CHILDHOOD MALTREATMENT AND MECHANISMS OF VULNERABILITY WITHIN ANHEDONIA AND DEPRESSION

by

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Abstract

Anhedonia is one of the defining features of Major Depressive Disorder (MDD), and may be characteristic of an especially severe depression. Because MDD is highly heterogeneous, anhedonia may represent an easier target for research on how childhood maltreatment is associated with MDD and anhedonia and on the underlying mechanisms of dysfunction within this disorder. The goal of the current study is to test the hypothesis that the association between childhood maltreatment and anhedonia is mediated by two endophenotypes: (a) blunted neuroendocrine response to stress, and (b) blunted responsivity to reward. Further, consistent with the related neurobiological underpinnings of threat and reward systems, we hypothesize that in our full sample, individual differences in stress reactivity will be correlated with individual differences in reward responsivity. The current study includes 89 adults (39 with MDD, 47 non-depressed) who were well-characterized in terms of their diagnostic and symptom profiles, and who participated in a laboratory stress challenge (the Trier Social Stress Task; TSST) and a computerized Probabilistic Reward Task (PRT). Our hypothesized mediation model was not supported by the results. However, I did find that blunted reward learning was correlated with blunted stress reactivity. Further, different forms of childhood maltreatment were preferentially associated with different symptoms of anhedonia. Contrary to hypotheses, I also found that within the depressed group, childhood maltreatment, depression severity, and anhedonia were positively correlated with response bias on the PRT. Also contrary to hypotheses, within the depressed group stress reactivity was positively associated with anhedonic symptoms, although these results were not statistically significant. Although our overall model was not supported by the results, my findings suggest that reward responsivity, stress reactivity, and anhedonia remain important research targets in understanding the etiology of MDD. These findings also help to shed light on the negative outcomes associated with childhood maltreatment.
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List of Abbreviations

ACTH................................................................................................. Adrenocorticotrophic hormone
AUCi................................................................................................. Area under the curve relative to increase
AVP........................................................................................................ Vasopressin
CECA................................................................................................. Childhood Experiences of Care and Abuse scale
CRF........................................................................................................ Andrenocorticotrophic hormone-releasing factor
DSM................................................................................................. Diagnostic and Statistic Manual of Mental Disorders
DST................................................................................................. Dexamethasone Supression Test
HPA................................................................................................. Hypothalamic-pituitary adrenal
MADRS.............................................................................................. Montgomery-Asberg Depression Rating Scale
MASQ................................................................................................. Mood and Anxiety Symptom Questionnaire
MASQ AA........................................................................................ MASQ Anxious Arousal scale
MASQ AD......................................................................................... MASQ Anhedonic Depression scale
MASQ GD......................................................................................... MASQ General Distress scale
MDD................................................................................................. Major Depressive Disorder
PRT................................................................................................. Probabilistic Reward Task
RDoC................................................................................................. Research Domain Criteria
SHAPS.............................................................................................. Snaith-Hamilton Pleasure Scale
TSST................................................................................................. Trier Social Stress Task
Chapter 1

Introduction

Major depressive disorder (MDD) is a common and burdensome condition in Canada (Patten et al., 2015). Recent epidemiological research has indicated that the point prevalence of a current MDD episode in Canada is about 3.9 percent, with higher rates among females and younger age groups (Patten et al., 2015). Lifetime prevalence of this devastating disorder is even higher, at an estimated 9.9 percent, when excluding individuals with other mood disorders such as bipolar disorder (Patten et al., 2015). Depression is one of the leading causes of disability worldwide, and the second-leading contributor to the global burden of disease (World Health Organization, 2008). Every year in Canada, 6.6 percent of individuals with current MDD attempt suicide, and 16.6 percent of individuals with a history of MDD will attempt suicide at some point in their lives (Patten et al., 2015). Individuals with a history of depression are also at significantly greater risk for a variety of physical health problems such as cardiovascular disease, cancer, and disrupted immune functioning (Lahey, 2009, Mroczek, Spiro, & Turiano, 2009, Park et al., 2013). The burden that depression places on the North American healthcare system is about 60 billion dollars per year, and much of that is due to lost productivity in the workplace (Wilson, Joffe, & Wilkerson, 2000). Approximately 60 to 90 percent of individuals who have one episode of depression will have future episodes (APA, 2000), meaning this condition is often chronic and is debilitating throughout a person’s lifetime. Therefore, etiological research is important in order to gain a more complete understanding of the development of this disorder, which is expected to lead to the development of more effective and targeted treatments in the future.

The syndromal presentation of MDD varies a great deal among individuals, which can give rise to difficulties in clarifying its underlying etiology, as well as in providing effective treatment. More
specifically, the diagnostic category of MDD from the Diagnostic and Statistic Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013), which is based on clinical consensus, may fail to capture key underlying mechanisms of dysfunction, and the boundaries of this category, and diagnostic categories in general, tend to not be predictive of recovery and treatment response (Insel et al., 2010). Therefore, the Research Domain Criteria (RDoC) were developed to focus instead on transdiagnostic domains of functioning that can be measured objectively and that have clear neurobiological targets (Insel et al., 2010; Cuthbert & Kozak, 2013). The RDoC framework relies on three important assumptions (Insel et al., 2010). First, psychopathology is conceptualized as brain disorders and can be addressed as disorders of brain circuits. Second, it is assumed that neural circuitry dysfunction can be identified and measured objectively. Third, it is assumed that data gathered from these measures will be associated with specific biosignatures that will be supplemental to clinical symptoms and signs (Insel et al., 2010).

An example of a domain of functioning with critical relevance to MDD is anhedonia. Anhedonia, one of two core features of MDD, has been generally defined as a decrease in the ability to experience pleasure and joy in the presence of stimuli that normally elicit these responses (Fawcett et al., 1983; Agrawal et al., 2012). Clinically, anhedonia is assessed with symptom measures that include items that tap into this definition (e.g., “Felt like nothing was enjoyable;” “Did not look forward to things with enjoyment;” “Did not enjoy spending time with family and close friends”). Anhedonia is not necessary for a diagnosis of MDD, however, and approximately 70% of MDD patients meet criteria for this symptom (Buchwald & Rudick-Davis, 1993). The presence of anhedonia has been recognized as being indicative of a more severe form of the disorder (Rush et al., 1994, Agrawal et al., 2012). Therefore, the homogeneity of anhedonia makes it a more powerful construct when investigating the etiological mechanisms that may be relevant to MDD as a whole.
The overarching goal of the current study was to examine the role of two mediating endophenotypes – responsivity to reward and sensitivity to stress – that may underlie anhedonia in individuals with and without a diagnosis of MDD. The term ‘endophenotype’ refers to biological traits or behavioural symptoms of a disorder that have a genetic connection. The model that I tested is provided in Figure 1. Specifically, I predicted that blunted reward responsivity and blunted stress reactivity would be correlated with one another, and both would be associated with higher levels of clinically-defined anhedonia. I also expected both to be related to a history of childhood maltreatment, and to mediate the relation of maltreatment to heightened anhedonia.

Figure 1. The mediating role of stress reactivity and reward responsivity on the relation between each type of childhood maltreatment and anhedonia symptoms in individuals with MDD and controls.

Childhood maltreatment encompasses experiences of emotional maltreatment (e.g., rejection, teasing, degradation, terrorization, isolation, neglect), physical maltreatment (e.g., pushing, slapping, hitting), and sexual maltreatment (any unwanted sexual experiences) that occurred prior to age 18. Epidemiological studies have confirmed that individuals with a history of childhood maltreatment are three to four times more likely to develop depression at some point in their lifetime than those without (MacMillan et al., 2009). Further, individuals with a history of childhood maltreatment are significantly
more likely to be diagnosed with the ‘endogenous’ subtype of depression, which is characterized primarily by severe anhedonia, than those without (Harkness & Monroe, 2002). Additionally, non-depressed individuals who have experienced childhood maltreatment and stress display more anhedonic symptoms than those without (Dillon et al., 2009). The specific mechanisms that translate a history of childhood maltreatment to MDD have received empirical attention (e.g., Li, D’ARcy, & Meng, 2016; Bassani, Antypa, & Serretti, 2013); however, the heterogeneity of MDD can give rise to difficulties in attempting to clarify the precise etiological role of childhood maltreatment, and it is possible that different symptom clusters within MDD may have different etiologies (Rush et al., 2006). Defining anhedonia as the outcome may help in focusing research, as its comparative homogeneity provides an easier target than MDD as a whole for clarifying the etiological role of childhood maltreatment in this disorder (Agrawal et al., 2012; Pizzagalli et al., 2007; Bogdan & Pizzagalli, 2006).
Chapter 2

Literature Review

Endophenotypes in Anhedonia

The RDoC framework proposes five main domains of functioning: Positive Valence Systems, Negative Valence Systems, Cognitive Systems, Systems for Social Processes, and Arousal/Regulatory Systems. Each domain encompasses other lower-order constructs, including reward processing (within Positive Valence Systems) and threat processing (within Negative Valence Systems). Reward processing includes the value that an individual places on a reward, their perceived probability of obtaining a reward, and the mechanisms that underlie their response to goal relevant cues or to receiving a reward. Threat processing includes reactivity to potential stressors, acute stressors, and sustained stressors.

It has been proposed that within MDD, two main RDoC constructs may act as mediators and partially account for the relation between childhood maltreatment and anhedonia: (1) blunted reward responsivity and (2) blunted stress reactivity (Monroe & Harkness, 2005; Pizzagalli et al., 2005; Vrieze & Claes, 2009). These have been proposed to be correlated endophenotypes that share a common genetic diathesis and underlying brain mechanisms.

