baca-Garcia, & Sher, 2010; Brodsky, Oquendo, Ellis, Haas, Malone, & Mann, 2001). At the biological level, effects of CM include high levels of stress hormones that alter neural systems responsible for stress reactivity, self-regulation, impulse control, and planning behavior (Hart & Rubia, 2012; Teicher, Samson, Anderson, & Oshashi, 2016). Neuroimaging studies investigating emotion processing in CM populations have consistently revealed that childhood trauma is linked to heightened neural reactivity to threat-related information (for review, see Hein & Monk, 2016), particularly in the right amygdala (Grant, Cannistraci, Hollon, Gore, & Shelton, 2011; Nooner, Mennes, Brown, Castellanos, Leventhal, Milham, & Colcombe, 2013). Individual differences in threat processing have recently been identified as a transdiagnostic mechanism contributing to the emergence of psychopathology (Weissman, Jenness, Colich, Bryant Miller, Sambrook, Sheridan, & McLaughlin, 2019).

Alongside these findings of elevated emotionality in CM populations, a growing body of research indicates higher levels of behavioral impulsivity on laboratory tasks (e.g., DePrince, Weinzierl, & Combs, 2009; Mezzacappa, Kindlon, & Earls, 2001; Mueller, Maheu, Dozier, Peloso, Mandell, Leibenluft, & … Ernst, 2010; Pollak, Nelson, Schlaak, Roeber, Wewerka, Wiik,... & Gunnar, 2010; Sonuga-Barke & Rubia, 2008) and altered neural activation during cognitive control tasks (Bremner, Vermetten, Vythilingam, Afzal, Schmahl, Elzinga, & Charney, 2004; Herzog, Niedtfeld, Rausch, Thome, Mueller-Engelmann, Steil, ... & Schmahl, 2017; Mackiewicz Seghete, DePrince, Banich, 2018; Mackiewicz Seghete, Kaiser, DePrince, Banich, 2017). However, many individuals demonstrate the capacity for resilient outcomes in one or more domains despite the presence of chronic and severe adversity (Cicchetti, Rogosch, Lynch, & Holt, 1993). A recent study indicates that greater recruitment of PFC control regions and stronger modulation of amygdala reactivity during emotional viewing and reappraisal are protective against psychopathology (e.g., Rodman, Jenness, Weissman, Pine, & McLaughlin, 2019). It remains unknown whether or not individual differences in impulsive reactions to emotions and associated neural activation are also protective against negative impacts of early adversity, and NSSI in particular.

The current study sought to determine whether the relationship between CM and NSSI is moderated by impulsive reactions to emotions and associated neural activation. In a sample of adolescent females who report NSSI behaviors, we measured impulsive reactions in the context of negative emotional distractions while participants underwent functional magnetic resonance imaging. We predicted that better inhibitory control abilities during emotional situations or contexts would mitigate, or reduce, the relationship between CM and NSSI frequency. Further, we predicted that for participants with elevated right amygdala activation during inhibitory control in the context of negative emotional distractions, high levels of CM would correspond with the highest NSSI frequency.

Methods

Participants

Participants included fifty adolescent females ages 12 to 17 years ($M = 15.15$ years, $SD = 1.09$ years) with a history of NSSI. Participants were recruited from clinics and hospital services of the University of Minnesota, Medical Center and Masonic Children's Hospital, by letters and study brochures at local clinics for adolescents with mood disorders, at the Minnesota State Fair Driven to Discover Research Facility, as well as by flyers posted in the community and advertisements posted on Google and social media sites.

All participants provided informed assent, and parents gave consent, in compliance with the University of Minnesota's Institutional Review Board. All participants were compensated for their time. For this study, exclusion criteria included: male sex, being pre-menarche, IQ lower than 80, current or past history of neurological disorders or trauma, known major medical or mental illness (i.e., primary psychotic disorder, bipolar spectrum disorder, autism spectrum disorder, current substance use disorder, active suicidality), or MRI contraindications (including pregnancy, claustrophobia, metal in the body, or extreme obesity). Demographic information for the current sample is provided in Table 1.

All participants completed a comprehensive diagnostic assessment conducted by trained clinicians or graduate students under the supervision of a licensed psychologist. Interviews were conducted separately with adolescents and parents for the Kiddie Schedule of Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997). Primary parent/guardians of participants reported perceptions of their child's internalizing and externalizing problems on the Child

Behavior Checklist (CBCL; Achenbach, 1991), which includes broad-band psychopathology scales adjusted for age and sex norms. NSSI was measured using the Self-Injurious Thoughts and Behaviors Interview (SITBI; Nock, Holmberg, Photos, & Michel, 2007). The SITBI is a structured clinical interview that assesses the presence and frequency (number of episodes), and has been shown to have strong interrater reliability (average κ = .99), test–retest reliability across 6 months (average κ =.70), and convergent validity with respect to other measures of suicide ideation (average κ = .54) and suicide attempt (κ = .65; Nock et al., 2007).

Table 1. *Demographics and sample characteristics for adolescents with NSSI and trauma history*

Sample Characteristics	*N* = 50
Age, *M* (*SD)*	15.15 (1.09)
Race, *n* (%)	
White	38 (76)
African American	0 (0)
Asian	2 (4)
Native American	2 (4)
Multiracial	8 (16)
Other	0 (0)
Hispanic, *n* (%)	5 (10)
WASI-II IQ, *M* (*SD*)	*N* = 40, 107.85 (8.82)
CTQ Total Score, *M* (*SD*)	*N* = 39, 42.49 (15.78)
CBCL Internalizing T-Score, *M* (*SD*)	*N* = 47, 63.96 (9.79)
CBCL Externalizing T-Score, *M* (*SD*)	*N* = 47, 53.70 (10.92)
DSM-IV Diagnoses, *n* (%)	
Mood Disorder	Current: 45 (90)
	Ever: 48 (96)
Anxiety Disorder	Current: 29 (58)
	Ever: 37 (74)
Attention Deficit/Hyperactivity Disorder	Current: 19 (38)