Reward Responsivity

Anhedonia and reward processing within MDD. Clinically, anhedonia tends to be defined in terms of consummatory, or hedonic, pleasure (“liking”), and this is largely how it was defined and assessed for the purposes of this study. However, it is important to recognize that although anhedonia is more homogenous than MDD, it is still a multidimensional construct. The anticipatory (“wanting”) component of anhedonia, which is conceptualized as the ability to work for reward and to learn to obtain rewards, has also been widely examined in depression research (Rizvi et al., 2016; Treadway & Zald,
Although distinct, anticipatory and consummatory anhedonia should not necessarily be viewed as orthogonal. Rizvi et al. (2016) modified a multi-stage reward process model originally described by Kring and Barch (2014), where reward involves (1) building a stimulus-reward association, which leads to (2) interest or wanting a reward, (3) anticipation for the reward, (4) motivation to engage in activities to obtain the reward, (5) expending effort to engage in the activities necessary for obtaining the reward, (6) hedonic response (consummatory pleasure from receiving the reward), and (7) integrating this information to update reward presence and values. The authors assert that while it may be conceptually useful to view these as stages in a linear process, different facets of the reward process can also occur simultaneously and can influence one another.

Preclinical research in animals has suggested that these different facets of the reward system are subserved by different neural circuitry. Although there are numerous regions of the brain that are relevant in reward responses, the fronto-striatal neuro circuit plays a central role (Nusslock & Alloy, in press; Berridge et al., 2009; Haber and Knutson, 2010; Kringelbach and Berridge, 2009; Schultz, 2000). Both human and animal research has demonstrated that areas within this circuit such as the ventral striatum, nucleus accumbens, orbitofrontal cortex, medial prefrontal cortex, and anterior cingulate cortex are critical in the processes underlying reward responsivity, incentive-based learning, assessing reward-related probabilities, and goal-directed behaviour (Nusslock & Alloy, in press). In general, down-regulation of this system results in reductions in motivation, reward responsivity, and goal-directed behaviour. Additionally, it can lead to increased sadness and anhedonia (Nusslock & Alloy, in press). However, research has shown that the dopaminergic fronto-striatal reward circuit appears to be primarily associated with the anticipatory or motivational aspects of reward processing, whereas hedonic capacity is more strongly associated with endogenous opioids (Treadway & Zald, 2011; Nusslock & Alloy, in press).

For example, research has shown that when dopamine is depleted or there are lesions in dopamine synapses, rats and mice do not show any impairment in their liking of sucrose (Cannon & Palmiter, 2003;
Berridge & Robinson, 1998). Alternatively, reducing or altering dopaminergic functioning in rats strongly impacts motivation to seek food and other rewards (Salamone et al., 2007).

Research on the reward system in depression has found that participants with MDD show deficits in the consummatory and anticipatory aspects. In terms of the consummatory aspect, MDD patients self-report lower levels of consummatory pleasure (Franken, Rassin, & Muris, 2007), and also exhibit a weaker neural response to the consumption of a reward (Hajcak et al., 2013; Rzepa, Fisk, & McCabe, 2017) than non-depressed individuals. For example, Pizzagalli et al. (2009) found that participants with MDD showed significantly weaker responses to receiving a reward in left nucleus accumbens and caudate compared to controls (also see Rzepa, Fisk, & McCabe [2017] for a similar result in a sample of adolescents with depressive symptoms).

In contrast, other studies using different paradigms have shown no difference between MDD and control groups in the ‘liking’ of rewards. For example, in four separate ‘sweet taste test’ studies, individuals with MDD demonstrated no differences from controls in preference and enjoyment of sucrose (Amsterdam et al., 1987; Berlin et al., 1998; Dichter et al., 2010; Kazes et al., 1994). This result is particularly noteworthy because, in the non-human animal literature reduced sucrose preference is widely used as a behavioral indicator of anhedonia (Treadway & Zald, 2013). Similarly, Sherdell and colleagues (2012) found that participants with MDD experienced similar levels of ‘liking’ of humorous cartoons as healthy controls, but demonstrated reduced anticipation for a reward (humorous cartoons) and reduced motivation for effort expenditure. Therefore, at present it is unclear whether individuals with MDD differ from non-depressed individuals in the ‘liking’ of rewards, and differences in results on liking tasks appear to emerge between studies that examine neural responses to reward and those that rely on self-reported liking.

Consistent evidence for impairment in the anticipatory aspect of reward in MDD comes from several sources. MDD patients are poorer than non-depressed individuals at detecting rewards and at
incorporating the experience of rewards into reward-learning associations (Pizzagalli, 2014). Further, in the studies cited above, blunted neural responses were found during the anticipatory phase of reward processing in depression groups (Pizzagalli et al., 2009; Rzepa, Fisk, & McCabe, 2017). In behavioural studies, the anticipatory aspect of reward has been assessed using experimental tasks that assess learning in the context of reward. One example of such a task in the Probabilistic Reward Task (Pizzagalli, Jahn, & O'Shea, 2005). This signal-detection task assesses participants’ ability to modulate behaviour towards monetary rewards based on reward history (reward learning), and is used as a way to operationalize hedonic capacity in research (Pizzagalli et al., 2005). The two most commonly used PRT parameters are response bias scores and reward learning scores. Response bias scores indicate how good a participant was at the PRT and is similar to their average score across the three trials. Reward learning indicates the extent to which a participant was able to improve throughout the task. Research with the PRT has suggested that blunted reward learning (e.g., a lack of improvement throughout the task) is associated with depression and may underlie anhedonia in individuals with MDD (Pizzagalli et al., 2005). Research has also shown that having a history of MDD was predictive of blunted reward learning as assessed by the PRT over and above residual symptoms of depression and anhedonia (Pechtel et al., 2013).

Anhedonia and reward responsivity. Numerous research findings demonstrate a strong link between anhedonic symptoms (both anticipatory and consummatory) and blunted reward responsivity. Neuroimaging research has suggested that anhedonic individuals may have dysfunction in the basal ganglia, specifically the nucleus accumbens, caudate, and putamen – areas of the brain associated with reward, reinforcement learning, and goal-directed action (Keedwell et al., 2005; Pizzagalli et al., 2009; Dillon et al., 2009). Additionally, Pizzagalli et al. (2005) found that participants who had elevated depressive and self-reported anhedonic symptoms showed diminished reward learning, and specifically failed to develop a response bias to the more frequently rewarded stimulus in the PRT, compared to healthy controls. Moreover, the relation of blunted reward learning to anhedonic symptoms held over and
above general distress and other symptom profiles of depression, such as anxiety (Pizzagalli et al., 2007), suggesting that blunted reward processing is preferentially associated with anhedonic symptoms. Therefore, I hypothesize that in this study blunted reward learning in the PRT will be associated preferentially with high scores on symptom measures of anhedonia as opposed to general depression severity or other symptom profiles of depression.

**Reward responsivity and childhood maltreatment.** As indicated previously, childhood maltreatment is associated with an anhedonic symptom presentation in individuals with MDD (Harkness & Monroe, 2002; Dillon et al., 2009). Research has also found associations between childhood maltreatment and blunted reward responsivity. Dillon et al. (2009) found that in addition to more depressive and anhedonic symptoms, women with a history of childhood maltreatment also rated reward cues as being less positive and exhibited a weaker response to anticipatory reward cues in the left globus pallidus. This area of the brain plays a role in integrating incoming reward information and relaying it to the motor cortex. Thus, the authors of this study proposed that pallidus dysfunction might result in diminished ability to predict reward cues and to engage in goal-directed behaviour. Further, Pechtel and Pizzagalli (2013) found that women with a history of childhood sexual abuse showed significant deficits in incentive-based decision-making, supporting the theory that maltreatment is related to developing deficits in reward learning. However, the current study is the first to test the hypothesis that depressed individuals with a history of childhood maltreatment show deficits in reward learning that are specifically related to higher levels of clinical anhedonia.

**Stress Reactivity**

**MDD and HPA axis functioning.** The stress response system is subserved biologically by the hypothalamic-pituitary-adrenal axis (HPA axis; see Figure 2; Pariante & Lightman, 2008; Schatzberg et al., 2014). When a stressor stimulates the hypothalamus to secrete adrenocorticotropic hormone-releasing factor (CRF) and vasopressin (AVP), it results in secretion of adrenocorticotropic hormone
(ACTH) from the pituitary, which in turn results in secretion of the glucocorticoid cortisol from the adrenal cortex. Cortisol then inhibits CRF and AVP and triggers a negative feedback loop to inhibit further stress response (Pariante & Lightman, 2008; Schatzberg et al., 2014). Under normal conditions, this response is adaptive and can help the organism to react to immediate stressors with a fight or flight response. Additionally, the HPA axis plays an important role in regulating a variety of body functions, including neuronal survival, neurogenesis, memory acquisition, and the appraisal of emotionally-charged stimuli (Pariante & Lightman, 2008). The function of the HPA-axis in humans is often assessed by measuring the final output of this system (cortisol) in saliva.

*Figure 2.* The Hypothalamic-pituitary adrenal (HPA) axis. When a stressor stimulates the hypothalamus to secrete adrenocorticotropic hormone- releasing factor (CRF) and vasopressin (AVP), it results in secretion of adrenocorticotropic hormone (ACTH) from the pituitary, which in turn results in secretion of the glucocorticoid cortisol from the adrenal cortex. Cortisol then inhibits CRF and AVP and triggers a negative feedback loop to inhibit further stress response.
A large body of research has provided evidence that many psychiatric disorders, including depression, are associated with dysregulation of the HPA axis (Pariante & Lightman, 2008). Research on MDD has examined numerous parameters of stress reactivity, including diurnal cortisol, cortisol reactivity to pharmacological challenge, the Dexamethasone Suppression Test (DST), and cortisol reactivity to a laboratory psychosocial stress task. However, a limitation of pharmacological challenge, diurnal cortisol, and the DST is that they do not take into account natural responses to a psychological stressor in the immediate environment, and thus lack ecological validity (Harkness et al., 2011). As a result, recent research has tended to focus on psychological stress tasks, such as the Trier Social Stress Task (TSST; see Figure 3). The TSST requires participants to give a speech and perform a difficult verbal arithmetic task in front of a panel of two judges, and salivary cortisol is collected at several time points throughout the duration of the task. The TSST is one of only a small number of stress tasks that combines high uncontrollability with high social-evaluative threat, and tasks that include these two components tend to be associated with the largest HPA axis response and longer recovery times (Harkness et al., 2011; Dickerson & Kemeny, 2004). Because of these advantages, this study used the TSST in order to assess cortisol reactivity to stress.