	Ever: 19 (38)
Eating Disorder	Current: 7 (14)
	Ever: 8 (16)
PTSD	Current: 13 (26)
	Ever: 18 (36)
NSSI Frequency	
Past year, range, median, *M* (*SD*)	0 – 300, 5, 18.53 (50.74)
Lifetime, range, median, *M* (*SD*)	1 – 930, 20, 78.85 (167.76)
NSSI Method (*N* = 50)	
Cutting, *n* (%)	45 (90)
Severe scratching, *n* (%)	18 (36)
Banging/hitting self, *n* (%)	11 (22)
Interfering with wound , *n* (%)	10 (20)
Burning, *n* (%)	8 (16)
Rubbing skin, *n* (%)	7 (14)
Carving, *n* (%)	6 (12)
Pulling hair, *n* (%)	4 (8)
Biting self, *n* (%)	3 (6)
Sticking with needles, *n* (%)	3 (6)
Swallowing substances, *n* (%)	2 (4)
Pinching, *n* (%)	2 (4)

Data from an additional 9 individuals were collected but excluded from the final analysis due to excessive head motion (n = 4), scan failures (n = 2), or missing task data (n = 3).

Measure of Maltreatment History

Data on CM status, type, and number of types was collected using the Childhood Trauma Questionnaire (CTQ; Bernstein, Fink, Handelsman, Foote, Lovejoy, Wenzel, … & Ruggiero, 1994). The CTQ is a 28-item self-report measure designed to screen for five types of maltreatment: emotional abuse, emotional neglect, physical abuse, physical neglect and sexual abuse. Each type of trauma is classified as having been absent in that subject's childhood or having had occurred to a low, moderate, or severe extent. Three items screen for false negative reports of maltreatment. Data were available for 39 participants.

Behavioral fMRI Imaging Paradigm, Data Acquisition and Analysis

The same behavioral task (i.e., IAPS Go/No-Go), imaging paradigm, acquisition, and analysis steps were used as Chapter III.

Analytic Plan

Single-subject fMRI data were entered into a general linear model using gamma-convolved predictors for the four image-background conditions (negative valence, positive valence, neutral valence, scrambled images), and a predictor for the all-Go trial blocks, with rest blocks serving as the unmarked baseline. Additional predictors of noninterest included a predictor for an unused buffer period (short fixation period at the beginning of the task). Impulsive reactions in the context of negative emotional distraction were indexed via the contrast of negative valence > neutral valence. Percent signal change of the right amygdala for negative valence > neutral valence conditions was extracted for each participant using FSL's Featquery tool.

Next, we planned to explore whether CM severity and NSSI frequency related to task performance and/or brain activation across all participants, and whether indices of impulsive reactions to emotions moderated the relationship between CM severity and NSSI frequency. We planned to first run multi-subject regression analyses on general behavioral and neural task effects for negative valence > neutral valence conditions, controlling for age. Then, we planned to use a correlation test to assess the relationship between CM severity and NSSI frequency, and to use hierarchical linear regression analyses to investigate whether the interaction term between CM and indices of impulsive reactions to emotions (e.g., d-prime difference score for negative compared to neutral conditions, average Go trial reaction time difference score for negative compared to neutral conditions, right amygdala reactivity to negative compared to neutral conditions) significantly predict NSSI frequency, which would indicate a moderating effect on the relationship between CM and NSSI.

Prior to running these tests, we examined the distribution of CTQ scores and NSSI frequency over the past year to assess whether they met the assumptions associated with linear regression models. In instances when assumptions were not met, we removed outliers and applied appropriate transformations. Next, if assumptions of OLS regression were still not met, non-parametric tests were used. We used SPSS/ PASW 25.0 (SPSS, Chicago, IL) to conduct behavioral analyses.

Results

Prior to exploring relationships in our data, we examined whether our data met the assumptions of linear regression. First, we checked data for outliers. There were two participants who were identified as extreme outliers for NSSI frequency over the past year (absolute *z* values larger than 3). One of these participants was also an outlier for CTQ total score; no other outliers for CTQ total score were identified. Outliers were removed from further analyses.

Next, we tested the data tested for normalcy. Both NSSI frequency over the past year and CTQ total score were non-normal (Kolmogorov-Smirnov *p*'s < .001) and skewed right. To try to address the non-normal distributions, we attempted multiple forms of transformation. Application of square root transformations to both NSSI frequency and CTQ did not result in normalcy for either distribution (Kolmogorov-Smirnov $p = .02$ and .01, respectively). Application of $\log_{10}$ transformations to both NSSI frequency (plus a constant to avoid zero values) and CTQ also did not result in normalcy for either distribution (Kolmogorov-Smirnov $p = .04$ and .01, respectively).

We examined whether CM severity and NSSI frequency related to task indices of impulsive reactions to emotions across all participants using non-parametric correlations. CM severity did not relate to d-prime difference score [*rho*(34) = -.15, *p* = .38], No-Go accuracy difference score [*rho*(34) = -.07, *p* = .70], or Go reaction time difference score [*rho*(34) = .18, *p* = .31]. When the effect of age was controlled for, the relationship was still non-significant for d-prime difference score [*rho*(33) = -.14, *p* = .42], No-Go accuracy difference score [*rho*(33) = -.04, *p* = .80], and Go reaction time difference score [*rho*(33) = .18, *p* = .29]. NSSI frequency over the past year also did not relate to d-prime difference score [*rho*(34) = -.15, *p* = .38], No-Go accuracy difference score [*rho*(34) = -.17, *p* = .32], or Go reaction time difference score [*rho*(34) = .08, *p* = .64]. When the effect of age was controlled for, the relationship was still non-significant for d-prime difference score [*rho*(33) = -.17, *p* = .34], No-Go accuracy difference score [*rho*(33) = -.21, *p* = .24], and Go reaction time difference score [*rho*(33) = .07, *p* = .70].

Given the non-normal distribution of CM severity and NSSI frequency, we were unable to assess whether either variable related to brain activation using standard regression analyses available in neuroimaging software packages. We used non-parametric correlations to examine the relationship between CM severity, NSSI frequency, and extracted right amygdala signal change for negative valence > neutral valence conditions. Amygdala signal change did not relate to CM severity [*rho*(34) = .11, *p* = .54], nor NSSI frequency [*rho*(34) = .14, *p* = .43]. Relationships remained non-significant after accounting for the effect of age [*rho*(33) = .15, *p* = .40; *rho*(33) = .10, *p* = .57, respectively].

Since we were unable to successfully normalize the data distributions, we evaluated whether there was a relationship between NSSI and CM using a non-parametric correlation. Based on prior literature, we expected a positive correlation between NSSI and CM. The relationship was non-significant both when all participants' data were included [*rho*(36)=.15, *p* =.37] and when the outliers were removed [*rho*(34)=.08, *p* =.63]. Given potential developmental effects, we also ran a nonparametric partial correlation, controlling for age. When the effect of age was partialled out, the relationship was still non-significant both when all participants' data were included [*rho*(35)=.17, *p* =.30] and when the outliers were removed [*rho*(33)=.12, *p* =.50].

Given the non-significant correlation between NSSI and CM observed in this dataset, we were unable to test for moderation of the relationship by impulsive reactions to emotions.

Discussion

Based on prior literature, we predicted more severe CM would relate to more frequent NSSI behaviors. We intended to investigate whether impulsive reactions to emotions, indexed by impulsive responses on a Go/No-Go task in the context of negative emotional distraction, augment this relationship. Unfortunately, we were unable to pursue our planned analyses because our data did not reveal a significant relationship between CM and NSSI behaviors. CM and NSSI frequency did not relate to impulsive behavior to emotions; however, this null relationship may have been due to methodological limitations.

It is evident from the extant literature that individuals exposed to CM are more likely to self-injure. However, much of the prior literature on the relationship between CM and NSSI behaviors has focused on whether or not one engages in NSSI behaviors, and has not evaluated the relationship between CM history and frequency of these behaviors (e.g., Glassman, Weierich, Hooley, Deliberto, & Nock, 2007; Swannell, Martin, Page, Hasking, Hzell, Taylor, & Protani, 2012; Whitlock, Eckenrode, & Silverman, 2006; Yates et al., 2008). Further, several studies have indicated that the relationship is only significant when the presence, but not frequency of NSSI, is evaluated (Armey, Nugent, & Crowther, 2012; Gratz & Chapman, 2007; Kaess, Parzer, Mattern, Plener, Bifulco, Resch, & Brunner, 2013). Other research has been mixed. For instance, one prior study suggested a relationship for physical but not sexual abuse and frequency of NSSI (Titelius, Cook, Spas, Orchowski, Kivisto, O'Brien, … & Seymour, 2018), while another reported a relationship for sexual but not physical abuse and frequency of NSSI (Di Pierro, Sarno, Perego, Gallucci, & Madeddu, 2012). Conflicting results may be due to difficulty accurately estimating NSSI frequency and CM exposure.

More recent studies with study designs that may have allowed for more accurate estimates of NSSI frequency and CM exposure have identified significant relationships between CM exposure and elevated NSSI frequency (Auerbach, Kim, Chango, Spiro, Cha, Gold, …, & Nock, 2014; Martin, Raby, Labella, & Roisman, 2017; Titelius et al., 2018). Martin and colleagues prospectively assessed childhood experiences of abuse and neglect (2017). In our sample and in many previous studies, CM has been characterized using retrospective self-report measure, which have been shown to have only slight to fair agreement with prospective caregiver-, research-, and clinician-report of childhood maltreatment (Newbury, Arseneault, Moffitt, Caspi, Danese, Baldwin, & Fisher, 2018). Also, Auerbach' and Titelius' research groups assessed frequency of NSSI behaviors over the past 1 and 6 months, respectively, in inpatient samples (2014; 2018). Reports of NSSI frequency may be more accurate when participants are asked to recall their behavior over a shorter time period and during a period when they are receiving psychiatric monitoring. In contrast, we assessed the relationship between CM and NSSI frequency using an estimate from the past year, as two-thirds of our sample had not reported engaging in self-harm within the past month. Retrospective reporting of behaviors over a long period introduces memory bias. Memory bias may be partially responsible for the skewed and non-normal distribution of NSSI episodes reported in our sample. We may not have been able to detect a relationship between NSSI frequency and impulsive reactions to emotions in this sample because of the biased reporting of NSSI frequency. Researchers are beginning to use ecological momentary assessment methods in studies of NSSI, but primarily have small sample sizes and short assessment periods (for review, see Rodríguez-Blanco, Carballo, & Baca-García, 2018). Future studies should utilize prospective designs, including ecological momentary assessment methods, to more accurately measure maltreatment and NSSI experiences.

Another challenge we faced when measuring NSSI behaviors is that a count of episodes over the past year does not account for variation in severity of episodes. For instance, one individual may have engaged in superficial scratching of the skin on a daily basis, while another individual may have engaged in cutting behavior on several occasions that required medical intervention. It is unknown whether impulsive reactions to emotions are more implicated for frequent but less severe self-injury or for severe forms of self-injury. We were unable to account for both frequency and type of NSSI episode in the current sample; however, future studies with larger samples should examine the influences of both frequency and severity of NSSI behaviors.