Figure 3. Comparing hypothetical blunted, typical, and reactive cortisol reactivity profiles in response to the TSST.
Meta-analytic evidence suggests that MDD is associated with a flat (i.e., blunted or hyporeactive) pattern of cortisol reactivity, as well as impaired cortisol recovery, following a laboratory stress challenge such as the TSST, relative to healthy controls (Burke et al., 2005). Individuals who may be at genetic risk for developing depression, and thus may be at risk for developing a more severe form of the disorder, tend to express trait desensitization of glucocorticoid receptors (Holsboer, 2000; Modell, Lauer, Schreiber, Huber, Krieg, & Holsboer, 1998). As a result of reduced glucocorticoid negative feedback, high CRH release as a result of prior chronic stressors (such as childhood maltreatment) can lead to down-regulation of CRH-receptors on ACTH cells, producing a blunted cortisol response to stress (Holsboer, 2000; Modell et al., 1998). Burke et al. (2005) also found that this blunted pattern is particularly pronounced in older, more severely depressed participants. In contrast, individuals with more mild depressive symptoms are able to maintain increased secretion of glucocorticoids to an acute stressor, despite negative feedback (Holsboer, 2000; Modell et al., 1998). Further support from this stems from findings showing that significant blunting of the cortisol response to stress has been found in pre-pubertal children with MDD, a group that would also be expected to have a strong genetic loading (Hankin, Badanes, Abela, & Watamura, 2010).

To my knowledge, no studies exist examining the specific cortisol reactivity pattern in the TSST that is associated with an anhedonic symptom presentation in MDD, in particular. As mentioned previously, anhedonia is indicative of a more severe depression, which has been associated with a blunted pattern. Further, blunted cortisol responses to the TSST were associated with reduced nucleus accumbens responses to reward in a neuroimaging study of sexual stimuli (Oei et al., 2013). Therefore, I hypothesize that higher levels of anhedonia will be associated with a blunted cortisol response to the TSST.

**Stress reactivity and childhood maltreatment.** Studies examining cortisol reactivity to social stress in individuals with and without a history of childhood maltreatment have generally found evidence
of blunted (i.e., hyporeactive) patterns. For example, Suzuki et al. (2014) found that a history of childhood maltreatment was associated with blunted cortisol reactivity and this relation held regardless of MDD status. Similarly, in a study on cortisol reactivity to a social stress task in female adolescents, MacMillan et al. (2009) found that girls with maltreatment exhibited a blunted cortisol response to a stressor compared to the control group, and this response occurred regardless of depression symptoms.

Peckins et al. (2012) examined the association between concurrent and lifetime exposure to violence with cortisol reactivity to a social stress task. They found that in boys only, exposure to violence was associated with a blunted cortisol response compared to controls, and this effect occurred over and above MDD and other psychiatric symptoms. In a sample of non-clinical adult females, Carpenter et al. (2010) found that a history of physical abuse was associated with a significantly blunted cortisol response to a social stress task. Goldman-Mellor, Hamer, and Steptoe (2012) found that individuals who were exposed to early-life stress who also had recurrent psychological distress in adulthood exhibited significantly blunted cortisol reactivity to a cognitive stressor compared to those who had not experienced early-life stress. In contrast to the studies reported above, however, they found that adults with early-life stress who did not have recurrent psychological distress showed elevated cortisol reactivity compared to other groups. A similar pattern was provided when Harkness et al. (2011) examined the relation between childhood maltreatment and stress reactivity, stratified by depression severity. They found that in individuals with a history of maltreatment, MDD that was early in its course and mild in severity was associated with an elevated cortisol response to stress (i.e., hypercortisolemia), whereas recurrent or more severe depression was associated with blunted cortisol responses, particularly in those with a maltreatment history. Therefore, in the present study, I hypothesized that childhood maltreatment would be associated with a blunted cortisol response to a stress task, particularly in those with MDD and high levels of anhedonia.
Relation Between the Reward and Stress Systems

As noted previously, it has been theorized that reward responsivity and stress reactivity may be correlated endophenotypes that share a common neurobiological substrate and related neural circuitry. Research using animal models has found that a variety of stressors (e.g., chronic and mild stress, inescapable stress, and early maternal separation) result in reduced sensitivity to reward and behavioural signs of the liking component of anhedonic, such as reduced preference for sucrose solution and increased thresholds for rewarding brain stimulation (Matthews & Robbins, 2003; Pohl, Olmstead, Wynne-Edwards, Harkness, & Menard, 2007; Willner, 2005). Additionally, results from neuroimaging studies with humans have shown that healthy individuals exposed to threat of electric shocks or social stress tasks show disrupted hedonic capacity, reward anticipation and learning, and reduced activation of brain areas associated with reward processing in response to reward compared to non-stressed participants (Bogdan & Pizzagalli, 2006; Bogdan et al., 2011).

Research has also found associations among stress, reward responsivity, and anhedonia. In addition to finding that threat-of-shock resulted in reduced reward anticipation, Bogdan and Pizzagalli (2006) also found that self-reported symptoms of anhedonia predicted these stress-induced effects over and above other symptoms, such as anxiety. Further, Pizzagalli et al. (2007) compared participants’ self-reports of recent stress with their performance on a signal detection task used to assess hedonic capacity. They found that participants who indicated that they viewed their current lives as stressful, unpredictable, and overwhelming reported elevated anhedonic symptoms and showed diminished hedonic capacity (liking of rewards) compared to healthy controls. The current study is the first to look at stress reactivity and reward responsivity as potential mediators that account for the relation between childhood maltreatment and anhedonia, and the first to examine how these domains of functioning are related to one another within the context of maltreatment.
**Differential Characteristics of Childhood Maltreatment**

Much of the previous research on the relations of childhood maltreatment to reward responsivity, stress reactivity, and anhedonia either focus on one type of maltreatment (e.g., sexual or physical or emotional) or examine all types of maltreatment as a composite risk factor for these outcomes (e.g. Pachtel & Pizzagalli, 2013; Harkness et al., 2011; Agrawal et al., 2012; Heim et al., 2001). Therefore, a critical gap in the existing literature is to examine whether different types of maltreatment present a differential risk for blunted stress reactivity, blunted reward responsivity, and resulting anhedonic symptoms.

Research investigating the relation between childhood maltreatment and depression in general has indicated that emotional abuse may pose a greater degree of risk for depression than other abuse types (Chapman et al., 2014; Alloy et al., 2006; Spinhoven et al., 2010; Widom et al., 2007). For example, in a retrospective cohort study of 9460 adults, Chapman et al. (2014) found that emotional maltreatment conferred a greater risk for both recent depressive episodes and a history of recurrent MDD than either physical or sexual maltreatment. Similarly, in a longitudinal lifespan study of 2288 individuals, Spinhoven et al. (2010) reported that emotional abuse and emotional neglect were more highly related to later depressive episodes and a higher incidence of other depressive disorders than physical or sexual abuse. Therefore, in the current study, I predict that emotional abuse will be more strongly associated with depression and anhedonia than physical or sexual abuse.

**Research Goals and Hypotheses**

The goals of my Master’s thesis are to test the model presented in Figure 1. Specifically, I examine: 1) the differential relation of sexual, physical, and emotional maltreatment to an anhedonic symptom presentation in both MDD patients and controls over and above the contribution of general symptoms of depression and anxiety; 2) the differential relation of sexual, physical, and/or emotional maltreatment to (a) cortisol response to a laboratory social stress task and (b) reward learning on a
probabilistic reward task; 3) the relation of cortisol response in a laboratory social stress task and reward learning on a probabilistic reward task to an anhedonic symptom presentation over and above the contribution of general symptoms of depression and anxiety; 4) the correlation between parameters of stress reactivity and reward responsivity, and (5) the mediating role of stress reactivity and reward responsivity on the relation between each type of childhood maltreatment and anhedonia symptoms in individuals with MDD and controls.

I hypothesized that 1) emotional abuse would be more strongly related to anhedonia than other forms of abuse in depressed individuals and controls; and that 2) emotional abuse would be more highly associated with a blunted cortisol response to a social stress task and blunted reward learning on a probabilistic reward task than other abuse forms. I also hypothesized that 3) both reward responsivity and stress reactivity would be significantly associated with symptoms of anhedonia in the full sample and the depressed group; and that 4) blunted cortisol response to a social stress task and blunted reward learning on a probabilistic reward task would be correlated with each other. Finally, I hypothesized that (5) blunted cortisol reactivity and reward responsivity would partially account for the relation between childhood maltreatment and anhedonia, and that this mediation will be stronger in the context of emotional abuse. This research was conducted as part of a larger ongoing project that examined the overall effects that childhood maltreatment and anhedonic symptom presentation have on stress reactivity and blunted reward responsivity.
Chapter 3

Methods

Participants

Participants were 39 depressed individuals and 47 healthy controls between the ages of 18 and 66 ($M = 28.79$, $SD = 12.99$; 59% female) who participated as part of a larger ongoing study of biomarkers in depression. All participants were recruited through advertisements placed in public places (e.g., coffee shops, community centres, etc.). Participants were required to pass a preliminary phone screen before being given an appointment to ensure that they met study requirements. Participants in the depressed group met DSM-IV criteria for current MDD, and participants in the non-depressed group had no current or lifetime psychiatric diagnoses. Exclusion criteria included schizophrenia and other psychotic disorders, bipolar disorder, substance dependence, a medical disorder that could cause depression, or need for inpatient care. Women who were pregnant, as well as habitual smokers, were also excluded because of hormonal differences that could affect the validity of their cortisol samples (Rohleder & Kirschbaum, 2006).

Procedure

The study took place at Providence Care, Mental Health Services. Participants engaged in two 2-hour sessions separated by one week: Session 1 consisted of (a) consent, (b) diagnostic interview, (c) questionnaires; (d) child maltreatment interview. In Session 2, participants completed (a) a laboratory stress task; and (b) a probabilistic reward task. As part of the larger study, participants also provided a blood sample during Session 1 and came in for a third appointment for an MRI scan. I and other clinical psychology and neuroscience graduate students supervised by Dr. Harkness conducted the interviews. Participants received $50 compensation for the procedures specific to my study, and $150 if they completed all components of the study, including the MRI appointment. Participants were also provided
with a list of clinical resources within the community.

**Measures**

**Depression.** The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-IV; First, Spitzer, Gibbon, & Williams, 2002) was used to determine diagnoses of depressive disorders and comorbid conditions. At this time, we also assessed demographic variables, and psychotropic and steroidal medication history. The 10-item clinician-rated Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979) was used to assess the severity of depression symptoms. The MADRS assesses a variety of symptoms including sadness, tension, appetite and sleep disturbance, difficulties with concentration, and suicidal ideation. Items are rated on a 7-point Likert scale, with ‘0’ representing the absence of a symptom and ‘6’ indicating that the symptom is endorsed or observed as severe. MADRS scores were used for preliminary descriptive analyses and when reporting clinical characteristics of the sample.

**Anhedonia.** The Snaith Hamilton Pleasure Scale (SHAPS; Snaith et al., 1995) is a 14-item self-report scale that exclusively measures self-reported consummatory pleasure, or liking of a reward (e.g., “I would enjoy being with my family or close friends”). This scale has excellent reliability and validity in both clinical and research populations (Franken, Rassin, & Muris, 2007).

Participants also completed the 90-item Mood and Anxiety Symptom Questionnaire (MASQ; Watson & Clark, 1991). The MASQ has strong reliability and validity, and has specific relevance to identifying anhedonia as a trait vulnerability in MDD (Watson et al., 1991). The anhedonic depression (AD) subscale of the MASQ taps into multiple symptoms of anhedonia, including hedonic capacity (e.g., “Felt like nothing was very enjoyable”), reward anticipation (e.g., “Looked forward to things with enjoyment”), and motivation difficulties (e.g., “Felt like it took extra effort to get started”). Thus, the MASQ AD can be useful for the assessment of the broader conceptualization of anhedonia and may tap into constructs that are overlooked by the SHAPS.
In addition to measuring anhedonia, the MASQ uses Watson and Clark’s (1991) tripartite model of anxiety and depression, and also provides subscale scores for general distress (GD), and anxious arousal (AA). GD is a variable that encompasses overlapping symptoms between depression and anxiety, and is thought to reflect underlying negative affect (NA; Watson & Clark, 1994; Keogh & Reidy, 2000). NA is the stable trait tendency to experience a variety of negative emotions, including worry anxiety, and self-criticism (Watson & Clark, 1994). AA is a variable that encompasses symptoms of somatic anxiety, tension, and hyperarousal (Watson & Clark, 1994). In order to examine if any observed effects were specific to an anhedonic symptom profile over and above other depressive symptoms/depression severity, I also examined general distress (GD) and anxious arousal (AA).

Childhood Maltreatment. The Childhood Experience of Care and Abuse scale (CECA; Bifulco, Brown, & Harris, 1994) is a semi-structured interview assessing the quality of parental care and abuse up to age 18. Audio recordings of the interviews were written up and rated by independent undergraduate research assistant judges and approved by Dr. Harkness. Raters used the CECA rating manual, which contains hundreds of case examples, to anchor their ratings. Scales are rated from 1-marked to 4-little/none on the different forms of abuse: (a) antipathy – hostility, criticism, and/or coldness toward the child, (b) neglect – failing to provide for child’s physical and/or emotional needs, (c) physical abuse – violence directed toward the child by parents; (d) sexual abuse – non-consensual sexual contact by any perpetrator. For statistical analyses, ratings for each scale were dummy coded to form 1-severe abuse (a rating of 1-marked or 2-moderate) vs. 0-non-severe/no abuse (a rating of 3-some or 4-little/none) categories. These scores are dichotomized because the continuous scores are highly skewed (the modal rating is ‘4 – little/none’). This skew cannot be corrected by transforming the variables, so we dichotomize them instead.

1 – 4 distribution is typically very skewed, with the majority of participants falling in the ‘4 – little/none’ category. Antipathy and neglect were combined to form a composite variable representing the
presence versus absence of severe emotional abuse.

**Probabilistic Reward task**

In the Probabilistic Reward task (Pizzagalli, Jahn, & O'Shea, 2005), participants were presented with cartoon face stimuli on a computer screen, and they indicated by key press whether the mouth was short (11.5mm) or long (13mm) (See Figure 4). Stimuli were presented for 100ms in three blocks of 100 trials. To elicit a response bias, correct identification of the long mouth was rewarded (“Correct! You won 20 Cents”) three times more frequently (“rich stimulus”) than correct identification of the short mouth (“lean stimulus”). In each block, only 40 correct trials (30 rich, 10 lean) were rewarded to ensure that participants were exposed to similar reinforcement schedules. Therefore, participants had to integrate reinforcement history over time to optimize their responses. Participants were informed that their goal was to win as much money as possible. They were told that not all correct responses would receive reward feedback, but they were not told that one stimulus would be disproportionately rewarded.

![Figure 4](image-url)  
*Figure 4. Stimuli from the Probabilistic Reward Task (PRT). For each trial, the participant must decide whether a short or a long mouth was presented (reproduced from Pizzagalli et al., 2009).*

**Parameters for analyses.** Three central parameters were calculated. The first is Response Bias (\( \log b = \frac{1}{2} \log (\text{Richcorrect} \times \text{Leanincorrect} / \text{Richincorrect} \times \text{Leancorrect}) \)). High response bias indicated
high rates of correct identification (hits) for the rich stimulus (the one that was rewarded more frequently), and high miss rates for the lean stimulus (the one that was rewarded less frequently). The Response Bias total score (based on Response Bias for all three blocks of the task) was used for analyses, and essentially indicates how good the participant was at responding to the rewarding stimuli. The second parameter that was calculated was Discriminability (Log d = ½ log (Richcorrect*Leancorrect/Richincorrect*Leanincorrect)). This assessed participants’ ability to distinguish between the short and long mouths. This is important to compute to determine whether group differences in response bias were better accounted for by task difficulty. Because MDD can result in cognitive and attentional deficits, it is important to ensure that group differences are occurring as a result of decreased responsiveness to reward and not because participants were unable to differentiate between stimuli as a result of cognitive symptoms or some other reason. The third parameter is Response Bias Delta, which assessed each participants’ rate of learning throughout the task (e.g., how much their performance in Block 3 improved from their performance on Block 1). This was calculated by subtracting their Response Bias scores on Block 1 from their Response Bias scores on Block 3.

Salivary Hormone and Stress Challenge Test

Trier Social Stress Task (TSST). The TSST (see Figure 2) begins with an initial sample that is taken within five minutes of the participant arriving at the lab (Sample A). This sample is followed with a 30 min rest period, followed by a second sample (Sample B). After this second sample, the participant is led to a room where a committee of two people are sitting behind a table. The participant learns that he or she will have to deliver a speech for a job application to the committee, which will be videotaped as per TSST protocol. The participant is led back to the first room and given 10 minutes to prepare, after which a third sample is collected (Sample C). The participant then gives the five-minute speech; after which they are asked to serially subtract the number 13 from 1022 as quickly as possible without making any mistakes. If a mistake is made the participant is told by the committee that they must start over. The
committee also prompts the participant to maintain eye contact and calculate more quickly. Following the arithmetic test, the participant is led back into the preparation room to provide a fourth sample (Sample D). The participant is then debriefed and relaxes quietly (with neutral reading material available) for 60 minutes to allow for hormone recovery (Samples E-H).

**Saliva collection.** Samples were collected by passive drool (Shirtcliff, Granger, Schwartz, & Curran, 2001) between 2:00-4:30pm to avoid post-awakening increases in hormones (Groschl, Rauh, & Dorr, 2003) in 5 ml polypropylene vials (PGC Scientifics Corporation, MD). We asked that participants avoid teeth brushing, vigorous exercise, smoking, caffeine, and eating or drinking other than water for 2 hours before the study (Kivlighan et al., 2004). Samples were immediately placed in a freezer for short-term storage and then mailed on dry ice without identifying information about MDD or childhood maltreatment status to Dr. Wynne-Edwards’ laboratory in the Health Research Innovation Centre at the University of Calgary for secure frozen storage and assay.

**Cortisol assay and determinants.** Dr. Wynne-Edwards’ laboratory has developed and used novel methods of Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) for the quantitation of salivary cortisol in a wide variety of species (Jensen, Hansen, Abrahamsson, & Nørgaard, 2011; Erickson, Singh, Sathananthan, Vella, & Bryant; 2012; Wynne-Edwards, Edwards, & Hancock, 2013). Samples were thawed under gentle shaking in 20 degrees Celsius water and then centrifuged (1500g, 15 minutes) to remove mucopolysaccharides and detritus. Resulting supernatant was spiked with bio-identical deuterated internal standard, subjected to protein precipitation by zinc sulfate, and then reconstituted for LC-MS/MS using the method of Koren et al. (2012), with calibrators prepared in water, and quality controls prepared in a pool of charcoal-stripped human saliva. Quantitation used area ratio for the steroid relative to the deuterated internal standard, read against a calibration curve tailored to these samples.