Another limitation of the present study is that the sample was not randomly selected, and therefore results cannot be generalized to the broader population of individuals showing NSSI. Participation in the study involves multiple assessment visits, which involved adolescent and care-giver participation, each year for three years in total. It is likely that these study demands may have restricted the sub population who were able to participate, perhaps especially those with higher trauma scores, therefore, reducing the association between CM and NSSI. High-risk individuals are less likely to participate in studies compared to lower-risk individuals due to limited resources and motivation to visit a laboratory on numerous occasions related to high levels of instability and continuing family crises (Kinard, 2001; Reznick, 2013). Adolescents with maltreating caregivers, in particular, may be even less likely to participate in a study that requires both members of the dyad to be involved due to demands on their strained relationship. In our sample, a much lower proportion (i.e. 16%) reported severe maltreatment experiences relative to prior research (Yates et al., 2008). It is likely that we were unable to detect a relationship between CM experiences and impulsive reactions to emotions in this sample because of the limited variability of reported CM. In addition, by excluding actively suicidal adolescents from the study, we could have introduced selection bias that was not present in previous studies of inpatient self-injurers, that showed a positive relationship between CM and NSSI (i.e., Auerbach et al., 2014 & Titelius et al., 2018). It is possible that the relationship is only significant in a more representative sample. Further, it is possible we did not find a relationship between CM and amygdala reactivity for this same reason. A recent assessment of the influence of sample composition on observation of known developmental trajectories in neuroimaging data indicated that non-representative samples, in terms of socioeconomic status, race/ethnicity, and sex, can obscure fundamental neural processes (LeWinn, Sheridan, Keyes, Hamilton, & McLaughlin, 2017). Therefore, future studies with larger and more representative samples are needed.

Together, it is possible we did not find the expected relationships due to the limitations pertaining to accurate measurement of NSSI frequency and severity and also CM exposure in addition to the non-representative sample. While this study is one of the few studies that directly examines impulsivity and its neural underpinnings in adolescents who engage in self-injury, we were unable to determine whether the resistance to engaging in impulsive behavior, especially under conditions of negative affect, is protective against negative impacts of early adversity, and NSSI in particular.

Chapter 5: General Discussion

In this dissertation, I examined developmental risk factors and outcomes associated with impulsive reactions to emotions, and investigated whether resistance to impulsive reactions to emotions may reduce risk for negative impacts of early adversity. By studying two separate samples, I was able to address these research questions in both adolescents and adults, and in relatively psychiatrically healthy individuals and in individuals affected by mental illness. Comparison of results across samples is imperfect given that they differ on multiple dimensions. Nevertheless, the current dissertation addresses several gaps in the literature while also exposing new and outstanding questions that can be addressed in future studies.

Risk factors for impulsive reactions to emotions

Child maltreatment

First, I explored whether the experience of child maltreatment (CM) was related to impulsive reactions to emotions in adults. Contrary to my predictions, inhibitory control in the adults with a history of CM was not affected by the emotional valence of the distractor, whereas the comparison adults showed impaired impulse control in the context of negative distractor images. The decreased impulse control observed in the comparison group was accompanied by increased recruitment of frontal brain regions, including regions associated with inhibitory control (e.g., right interior frontal gyrus). This suggests the possibility that, based on their early experiences, this sample of maltreated adults may have developed more efficient neural systems for maintaining inhibitory control even in the context of negative emotion. Previous studies of adults exposed to early adversity provide some support for this assertion. Schweizer and colleagues showed that the neural underpinnings of emotion regulation in healthy 19-21 year-olds exposed to moderate childhood adversities may be operating more efficiently than in those with low adversity (Schweizer, Walsh, Stretton, Dunn, Goodyet, & Dalgleish, 2016). Our sample is similar to this one in several respects, including the age at study and the relatively low incidence of clinical psychopathology, suggesting that we were studying individuals who were quite resilient in their functioning despite prospectively documented early adversity. In contrast, in samples of psychiatrically ill (i.e., elevated depression and PTSD symptoms) maltreated adults showed greater activation in multiple prefrontal brain regions during emotionally-charged executive function tasks (Herzog, Niedtfeld, Rausch, Thome, Mueller-Engelmann, Steil, ... & Schmahl, 2017; Mackiewicz Seghete, Kaiser, DePrince, Banich, 2017). Together, these studies may indicate that impulse control is not disrupted by negative contexts, despite less recruitment of neural systems typically implicated in inhibitory control, in healthy adults with histories of early adversity and/or abuse. Thereby, the increased ability to regulate emotions while simultaneously avoiding distractions and engaging in goal-directed behavior, underpinned by efficient processing in cognitive-affective neural systems, may foster resilience in adulthood.

I was unable to assess effects of negative contexts on impulse control in resilient *adolescents* exposed to early adversity and/or abuse. In the adolescent sample included in my dissertation, CM experiences were only reported in adolescents who reported NSSI behaviors, and not in the comparison sample. Therefore, I did not have a resilient sample of adolescents to study. It is possible that adolescents who demonstrate resilient functioning despite early adversity may have developed more efficient neural circuits for emotion regulation and have learned to maintain inhibitory control even in negative contexts. However, it is also possible that the development of efficient neural circuitry occurs across adolescence and is therefore only observed in adulthood.

Unfortunately, I was also unable to assess the relationship between CM experiences and neural indices of inhibitory control in psychiatrically ill adolescent females. I could not run a whole-brain regression analysis to examine correlates of reported CM experiences because the distribution was significantly skewed and non-parametric tests are not available in neuroimaging software packages. Nonetheless, non-parametric tests on extracted right amygdala signal change as well as on behavioral indices of inhibitory control from the task indicated that reported CM in adolescents did not relate to inhibitory control in negative contexts. Non-parametric tests also failed to identify a relationship between reported CM experiences and reported NSSI frequency in this sample. Future studies with representative samples and robust measures of NSSI frequency and CM experiences are needed to explore the relationships between CM, inhibitory control in negative contexts, and NSSI in adolescents.