**Parameters for analyses.** The first variable that was calculated for statistical analyses was Area
Under the Curve with respect to Increase (AUCi). AUCi represents the total cortisol secreted during the TSST over baseline levels, calculated as the sum of the area of the seven trapezoids bounded by the participants’ baseline and framed by the cortisol concentration in the eight saliva samples. Because AUCi takes baseline into account it is the best marker of overall reactivity to the stressor (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). However, someone who shows a very slow and gradual release of cortisol over the sampling period may have identical AUCi values to someone who peaks and recovers in very quickly. That is, AUCi does not model the heterogeneity of cortisol trajectories that may have important significance in distinguishing individuals with particular endophenotypes. I also created a variable for ‘cortisol reactivity’, which subtracts Sample A from Sample D and measures a participants reactivity to the TSST relative to their baseline. Numerous different indices of stress reactivity have been used in prior research, including reactivity (where the average peak in activity is; for summary see Khoury et al., 2016).

Statistical Analyses

**Preliminary analyses.** Prior to addressing the hypotheses, group differences between controls and MDD participants were analyzed in terms of gender, age, and ethnicity. I also assessed the relation of age, gender, and ethnicity to the primary study variables, specifically depression severity, anhedonia, childhood maltreatment, reward responsivity, and stress reactivity. Further, I examined the relation of depression status and severity to these primary study variables.

**Hypothesis 1.** A series of independent samples t-tests was used to assess if anhedonic symptoms were higher in individuals with and without emotional, physical, or sexual abuse. Multiple regression modeling was then used to assess which forms of abuse were significantly associated with anhedonic symptoms while controlling for other abuse types. Analyses were conducted in the full sample and in the depressed group only.

**Hypothesis 2.** A series of independent samples t-tests was used to assess if (a) reward
responsivity based on PRT scores or (b) stress reactivity to the TSST differed based on the presence or absence of emotional, physical, or sexual abuse. Analyses included separate models using response bias and reward learning scores for the PRT, and using AUCi and cortisol reactivity from the TSST. Multiple regression modeling was then used to examine which types of abuse were associated with reward responsivity and stress reactivity while controlling for other abuse types. Analyses were conducted in the full sample and in the depressed group.

**Hypothesis 3.** Correlation analyses were used to examine if measures of reward responsivity (response bias and reward learning) were associated with measures of stress reactivity (AUCi and cortisol reactivity). Analyses were conducted in the full sample and in the depressed group.

**Hypothesis 4.** Mediated linear regression modeling was used to determine if stress reactivity and reward responsivity mediated the relation between childhood maltreatment and anhedonia within MDD, using Preacher & Hayes’ (2015) PROCESS macro for SPSS. A multiple mediation model was used, and this analysis was only conducted for versions of the model that met mediation assumptions. In order to meet our requirements, (1) the independent variable (childhood maltreatment) needed to show a significant association with the mediator variable(s) (reward responsivity/stress reactivity), and (2) the mediator variable needed to be significantly related to the dependent variable (anhedonia) (MacKinnon & Fairchild, 2009).
Chapter 4

Results

Preliminary Depression Group Differences on Demographic and Clinical Characteristics

Means and standard deviations for group differences on gender, age, ethnicity, MADRS scores, MASQ AD scores, MASQ AA scores, MASQ GD scores, and SHAPS scores are listed in Table 1, in addition to clinical characteristics of the depressed group. There were no significant differences between controls and depressed individuals for any of the demographic variables (e.g., gender, age, or ethnicity). As expected, the depressed group had significantly greater scores on all measures relating to depression severity and symptoms.
Table 1  
*Preliminary Depression Group Differences on Demographic and Clinical Characteristics* 

<table>
<thead>
<tr>
<th></th>
<th>Depressed (n = 39)</th>
<th>Control (n = 47)</th>
<th>( \chi^2 ) or ( t )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: Female n (%)</td>
<td>27 (69)</td>
<td>32 (68)</td>
<td>0.01</td>
</tr>
<tr>
<td>Age M (SD)</td>
<td>31.18 (13.49)</td>
<td>26.85 (12.36)</td>
<td>- 1.54</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td>5.23</td>
</tr>
<tr>
<td>White n (%)</td>
<td>27 (69)</td>
<td>32 (68)</td>
<td></td>
</tr>
<tr>
<td>Chinese n (%)</td>
<td>3 (8)</td>
<td>5 (11)</td>
<td></td>
</tr>
<tr>
<td>Other n (%)</td>
<td>9 (23)</td>
<td>10 (21)</td>
<td></td>
</tr>
<tr>
<td>MADRS M (SD)</td>
<td>26.45 (7.62)</td>
<td>1.34 (2.44)</td>
<td>- 21.31***</td>
</tr>
<tr>
<td>Range = 0 – 60</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MASQ AD M (SD)</td>
<td>83.77 (13.43)</td>
<td>55.15 (11.97)</td>
<td>- 10.44***</td>
</tr>
<tr>
<td>Range = 22 – 110</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MASQ AA M (SD)</td>
<td>33.18 (11.96)</td>
<td>19.74 (2.40)</td>
<td>- 7.53 ***</td>
</tr>
<tr>
<td>Range = 17 – 85</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MASQ GD M (SD)</td>
<td>233.54 (44.42)</td>
<td>134.55 (27.69)</td>
<td>- 12.61***</td>
</tr>
<tr>
<td>Range = 76 – 380</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHAPS M (SD)</td>
<td>4.87 (3.47)</td>
<td>0.17 (0.56)</td>
<td>- 9.18***</td>
</tr>
<tr>
<td>Range = 0 – 14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at first onset M (SD)</td>
<td>31.18 (13.49)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comorbidity: Yes n (%)</td>
<td>22 (56)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacological treatment:</td>
<td>14 (37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note. On the MADRS, MASQ, and SHAPS, higher scores indicate elevated symptoms; M = mean, SD = standard deviation.*

26
Table 2
Additional Clinical Characteristics of the Depressed Group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Depressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at first onset $M$ ($SD$)</td>
<td>31.18 (13.49)</td>
</tr>
<tr>
<td>Any Comorbidity: Yes $n$ (%)</td>
<td>22 (56)</td>
</tr>
<tr>
<td>Comorbid Specific Phobia: Yes $n$ (%)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Comorbid GAD: Yes $n$ (%)</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Comorbid Obsessive-Compulsive Disorder: Yes $n$ (%)</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Comorbid Post-Traumatic Stress Disorder: Yes $n$ (%)</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Comorbid Panic Disorder: Yes $n$ (%)</td>
<td>7 (8.1)</td>
</tr>
<tr>
<td>Comorbid Social Anxiety: Yes $n$ (%)</td>
<td>9 (10.5)</td>
</tr>
<tr>
<td>Previous episodes $M$ ($SD$)</td>
<td>2.32 (1.76)</td>
</tr>
<tr>
<td>Pharmacological treatment: Yes $n$ (%)</td>
<td>14 (37)</td>
</tr>
</tbody>
</table>

Note. On the MADRS, MASQ, and SHAPS, higher scores indicate elevated symptoms; $M$ = mean, $SD$ = standard deviation.

Preliminary Relation of Demographic Characteristics to Primary Study Variables

Gender. Gender was not significantly associated with emotional, physical, or sexual abuse, MASQ AD or SHAPS scores, or the PRT parameters (all $p$s > .22). However, males had significantly greater $AUC_i$ than females ($Ms = 150.79, 95.36$; $SDs = 17.77, 59.91$), $t$ ($83$) = -3.16, $p$ = .002. Males also had significantly greater cortisol reactivity than females ($Ms = 0.82, 0.03$; $SDs = 1.65, 0.66$), $t$ ($83$) = -
2.90, \( p = .003 \). Gender was thus included as a covariate for all subsequent analyses involving cortisol output and reactivity.

**Age.** Age was not significantly related to emotional, physical, or sexual abuse, MASQ AD or SHAPS scores, the PRT parameters, or cortisol reactivity. However, age was significantly negatively correlated with AUCi, with older individuals showing reduced cortisol output, Pearson’s \( r(86) = -.27, p = .025 \). Age was therefore included as a covariate in all subsequent analyses involving AUCi.

**Ethnicity differences.** There were no differences based on ethnicity for any of the primary study variables (all \( p > .27 \)).

**Relation of Depression to Primary Study Variables**

**Depression and childhood maltreatment.** Rates of emotional and sexual abuse were significantly higher in the depressed group than in the control group; however, groups did not differ in rates of physical abuse (see Table 2). In the full sample, those with emotional, physical, and sexual abuse had significantly higher MADRS scores than those without (see Table 3). Within the depressed group, those with versus without emotional and sexual abuse had higher scores, as a trend on the MADRS, and those with versus without physical abuse had significantly higher scores on the MADRS (see Table 3). When examining the association between each abuse type and MADRS scores while controlling for other abuse types, no types of abuse were significantly associated with MADRS scores (\( p > .173 \)). However, this is likely due to overlapping variance among the abuse types, especially emotional abuse and physical abuse.
Table 3  
*Depression Group Differences on Primary Study Variables*

<table>
<thead>
<tr>
<th></th>
<th>Depressed (n = 39)</th>
<th>Control (n = 47)</th>
<th>$\chi^2$ or $t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional maltreatment: Yes n (%)</td>
<td>16 (41)</td>
<td>7 (14)</td>
<td>7.58 **</td>
</tr>
<tr>
<td>Physical maltreatment: Yes n (%)</td>
<td>7 (18)</td>
<td>3 (7)</td>
<td>2.59</td>
</tr>
<tr>
<td>Sexual maltreatment: Yes n (%)</td>
<td>9 (23)</td>
<td>1 (2)</td>
<td>9.35***</td>
</tr>
<tr>
<td>Response Bias $M$ (SD)</td>
<td>0.15 (0.15)</td>
<td>0.14 (0.16)</td>
<td>-0.16</td>
</tr>
<tr>
<td>Reward Learning $M$ (SD)</td>
<td>0.01 (0.18)</td>
<td>0.14 (0.26)</td>
<td>2.24*</td>
</tr>
<tr>
<td>AUCi $M$ (SD)</td>
<td>95.64 (56.79)</td>
<td>123.55 (79.31)</td>
<td>1.71†</td>
</tr>
<tr>
<td>Cortisol Reactivity $M$ (SD)</td>
<td>0.07 (0.63)</td>
<td>0.41 (1.33)</td>
<td>1.43</td>
</tr>
</tbody>
</table>

*Note. M = mean, SD = standard deviation; † p < .095, * p < .050, ** p < .01, *** p < .005*
Table 3

Descriptive and Inferential Statistics for Childhood Maltreatment (CM) and MADRS Scores

<table>
<thead>
<tr>
<th></th>
<th>Full Sample</th>
<th>Presence</th>
<th>t</th>
<th>$\eta_p^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional $M (SD)$</td>
<td>10.07 (12.66)</td>
<td>21.62 (13.75)</td>
<td>-3.51***</td>
<td>.136</td>
</tr>
<tr>
<td>Physical $M (SD)$</td>
<td>11.83 (13.24)</td>
<td>23.00 (14.98)</td>
<td>-2.46*</td>
<td>.073</td>
</tr>
<tr>
<td>Sexual $M (SD)$</td>
<td>10.75 (12.90)</td>
<td>27.00 (10.87)</td>
<td>-3.95***</td>
<td>.168</td>
</tr>
</tbody>
</table>

Depressed Group

<table>
<thead>
<tr>
<th></th>
<th>Absence</th>
<th>Presence</th>
<th>t</th>
<th>$\eta_p^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional $M (SD)$</td>
<td>25.87 (6.86)</td>
<td>29.53 (5.71)</td>
<td>-1.70†</td>
<td>.078</td>
</tr>
<tr>
<td>Physical $M (SD)$</td>
<td>26.31 (6.51)</td>
<td>31.86 (5.11)</td>
<td>-2.10*</td>
<td>.114</td>
</tr>
<tr>
<td>Sexual $M (SD)$</td>
<td>26.15 (6.81)</td>
<td>30.78 (5.14)</td>
<td>-1.86†</td>
<td>.094</td>
</tr>
</tbody>
</table>

Note. $M =$ mean, $SD =$ standard deviation; † $p < .095$, * $p < .050$, ** $p < .01$, *** $p < .005$

**Depression and reward responsivity.** The depressed group did not have significantly different response bias scores than the control group, $t(84) = -0.16, p = .870, \eta_p^2 < .001$; however the depressed group did have significantly lower reward learning scores than the control group, $t(84) = 2.24, p = .029, \eta_p^2 = .075$ (see Table 2). This is further illustrated through the interaction between depression status and reward block (see Figure 5). A 2 (depression group; depressed and control) x 3 (reward block) Repeated Measures ANOVA was approaching a significant interaction, $F(2) = 2.63, p = .077$. Further analyses using a one-way (reward block) Repeated Measures ANOVA indicated that controls demonstrated a significant time effect, $F(2) = 5.76, p = .005$, whereas depressed individuals did not demonstrate a significant time effect, $F(2) = 0.27, p = .767$, indicating that compared to controls, depressed individuals failed to develop a preference for rewarding stimuli during the task.
Figure 5. Performance across the three trials of the PRT in the control group versus the depressed group.

In the full sample, response bias scores were not significantly correlated with scores on the MADRS, Pearson’s $r = .08, p = .545$; however, reward learning was significantly negatively correlated with scores on the MADRS, Pearson’s $r = -.28, p = .027$. Within the depressed group, response bias was approaching significance for a positive correlation with MADRS scores, Pearson’s $r = .35, p = .074$, where higher depression severity was associated with greater response bias. In contrast, reward learning was not significantly correlated with scores on the MADRS, Pearson’s $r = -.01, p = .953$.

**Depression and stress reactivity.** The depressed group had a lower AUCi than the control group at a trend, $t(68) = 1.71, p = .092$; however, the two groups did not differ in their cortisol reactivity, $t(69) = 1.44, p = .156$ (see Table 2). In the full sample, MADRS scores were not significantly correlated with either AUCi, Pearson’s $r = -.12, p = .317$, or reactivity, Pearson’s $r = -.16, p = .198$.

Within the depressed group, MADRS scores were not significantly correlated with either AUCi, Pearson’s $r = .28, p = .161$, or cortisol reactivity, Pearson’s $r = .09, p = .660$. However, it should be noted...
that the correlation with AUCi was moderate in magnitude and indicated that greater severity of depression was associated with greater total cortisol output. The lack of statistical significance may have been due to the small size of the MDD group, but this should be interpreted with caution.

**Hypothesis 1: Childhood Maltreatment and Anhedonia**

As expected, given the strong depression group differences in childhood maltreatment, those with versus without emotional abuse, physical abuse, and sexual abuse, had significantly higher SHAPS scores (see Table 4). Those with versus without emotional abuse, physical abuse, and sexual abuse, also had significantly higher MASQ AD scores (see Table 4).
### Table 4

**Childhood Maltreatment and Anhedonia**

<table>
<thead>
<tr>
<th>Full Sample</th>
<th>SHAPS</th>
<th>MASQ AD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absence</td>
<td>Presence</td>
</tr>
<tr>
<td>Emotional</td>
<td>1.83</td>
<td>3.90</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(3.16)</td>
<td>(3.62)</td>
</tr>
<tr>
<td>Physical</td>
<td>2.00</td>
<td>5.10</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(3.10)</td>
<td>(4.33)</td>
</tr>
<tr>
<td>Sexual</td>
<td>1.86</td>
<td>5.80</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(2.99)</td>
<td>(4.31)</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>4.82</td>
<td>5.23</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(3.62)</td>
<td>(3.35)</td>
</tr>
<tr>
<td>Physical</td>
<td>4.57</td>
<td>6.86</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(3.28)</td>
<td>(3.89)</td>
</tr>
<tr>
<td>Sexual</td>
<td>4.63</td>
<td>6.44</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(3.03)</td>
<td>(3.22)</td>
</tr>
</tbody>
</table>

*Note. M = mean, SD = standard deviation; * p < .050, ** p < .01, *** p < .005; † p = .056; ‡ p = .053; • p = .087.*

To determine whether, in the full sample, maltreatment was preferentially associated with scores on the anhedonia measures, as opposed to general depression and anxiety symptoms, we ran the above models controlling, separately, for scores on general distress (GD) and anxious arousal (AA). When controlling for GD, emotional abuse was not associated with the SHAPS, partial $r = .06$, $p = .610$, but was still associated with anhedonia (AD) at a trend, $r = .19$, $p = .096$. When controlling for AA, emotional
abuse was associated at a trend with the SHAPS, \( r = .19, p = .097 \), and significantly with the MASQ AD, partial \( r = .31, p = .005 \).

When controlling for GD, physical abuse was significantly associated with the SHAPS, partial \( r = .26, p = .023 \), but not the MASQ AD, \( r = .13, p = .269 \). Similarly, when controlling for AA, physical abuse was associated with the SHAPS, \( r = .29, p = .011 \), but not the MASQ AD, \( r = .18, p = .110 \).

Finally, when controlling for GD, sexual abuse was not significantly associated with the SHAPS, partial \( r = .18, p = .117 \), or the MASQ AD, partial \( r = .08, p = .483 \). However, when controlling for AA, sexual abuse was still significantly associated with the SHAPS, partial \( r = .24, p = .033 \) and was associated at a trend with the MASQ AD, partial \( r = .19, p = .087 \).

Contrary to hypotheses, within the depressed group, those with versus without emotional abuse, physical abuse, and sexual abuse, did not differ significantly on the SHAPS (see Table 4). Those with versus without emotional abuse or physical abuse also did not significantly differ on the MASQ AD scale (see Table 4). However, those with sexual abuse had higher MASQ AD scores than those without at a trend (see Table 4). When controlling for GD and AA, respectively, the association between sexual abuse and MASQ AD scores were not significant, partial \( rs = .20, .25, ps = .243, .146 \).

**Differential effects of maltreatment on anhedonic symptoms.** Forty-eight percent of individuals with severe emotional abuse also had severe physical abuse. Because emotional abuse and physical abuse were so highly comorbid and had a great deal of overlapping variance, I did not put them in the same model when comparing abuse types. Instead, in the full sample I analyzed four separate multiple linear regression models: (1) emotional abuse and sexual abuse as predictors of SHAPS scores, (2) emotional abuse and sexual abuse as predictors of MASQ AD scores, (3) physical abuse and sexual abuse as predictors of SHAPS scores, and (4) physical abuse and sexual abuse as predictors of MASQ AD scores.
When examining the association of emotional and sexual abuse with anhedonic symptoms, the full regression equation for the first model was significant, $R^2 = .17$, $F(2, 79) = 8.10$, $p = .001$. Sexual abuse was a significant predictor of SHAPS scores, $b = .33$, $t(77) = 3.07$, $p = .003$, but emotional abuse was not, $b = .17$, $t(77) = 1.60$, $p = .113$. The regression equation for the second model was also significant, $R^2 = .21$, $F(2, 79) = 10.41$, $p < .001$. Both emotional abuse, $b = .30$, $t(77) = 2.81$, $p = .006$, and sexual abuse, $b = .28$, $t(77) = 2.63$, $p = .010$, were significant predictors of MASQ AD scores.