Personality factors

Another potential risk factor for elevated impulsive reactions to emotions that I explored in my dissertation was alexithymia. Previous research has shown that levels of alexithymia positively correlate with the self-reported tendency to react impulsively to negative emotions (Fink, Anestis, Selby, & Joiner, 2010; Gaher, Arens, & Shishido, 2013) and are elevated in people with impulse control disorders (Cruise & Becerra, 2018; Hasking & Claes, 2020; Swannell, Martin, Page, Hasking, Hazell, Taylor, & Protani, 2012; Noël, Saeremans, Kornreich, Bechara, Jaafari, & Fantini-Hauwel, 2018; Pinaquy, Chabrol, Simon, Louvet, & Barbe, 2012). However, results of my dissertation did not reveal a relationship between alexithymia level and impulse control in negative contexts. Nor did my analyses show a relationship between alexithymia level and neural activation for impulse control during negative relative to neutral distraction. However, I did observe a relationship between alexithymia and general impulse control in adolescents reporting NSSI behaviors. Higher alexithymia levels were negatively related to d-prime for all background conditions, Go accuracy for negative, positive, and scrambled conditions, and No-Go accuracy for neutral and positive conditions. That is, those with more difficulty attending to, identifying, and verbally labeling their emotions were less accurate overall regardless of distractor type, had poorer impulse control when distractor images were neutral or positive valence, and had poorer sustained attention when distractor images were negative, positive, or scrambled. Therefore, rather than self-injuring adolescents with high levels of alexithymia appearing to act rashly in response to negative affect, as I had predicted, they appeared more impulsive in the context of emotionally neutral or positive stimuli and less vigilant in the context of non-emotional distractors and emotionally negative and positive distractors. As such, these findings suggest that while one's ability to understand and think about emotions may relate to their impulse control abilities, it does not relate only in the context of emotionally negative stimuli.

In my dissertation, I also explored the personality trait termed negative urgency (i.e., the tendency to engage in impulsive behavior under conditions of negative affect; Whiteside, Lynam, Miller, & Reynolds, 2005). My hypotheses regarding the relationship between self-reported negative urgency and emotional disruption of impulse control on the IAPS Go-No/Go task were not supported by the data. I was surprised by the null relationships because the task was designed to evaluate impulsive behavior under conditions of negative affect. Results suggest that the task and self-report measure may be tapping into different constructs. The task may not have adequately elicited negative affect in the participants. Further research examining physiological arousal during task completion should be conducted to address this possibility.

Outcomes associated with impulsive reactions to emotions

Adaptive Functioning

I was also interested in assessing outcomes associated with impulsive reactions to emotions in my dissertation. In the adult sample, I was able to evaluate whether behavioral and neural indices of impulsive reactions to emotions related to concurrent adaptive functioning (e.g., educational attainment, job status and work performance, and strength of interpersonal relationships). Individuals with higher levels of adaptive functioning had better impulse control on the laboratory task (i.e., higher No-Go accuracy). This effect was consistent with my predictions, as impulse control across various settings can be essential for refraining from maladaptive behaviors including drug use, violence, conflict, and withdrawal. However, this effect was not only observed in the context of negative emotional distractors. This lack of specificity to emotionally negative contexts supports the idea that the negative stimuli in this task were not especially emotionally arousing. This relationship could also reflect the general importance of impulse control for adaptive functioning, across different emotional contexts. At the neural level, adult adaptive functioning was significantly related to task-related activity (negative > neutral) of the right frontal pole and did not relate to amygdala connectivity. Together these data suggest that better overall impulse control as well as greater activation of neural regions involved in monitoring action outcomes (Koechlin, 2011) relates to more adaptive functioning in adults from a high-risk background.

Internalizing and Externalizing Psychopathology

Prior research indicates impulsive reactions to emotions are a core vulnerability to both externalizing and internalizing problems (Johnson, Carver, & Joormann, 2013). Therefore, in my dissertation I examined the relationships between both internalizing and externalizing symptoms and impulsive reactions to emotions, as measured by inhibitory control in the context of emotional distractor images. The results based on the adult sample did not support a relationship between impulsive reactions to emotions and psychopathology. Neither internalizing nor externalizing symptoms in the adults related to any behavioral metric of impulsive reactions to emotions. However, within the adolescent sample, both internalizing and externalizing symptoms related to performance on the Go/No-Go task. High levels of symptoms related to worse task performance (i.e., worse overall performance, lower inhibitory control, and poorer sustained attention). This discrepancy may be related to the differences in psychopathology within the two samples. Of note, the majority of adult participants showed internalizing symptoms (75%) and externalizing symptoms (80%) within the average range. Therefore, it is possible that the restricted range of psychopathology symptoms obscured the true relationship between emotional disruption of cognitive control and psychopathology within this sample, whereas the adolescent sample with a wider range of symptomatology revealed a significant relationship consistent with prior research.

Non-Suicidal Self-Injury

I also sought to determine whether NSSI was a clinical outcome associated with impulsive reactions to emotions in my dissertation. In contrast to the previous work in this area which has focused on adults, I specifically focused on adolescents. Results suggest that adolescent females who engage in NSSI behaviors report elevated impulsivity and show impaired inhibitory control as well as elevated dorsal medial PFC activation relative to adolescent females who do not engage in NSSI. The difference in self-reported impulsivity by those who self-injure corroborates previous findings (e.g., Baetens, Claes, Willem, Muehlenkamp, & Bijttebier, 2011; Janis & Nock, 2009; MacLaren & Best, 2010). However, similar to prior studies (e.g., Glenn & Klonsky, 2010; Janis & Nock, 2009; McCloskey, Look, Chen, Pajoumand, & Berman, 2012) self-reported impulsivity did not correlate with emotion-specific behavioral impulsivity measures. Although self-report data indicate group differences in impulsive reactions to emotions, behavioral data indicate group differences in impulsive reactions overall, and not specifically in negative emotional contexts. The observed difference in behavioral impulsivity, which has not been consistently reported in the literature, may be unique to adolescents with relatively high levels of NSSI and psychiatric complexity. The lack of group differences for impulsive reactions to emotions may be due to the fact that self-injurers are only impulsive in certain contexts. People who engage in NSSI typically report doing so as a form of emotion regulation in response to extreme emotional distress (Bentley, Nock, & Barlow, 2014). Further research examining emotional contexts that are more clearly arousing or distressing to self-injurers is warranted.