When examining the association of physical abuse and sexual abuse with anhedonic symptoms, the third regression model was significant, $R^2 = .20$, $F(2, 78) = 9.45$, $p < .001$. Both physical abuse, $b = .24$, $t(76) = 2.26$, $p = .027$, and sexual abuse, $b = .33$, $t(76) = 3.19$, $p = .002$, were significant predictors of SHAPS scores. The regression equation for the fourth model was also significant, $R^2 = .15$, $F(2, 78) = 6.93$, $p = .002$. Sexual abuse was a significant predictor of MASQ AD scores, $b = .33$, $t(76) = 3.07$, $p = .003$, but physical abuse was not, $b = .16$, $t(76) = 1.45$, $p = .151$.

**Hypothesis 2a: Childhood Maltreatment and Reward Responsivity**

Descriptive and inferential statistics for childhood maltreatment and reward learning are presented in Table 5. In the full sample, none of the forms of maltreatment were significantly associated with either response bias or reward learning. Within the depressed group, contrary to hypotheses, those with a history of emotional abuse had significantly higher response bias scores than those without a history of emotional abuse, but no differences in reward learning. Similarly, those with a history of physical abuse had higher response bias scores than those without. Individuals with a history of physical abuse also demonstrated significantly better reward learning than those without. Finally, those with sexual abuse did not demonstrate significantly different response bias scores than those without sexual abuse; and there were no significant differences in reward learning between those with sexual abuse and those without.
Table 5

*Childhood Maltreatment and Reward Responsivity*

<table>
<thead>
<tr>
<th>Sample</th>
<th>Response Bias</th>
<th>Reward Learning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence</td>
<td>Presence</td>
<td>t</td>
</tr>
<tr>
<td>Emotional</td>
<td>0.12</td>
<td>0.19</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(0.15)</td>
<td>(0.15)</td>
</tr>
<tr>
<td>Physical</td>
<td>0.12</td>
<td>0.20</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(0.15)</td>
<td>(0.16)</td>
</tr>
<tr>
<td>Sexual</td>
<td>0.14</td>
<td>0.13</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(0.16)</td>
<td>(0.13)</td>
</tr>
</tbody>
</table>

Depressed

<table>
<thead>
<tr>
<th>Sample</th>
<th>Response Bias</th>
<th>Reward Learning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence</td>
<td>Presence</td>
<td>t</td>
</tr>
<tr>
<td>Emotional</td>
<td>0.10</td>
<td>0.22</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(0.13)</td>
<td>(0.15)</td>
</tr>
<tr>
<td>Physical</td>
<td>0.12</td>
<td>0.25</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(0.14)</td>
<td>(0.14)</td>
</tr>
<tr>
<td>Sexual</td>
<td>0.15</td>
<td>0.16</td>
</tr>
<tr>
<td>M (SD)</td>
<td>(0.15)</td>
<td>(0.11)</td>
</tr>
</tbody>
</table>

*Note.* † p < .095, * p < .050, ** p < .01, *** p < .005
To determine which of emotional or physical maltreatment was most strongly associated with response bias, I examined the relation of emotional abuse to response bias, controlling for physical abuse, and vice versa. When doing this, neither emotional nor physical abuse were significantly associated with response bias ($p$s > .268). However, this is likely due to the amount of overlapping variance between emotional and physical abuse.

**Hypothesis 2b: Childhood Maltreatment and Stress Reactivity**

Descriptive and inferential statistics for childhood maltreatment and stress reactivity are reported in Table 6. In the full sample, none of the forms of maltreatment were significantly associated with either AUCi or cortisol reactivity. Similarly, within the depressed group, none of the forms of maltreatment were significantly associated with either AUCi or cortisol reactivity. However, although not statistically significant, a qualitative examination of effect sizes (see Table 6) suggests that within the depressed group, both emotional and physical abuse have a moderate positive association with AUCi and emotional abuse is also positively associated with cortisol reactivity. All other effect sizes were small.
Table 6

*Childhood Maltreatment and Stress Reactivity*

<table>
<thead>
<tr>
<th>Full Sample</th>
<th>AUCi</th>
<th>Reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absence</td>
<td>Presence</td>
</tr>
<tr>
<td>Emotional</td>
<td>114.92</td>
<td>115.55</td>
</tr>
<tr>
<td></td>
<td>(71.69)</td>
<td>(79.14)</td>
</tr>
<tr>
<td>Physical</td>
<td>111.17</td>
<td>147.97</td>
</tr>
<tr>
<td></td>
<td>(71.30)</td>
<td>(90.15)</td>
</tr>
<tr>
<td>Sexual</td>
<td>119.07</td>
<td>85.99</td>
</tr>
<tr>
<td></td>
<td>(75.87)</td>
<td>(41.46)</td>
</tr>
</tbody>
</table>

Depressed

<table>
<thead>
<tr>
<th></th>
<th>Emotional</th>
<th>Physical</th>
<th>Sexual</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absence</td>
<td>Presence</td>
<td>$t$</td>
</tr>
<tr>
<td>Emotional</td>
<td>83.94</td>
<td>110.85</td>
<td>- 1.19</td>
</tr>
<tr>
<td></td>
<td>(39.05)</td>
<td>(73.22)</td>
<td></td>
</tr>
<tr>
<td>Physical</td>
<td>90.51</td>
<td>128.54</td>
<td>- 1.22</td>
</tr>
<tr>
<td></td>
<td>(51.95)</td>
<td>(85.46)</td>
<td></td>
</tr>
<tr>
<td>Sexual</td>
<td>101.13</td>
<td>83.41</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>(63.17)</td>
<td>(44.79)</td>
<td></td>
</tr>
</tbody>
</table>

*Note.* † $p < .095$, * $p < .050$, ** $p < .01$, *** $p < .005$

**Hypothesis 3a: Reward Responsivity and Anhedonia**

In the full sample, response bias scores were not significantly correlated with the SHAPS, Pearson’s, $r = .15$, $p = .226$, or the AD scale of the MASQ, Pearson’s $r = .01$, $p = .949$. In the full sample, reward learning was not significantly correlated with scores on the SHAPS, Pearson’s $r = -.16$, $p = .218$.

As hypothesized, reward learning was negatively correlated with the AD scale of the MASQ at a trend,
Pearson’s $r = -.26, p = .074$. However, this relation was no longer significant when controlling for MASQ GD, partial $r = .10, p = .417$, or AA, partial $r = -.06, p = .657$.

Within the depressed group, contrary to hypotheses, response bias scores were positively correlated with scores on the SHAPS at a trend, Pearson’s $r = .32, p = .095$. When controlling for GD, SHAPS scores remained positively associated at a trend with response bias, partial $r = .34, p = .081$. This association was no longer statistically significant when controlling for AA, partial $r = .32, p = .105$. However, given the large partial $r$ value, it is likely that this stems more from low power due to the small sample size rather than a lack of association. Response bias scores were not significantly correlated with scores on the AD of the MASQ, Pearson’s $r = -.04, p = .824$. Reward learning scores were not significantly correlated with scores on the SHAPS, Pearson’s $r = .19, p = .342$ or the AD scale of the MASQ, Pearson’s $r = -.19, p = .338$.

**Hypothesis 3b: Stress Reactivity and Anhedonia**

In the full sample, neither measure of anhedonia was associated with AUCi ($ps > .647$) or cortisol reactivity ($ps > .315$). Similarly, within the depressed group, neither measure of anhedonia was associated with AUCi ($ps > .237$) or cortisol reactivity ($ps > .627$).

**Hypothesis 4: Relation Between Reward Responsivity and Stress Reactivity**

In the full sample, AUCi was not significantly correlated with response bias, Pearson’s $r = -.04, p = .758$; or reward learning Pearson’s $r = .07, p = .603$; and cortisol reactivity was not significantly associated with reward learning, Pearson’s $r = .05, p = .737$. However, stress reactivity and reward learning were significantly positively correlated, Pearson’s $r = .27, p = .046$.

Within the depressed group, AUCi was not significantly correlated with response bias, Pearson’s $r = .22, p = .348$; or reward learning Pearson’s $r = .07, p = .757$. Cortisol reactivity was also not associated with response bias, Pearson’s $r = .05, p = .824$; or reward learning Pearson’s $r = -.14, p = .544$. 

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Hypothesis 5: Mediation Analyses

The mediation analyses relied on two assumptions (MacKinnon & Fairchild, 2009): 1. Childhood maltreatment would be significantly associated with anhedonia; 2. Childhood maltreatment would be significantly associated with (a) reward responsivity and/or (b) stress reactivity. In the full sample, none of these assumptions were met. Within the depressed group, two models met our assumptions. The first model examined if the association between emotional abuse and SHAPS scores was mediated by response bias (see Figure 6). Neither emotional abuse, $b = 6.92, t(25) = 1.63, p = .115$, nor response bias, $b = -0.24, t(25) = -0.19, p = .847$, were significantly associated with SHAPS scores after the other was controlled for. A bias-corrected bootstrap confidence interval passed through zero (-2.83, 2.34), indicating that there was no significant indirect effect of response bias.

![Figure 6](image)

*Figure 6.* Model 1, where response bias was hypothesized to mediate the relation between emotional maltreatment and SHAPS scores.

The second model examined if the association between physical abuse and SHAPS scores was mediated by response bias (see Figure 7). Neither physical abuse, $b = 5.52, t(25) = 1.33, p = .197$, nor response bias, $b = 0.98, t(25) = 0.66, p = .514$, were significantly associated with SHAPS scores after the other was controlled for. A bias-corrected bootstrap confidence interval passed through zero (-0.06, 2.97), indicating that there was no significant indirect effect of response bias.
Figure 7. Model 2, where response bias was hypothesized to mediate the relation between physical maltreatment and SHAPS scores.
Chapter 5

Discussion

This is the first study to explore the hypothesis that reward responsivity and stress reactivity are correlated endophenotypes that are related to early adverse experiences and may be mechanisms that underlie anhedonia. Although the full model was not supported, my results did suggest that stress reactivity and reward responsivity are related constructs. The first goal of my study was to examine the differential relation of sexual, physical, and emotional maltreatment to an anhedonic symptom presentation in both MDD patients and controls over and above the contribution of general symptoms of depression and anxiety. I found that sexual abuse was associated with elevated depressive symptoms in general, whereas emotional and physical abuse were specifically associated with anhedonia. Additionally, emotional abuse was more strongly associated with the MASQ AD, whereas physical abuse was more strongly associated with the SHAPS.