Limitations and Future Directions

This dissertation has several limitations related to sample characteristics and task design. First, there was substantial heterogeneity in CM and NSSI, and due to the sample size of each study, I did not have sufficient power to investigate effects of this heterogeneity (e.g., type, frequency, duration of CM and NSSI). Previous research suggests that the timing, subtype, severity, frequency, and chronicity of CM can have unique predictive power (Cowell, Cicchetti, Rogosch, & Toth, 2015; Manly, Cicchetti, & Barnett, 1994), as can NSSI onset and chronicity (Riley, Combs, Jordan, & Smith, 2015). CM and NSSI populations are difficult to recruit and maintain in research studies for numerous reasons including inability to locate families that have high levels of instability and continuing family crises (Kinard, 2001). Families affected by adversity and CM may be particularly less likely to participate in longitudinal studies with multiple visits (which describes both of the larger studies from which my dissertation data was drawn) due to limited resources for traveling to the laboratory and demands on their strained relationships (Reznick, 2013).

Second, the adult sample may represent a resilient and not necessarily representative subset of maltreated individuals. Although this sample was drawn from a larger longitudinal study, which was representative of the community it was drawn from, the adults who participated in this phase of the research as adults may be higher functioning and less psychiatrically ill than the individuals who did not participate in this phase. Internalizing and externalizing symptoms were in the broad average range for 90% of the current sample, whereas 55% of adults with abuse histories have psychiatric disorder according to evidence from a community sample (Collishaw, Pickles, Messer, Rutter, Shearer, & Maughan, 2007).

Next, the adolescent sample examined in this dissertation may also be subject to selection bias, as the sampling was not random. Compared with a prospective, community sample, the reported incidence of CM was much lower than expected in our sample (Yates, Carlson, Egeland, 2008). Therefore, we cannot conclude that CM would not relate to impulsive reactions to emotions or to NSSI in a more representative sample. Future research of this kind should take care to use random sampling or match participants with and without maltreatment experiences as closely as possible on other pertinent measures. Finally, these samples had only one time point of impulsivity data available. Therefore, we cannot conclude whether impulsive reactions to emotions act as a risk factor or outcome for CM and NSSI. To better understand the developmental patterns and influences on impulse control during emotional contexts, longitudinal research with prospective measurement of adversity, psychopathology and adaptive functioning is needed, including neural and behavioral markers of impulse control in the context of emotional distraction.

While the behavior task used here afforded us the ability to compare inhibitory control in different emotional contexts, it had several limitations. First, because we used a task design that is unique compared to other tasks used to assess the impact of emotional stimuli on inhibitory control/impulsivity, we cannot directly compare results to those of others studies. In the majority of the extant work in this area, emotional stimuli are central to task (e.g.., emotional Stroop tasks, affective Go/No-Go tasks, modified stop-signal tasks), rather than included as background distractions. As such, performance reflects a variety of cognitive (i.e., regulation of attention, inhibitory control) and emotional processes (i.e., recognition and interpretation of emotional stimuli) simultaneously. In contrast, the task used in this dissertation was specifically designed to assess individual differences in disruption of goal-directed behavior by emotional distraction. A standard inhibitory control task was overlaid on top of emotionally salient images that were task irrelevant. In addition, the task design did not afford a comparison of behavioral and neural responses to negative contexts with and without impulse control demands. That is, due to the block-design nature of the task, neural activation to Go compared to No-Go trials was not possible, and the participants did not view or respond to negative emotional stimuli when not implementing inhibitory control. Rather than using a lengthy event-related fMRI task that would allow for this type of comparison, the researchers who created this task chose to maximize valuable data while minimizing participant fatigue. As such, the neural responses that were shown to differ in adults with and without CM histories and relate to negative urgency in adolescents could reflect a general bias to negative information rather than something specific about inhibitory control. However, given the behavioral differences between emotional background conditions on the No-Go trials, but no Go trials, we are assured that the task is measuring impulsive reactions to emotions. Finally, the negative images used in the task included sad, disgust, anger and fear content. Some research suggests that these different types of emotionally negative stimuli may have consistent and discrete neural correlates across studies (Vytal, & Hamann, 2010). Moreover, in adolescent NSSI samples, social exclusion and rejection seem to be particularly emotionally salient (e.g., Esposito, Bacchini, & Affuso, 2019; Groschwitz, Plener, Groen, Bonenberger, & Abler, 2016) and may therefore serve as a more ecologically emotional context when studying impulse control in this population.

Implications

This study was motivated by the ultimate goal to inform the design of treatment and intervention programs by providing a clearer understanding of the risk factors for and clinical correlates of impulsive reactions to emotions. Results provide evidence that greater control over impulsive reactions in the context of emotional and neutral stimuli relates to better current adaptive functioning in adults and lower levels of reported internalizing and externalizing symptoms in adolescents. In addition, general inhibitory control deficits were observed in adolescents with NSSI. Therefore, results support the dissemination and further development of intervention programs that specifically target impulse control in vulnerable populations.

Our neuroimaging results suggested that resilient, maltreated adults may have efficient neural systems for maintaining inhibitory control even in the context of negative emotion. Previous research has posited that adults who were abused as children may experience higher rates of emotional, mental, and physical health problems due to their difficulty regulating emotions while simultaneously engaging in goal-directed behavior, underpinned by a lack of flexible coordination in cognitive-affective brain circuits (Caldwell, Krug, Carter, & Minzenberg, 2014). Intervention research in this area will be valuable in determining if these neural and cognitive response patterns are malleable and if emotion regulation and attention training can reduce risk for emotional, mental, and physical health problems in individuals exposed to CM.

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Appendix 1: Study 1

For my dissertation, I proposed the following hypotheses and planned analyses that are not included in the written paper because they were not supported. For reference, IAPS Go/No-Go task data is summarized below.

	CM Group (n = 38)			
	Neutral	Negative	Positive	Scrambled
D-prime	2.52 (.83)	2.54 (.96)	2.62 (.85)	2.52 (.96)
Go Acc.	.96 (.07)	.95 (.07)	.96 (.08)	.95 (.08)
No-Go Acc.	.77 (.15)	.80 (.15)	.80 (.16)	.79 (.14)
Go RT	426 (42)	442 (38)	423 (39)	414 (34)

	Comparison Group (n = 34)			
	Neutral	Negative	Positive	Scrambled
D-prime	2.31 (1.05)	2.08 (.90)	2.37 (1.02)	2.39 (1.05)
Go Acc.	.91 (.12)	.91 (.12)	0.92 (.12)	.91 (.12)
No-Go Acc.	.78 (.19)	.72 (.20)	.76 (.20)	.78 (.20)
Go RT	408 (40)	424 (43)	412 (38)	402 (36)

1) I tested for group differences (child maltreatment [CM] vs. comparison) in amygdala activation during the IAPS Go-NoGo task (negative > neutral background contrast) using a general linear model within FSL software.
    a. Region of interest analyses probing the right and left amygdala failed to detect significant group differences in reactivity for the negative vs. neutral contrast (Right: $t(70)=-.367$, $p=.715$; Left: $t(70)=.002$, $p=.998$). My hypotheses regarding group differences in amygdala activity were not supported by the data.

2) I examined whether emotional disruption of cognitive control moderated the relationship between CM and internalizing symptoms using hierarchical multiple regression analysis. In the first step, centered CM status and the centered impulsive reactions to emotions index were used to predict internalizing symptoms (including age and sex as covariates). In the second step, the interaction term between CM and impulsive reactions to emotions was added to the regression model. Multiple models were run to test the separate indices of impulsive reactions to emotions (d-prime difference score, No-Go accuracy

difference score, Go reaction time difference score, neural reactivity mean contrast values, PPI extracted values).

   a. Results indicated that internalizing symptoms were not predicted by d-prime difference score nor its interaction with maltreatment history, No-Go accuracy difference score nor its interaction with maltreatment history, Go reaction time difference score nor its interaction with maltreatment history, neural reactivity mean contrast values nor their interactions with maltreatment history, the frontolimbic PPI extracted value nor its interaction with maltreatment history. My hypotheses were not supported by the data. Of note, internalizing symptoms (as measured by the ASR) were within the average range for 75% of participants. Therefore, it is possible that the restricted range of internalizing symptoms obscured any relationship between emotional disruption of cognitive control, CM history, and developmental outcomes.

3) I also examined whether emotional disruption of cognitive control moderated the relationship between CM and externalizing symptoms using hierarchical multiple regression analysis. In the first step, centered CM status and the centered impulsive reactions to emotions index were used to predict externalizing symptoms (including age and sex as covariates). In the second step, the interaction term between CM and impulsive reactions to emotions was added to the regression model. Multiple models were run to test the separate indices of impulsive reactions to emotions (d-prime difference score, No-Go accuracy difference score, Go reaction time difference score, medial prefrontal and amygdala neural reactivity, PPI extracted values).
   a. Externalizing symptoms were not predicted by d-prime difference score nor its interaction with maltreatment history, No-Go accuracy difference score, reaction time difference score nor its interaction with maltreatment history. My hypotheses were not supported by the behavioral data. Of note, externalizing symptoms (as measured by the ASR) were within the average range for 80% of participants. Therefore, it is possible that the restricted range of externalizing symptoms obscured any relationship between emotional disruption of cognitive control, CM history, and developmental outcomes.
   b. Externalizing symptoms were not predicted by prefrontal neural reactivity nor its interactions with maltreatment history, the frontolimbic PPI extracted value nor its interaction with maltreatment history.
   c. However, neural signal extracted from the right amygdala for the contrast of interest (i.e., negative > neutral) predicted externalizing symptoms ($F(4,67) = 3.38$, $p = .014$; Table 1), such that greater amygdala activation to negative distractors was associated with lower externalizing symptoms. Right amygdala activation did not moderate the relationship between CM and externalizing symptoms.
   d. Left amygdala activation did not predict externalizing symptoms.

Table 1
Summary of Hierarchical Regression Analysis for Variables Predicting Externalizing Symptoms (N = 72)

	Model 1		
Variable	*B*	*SE B*	Beta
Age	-0.17	0.35	-0.06
Sex	-2.75	2.44	-0.13
Maltreatment Status	1.74	2.48	0.81
R. amygdala	-5.52	1.57	-0.39**
R^2		.17	
F for model		3.38*	

Note. All variables were centered at their means.
*$p < .05$. ** $p < .01$.

4) To test whether emotional disruption of cognitive control moderated the relationship between CM and adult adaptive functioning, I used hierarchical multiple regression analysis. In the first step, centered CM status and the centered impulsive reactions to emotions index were used to predict adult adaptive functioning (including age and sex as covariates). In the second step, the interaction term between CM and impulsive reactions to emotions was added to the regression model. Multiple models were run to test the separate impulsive reactions to emotions indices (d-prime difference score, No-Go accuracy difference score, Go reaction time difference score, medial prefrontal and amygdala neural reactivity, PPI extracted values).
    a. Adult adaptive functioning was not predicted by d-prime difference score nor its interaction with maltreatment history, No-Go accuracy difference score nor its interaction with maltreatment history, Go reaction time difference score nor its interaction with maltreatment history. My hypothesis was not supported by the behavioral task data.
    b. Adult adaptive functioning was not predicted by medial prefrontal activation nor amygdala activation, nor their interactions with maltreatment group.

Appendix II: Studies 2 and 3

For my dissertation, I proposed the following hypotheses and planned analyses that are not included in the written paper because they were not supported. For reference, IAPS Go/No-Go task data is summarized below.

	NSSI Group (n = 50)			
	Neutral	Negative	Positive	Scrambled
D-prime*	2.49 (.76)	2.33 (.88)	2.49 (.86)	2.53 (.85)
Go Acc.*	.98 (.04)	.97 (.05)	.98 (.04)	.97 (.05)
No-Go Acc.*	.65 (.21)	.61 (.21)	.66 (.19)	.68 (.19)
Go RT	393 (40)	402 (50)	391 (38)	371 (45)
	Comparison Group (n = 21)			
	Neutral	Negative	Positive	Scrambled
D-prime*	2.83 (.56)	2.67 (.53)	2.94 (.56)	3.04 (.70)
Go Acc.*	.99 (.02)	.99 (.01)	1.00 (.00)	.99 (.01)
No-Go Acc.*	.72 (.16)	.67 (.16)	.73 (.16)	.77 (.19)
Go RT	379 (32)	395 (31)	381 (32)	264 (29)

1) I tested for group differences (NSSI vs. comparison) in PPI connectivity for the negative > neutral contrast.
    a. No regions that showed task-based connectivity with the right amygdala survived statistical thresholding across the entire sample of subjects, and no regions that showed group differences in task-based connectivity with the right amygdala survived statistical thresholding. These results did not support my prediction that the NSSI group would exhibit less negative connectivity between the prefrontal cortex and amygdala than the comparison group for the negative > neutral contrast.
2) I examined whether measures of emotional disruption of cognitive processes related to alexithymia. Several regression models were run to test the separate indices of impulsive reactions to emotions (*d'* difference score, No-Go accuracy difference score, Go reaction time difference score, neural reactivity mean contrast values).
    a. Regressions revealed no significant relationships between alexithymia and d-prime difference score (negative – neutral)(R^2=.01, F(2,48)=0.13, p =.88), the No-Go accuracy difference score (negative – neutral) (R^2=.04,

$F(2,48)=1.02$, $p = .37$), or the Go reaction time difference score (negative – neutral) ($R^2=.02$, $F(2,48)=0.39$, $p = .68$). Alexithymia also did not relate to neural activation (neg > neu) in any areas of the brain that survived cluster-wise and voxel-wise thresholding. My hypotheses regarding the relationship between alexithymia and emotional disruption of inhibitory control on the IAPS Go-No/Go task were not supported by the data.

b. Of note, in the NSSI group, alexithymia was significantly and negatively related to d-prime for all background conditions, to Go accuracy for negative, positive, and scrambled conditions, and to No-Go accuracy for neutral and positive conditions.

3) I examined whether emotional disruption of cognitive processes related to negative urgency using regression analysis. Multiple models were run to test the separate indices of impulsive reactions to emotions (*d'* difference score, No-Go accuracy difference score, Go reaction time difference score, neural reactivity mean contrast values).
    a. Regressions revealed no significant relationships between negative urgency and d-prime difference score (negative – neutral) ($R^2=.02$, $F(2,49)=0.60$ $p = .55$), the No-Go accuracy difference score (negative – neutral) ($R^2=.02$, $F(2,49)=0.57$, $p = .57$), or the Go reaction time difference score (negative – neutral) ($R^2=.01$, $F(2,49)=0.20$, $p = .86$). My hypotheses regarding the relationship between self-reported negative urgency and emotional disruption of inhibitory control on the IAPS Go-No/Go task were not supported by the data.

4) I also examined whether emotional disruption of cognitive control moderated the relationship between CM and internalizing symptoms using hierarchical multiple regression analysis. Because CM was not normally distributed and skew was not corrected with transformation, I created a median-split variable (high vs. low CTQ score). In the first step, CTQ score and the centered impulsive reactions to emotions index were used to predict internalizing symptoms (including age as covariates). In the second step, the interaction term between CTQ and impulsive reactions to emotions was added to the regression model. Multiple models were run to test the separate indices of impulsive reactions to emotions (*d'* difference score, No-Go accuracy difference score, Go reaction time difference score, right amygdala activation).
    a. Internalizing symptoms were not predicted by d-prime difference score nor its interaction with CTQ score, No-Go accuracy difference score nor its interaction with CTQ score, Go reaction time difference score nor its interaction with CTQ score, nor right amygdala activation nor its interaction with CTQ score. My hypothesis was not supported by the data.
    b. Of note, internalizing symptoms related to average Go accuracy [$r(59) = -.29$, $p = .02$], No-Go accuracy [$r(59) = -.31$, $p = .02$], and d-prime [$r(59) = -.39$, $p = .002$] across the full sample, when controlling for age. Within the NSSI sample, externalizing related to d-prime [$r(43) = -.29$, $p = .05$], when controlling for age.

5) I also examined whether emotional disruption of cognitive control moderates the relationship between CM and externalizing symptoms using hierarchical multiple regression analysis. Because CM was not normally distributed and skew was not corrected with transformation, I created a median-split variable (high vs. low CTQ score). In the first step, CTQ and the centered impulsive reactions to emotions index were used to predict externalizing symptoms (including age as covariates). In the second step, the interaction term between CTQ and impulsive reactions to emotions was added to the regression model. Multiple models were run to test the separate impulsive reactions to emotions indices (*d'* difference score, No-Go accuracy difference score, Go reaction time difference score, right amygdala activation).
    a. Externalizing symptoms were not predicted by d-prime difference score nor its interaction with CTQ score, No-Go accuracy difference score nor its interaction with CTQ score, Go reaction time difference score nor its interaction with CTQ score, nor right amygdala activation nor its interaction with CTQ score. My hypothesis was not supported by the data.
    b. Of note, externalizing symptoms related to average Go accuracy [$r(59) = -.27$, $p = .04$], No-Go accuracy [$r(59) = -.27$, $p = .04$], and d-prime [$r(59) = -.32$, $p = .01$] across the full sample, when controlling for age. Within the NSSI sample, externalizing related to No-Go accuracy [$r(43) = -.32$, $p = .03$] and d-prime [$r(43) = -.29$, $p = .05$], when controlling for age.