The second goal of my study was to examine the differential relation of sexual, physical, and/or emotional maltreatment to (a) cortisol response to a laboratory social stress task and (b) reward learning on a probabilistic reward task. Contrary to hypotheses, no forms of abuse were related to reward responsivity in the full sample. In the depressed group only, childhood maltreatment was positively associated with response bias scores. Also contrary to hypotheses, there were no significant associations between childhood maltreatment and stress reactivity in the full sample or specifically within the depressed group.

The third goal of my study was to examine the relation of cortisol response in a laboratory social stress task and reward learning on a probabilistic reward task to an anhedonic symptom presentation over and above the contribution of general symptoms of depression and anxiety. Contrary to hypotheses, in the full sample response bias was not associated with either measure of anhedonia, and reward learning was
not associated with SHAPS scores. However, as hypothesized, reward learning was negatively associated with the MASQ AD. Within the depressed group, our pattern of results was unexpected. We found that contrary to hypotheses, response bias was positively correlated with the SHAPS, indicating that those with blunted hedonic capacity actually showed a better ability to develop a response bias toward rewards. We also found that contrary to hypotheses, none of the stress reactivity parameters were associated with the anhedonia measures in either the full sample or the depressed group.

The fourth goal of my study was to examine the correlation between parameters of stress reactivity and reward responsivity in the full sample and specifically within depressed individuals. Consistent with hypotheses, in the full sample reward learning and cortisol reactivity were significantly positively correlated. Response bias was not associated with either AUCi or cortisol reactivity, and AUCi was not associated with reward learning.

Finally, the fifth goal of my study was to examine the mediating role of stress reactivity and reward responsivity on the relation between each type of childhood maltreatment and anhedonia symptoms in individuals with MDD and controls. Contrary to hypotheses, I did not find any evidence of mediation in the models that met my assumptions.

**Hypothesis 1: Childhood Maltreatment and Anhedonia**

To my knowledge, this is one of the first studies to examine the relations of different forms of childhood maltreatment on anhedonia in adulthood. In the full sample, individuals with emotional, physical, and sexual abuse had higher scores on both measures of anhedonia than those without abuse. My results also suggested that emotional abuse was preferentially related to anhedonia as measured by the MASQ AD over and above other symptoms of depression, such as general distress and anxious arousal. However, emotional abuse did not show this preferential association with anhedonia as measured by the SHAPS. This pattern of results was reversed for physical abuse. I found that physical abuse was preferentially associated with the SHAPS, but not the MASQ AD, over and above other depressive
symptoms. On the other hand, sexual abuse did not show a preferential association with anhedonia, and was instead associated with greater depression symptoms in general.

The finding that our results differed depending on which measure of anhedonia was being used suggests that different types of abuse may be related to different types of anhedonia. The SHAPS exclusively measures hedonic capacity, whereas the MASQ AD taps into hedonic capacity (e.g., “Felt like nothing was very enjoyable”) in addition to anticipation (e.g., “Looked forward to things with enjoyment”) and motivation (e.g., “Felt like it took extra effort to get started”). The lack of association between emotional abuse and the SHAPS after controlling for general distress may imply that emotional abuse is not associated with hedonic capacity over and above other depressive symptoms. However, emotional abuse may be preferentially associated with other aspects of anhedonia that are measured by the MASQ AD, such as motivation and anticipation. Alternatively, physical abuse was primarily associated with hedonic capacity as opposed to anticipation and motivation. Finally, sexual abuse did not have a preferential association with anhedonia, suggesting that this form of maltreatment may be a risk factor for a variety of depressive symptoms and general psychological distress. The mechanisms underlying the differential relation of emotional and physical abuse with different facets of anhedonia is unclear at present, and was not the focus for the current study. However, one possible explanation for the specific association of physical abuse with blunted hedonic capacity is that being a victim of frequent physical pain and injury may disrupt neural circuitry relevant to the ‘liking’ of rewards. Although I was unable to find prior research that examined this association in individuals with histories of physical abuse, research with chronic pain patients has suggested that chronic pain can result in dysfunction in the ventral striatum and medial prefrontal cortex (mPFC) – areas of the brain that are important for hedonic capacity (Baliki, Geha, Fields, & Apkarian, 2010; Berridge & Kringelbach, 2013; Leknes & Bastianm 2014; Martikainen et al., 2013). Alternatively, features of emotional abuse (such as parental neglect and antipathy) may more strongly affect cognitions about anticipating and receiving rewards instead of the
actual liking of those rewards. For example, if caregivers do not provide rewards or provide rewards in a highly inconstant manner (whether that be physical rewards such as food or social rewards such as affection), it is possible that this may alter psychological and neurological mechanisms that are related to reward anticipation and motivation.

The hypothesis that different forms of abuse may be relevant to the development of different features of anhedonia is further supported by drawing on research findings on how different forms of abuse are preferentially associated with different symptom profiles in MDD. For example, Arata, Langhinrichsen-Rohling, Bowers, and O’Brien (2007) studied the relation between different forms of abuse and symptoms of hopelessness, suicidality, and negative affect in addition to overall depression. Their results indicated that different forms of abuse and different combinations of abuse predicted different sets of MDD symptoms, as well as different severities of these symptoms. Additionally, Holshausen, Harkness, and Bowie (2016) found that depressed adolescents and young adults with psychotic symptoms were more likely to report a history of sexual abuse or multiple forms of abuse than those without psychotic symptoms. They also found that participants with psychotic symptoms were over twice as likely to report physical abuse, although this was not statistically significant. Although none of this research specifically looked at anhedonia, the results imply that abuse type may be an important predictor of differential effects that can result from chronic victimization. Future research could further investigate the association between abuse type and differential facets of anhedonia by using more precise tools for the measurement of anhedonia in order to more accurately assess how different constructs are related to maltreatment. Additionally, employing a longitudinal design would be useful in gaining insight to how anhedonia develops after the onset of victimization.

Within the depressed group, none of the abuse types were significantly associated with anhedonia as measured by the SHAPS. Similarly, neither emotional nor physical abuse was significantly associated with MASQ AD scores. However, individuals with sexual abuse were approaching significantly higher
MASQ AD scores than those without sexual abuse. This pattern of results was not consistent with my expectations: I had expected that even within the depressed group, all three types of childhood maltreatment would still be associated with more severe anhedonic symptoms, and this association would be especially strong for emotional abuse. Despite the lack of statistical significance, however, it is important to note that effect sizes for some differences were still in the moderate range, and in the hypothesized direction. In particular, within the depressed group the effect sizes for the relations of physical abuse and sexual abuse with the SHAPS are .069 and .053, respectively. Therefore, the trend of results suggests that within the depressed group, similar to the full sample, physical and sexual abuse are related to reduced hedonic capacity. Sexual abuse also showed a trend relation to the MASQ AD, suggesting that it is associated with anhedonia, broadly defined. In contrast, emotional abuse showed little trend for an association with either measure of anhedonia. This may suggest that once an individual is currently in a depressive episode, emotional abuse becomes a less important factor in the prediction of anhedonic symptoms.

Contrary to hypotheses, I did not find that emotional abuse was more strongly related to either depression status or symptoms of anhedonia than physical or sexual abuse. The hypothesis that emotional abuse would be a stronger predictor of anhedonia than other abuse types was based on a wealth of research suggesting that emotional abuse tends to confer the greatest risk for depression (Chapman et al., 2004; Alloy et al., 2006; Spinhoven et al., 2010; Widom et al., 2007). However, limited research has been conducted on how childhood maltreatment is specifically associated with anhedonia, and the findings from the present study may suggest that this relation is distinct (although not independent) from the relation between maltreatment and MDD as a whole. Consistent with my hypotheses, emotional abuse was a strong predictor of anhedonia in the full sample, and this may be especially true for anticipatory and motivational anhedonia. However, physical and sexual abuse were also strongly related to anhedonia, even when other abuse types were controlled for, and physical abuse showed a preferential relation with
hedonic features of anhedonia. Additionally, within the depressed group only, it was actually physical and sexual abuse that were the strongest predictors of anhedonic symptoms. This suggests that there are differences in predicting the onset of MDD versus predicting specific symptoms within MDD, and although emotional abuse is a particularly strong predictor of depression onset, it may not shape the way the syndrome is expressed.

To summarize, all three types of childhood maltreatment were associated with anhedonia in the full sample. However, emotional abuse appeared to be preferentially associated with the anticipatory and motivational aspects of anhedonia and physical abuse appeared to be preferentially associated with hedonic capacity. Although strongly related to anhedonic symptoms, sexual abuse was also related to more severe overall depressive symptoms and general distress. Within the depressed group, physical and sexual abuse were more strongly associated with anhedonia than emotional abuse, although none of these associations were statistically significant due to the small sample size. Despite prior research citing emotional abuse as the strongest predictor of MDD onset, these findings suggest that physical and sexual abuse may also play an important role in the symptomatic expression of depression.

**Hypothesis 2a: Childhood Maltreatment and Reward Responsivity**

Contrary to hypotheses, no forms of abuse were significantly associated with response bias or reward learning in the full sample. Further, within the depressed group, individuals with emotional and physical abuse had *higher* response bias scores than those without abuse, and individuals with a history of physical abuse also demonstrated *better* reward learning than those without. These results are contrary to all of the previous published research on this topic (e.g., Pizzagalli et al., 2005; Bogdan & Pizzagalli, 2006; Pechtel et al., 2013), which found that childhood maltreatment was associated with reduced capacity to develop a response bias toward rewards and reward learning. Although explanations of this result are very speculative due to the lack of similar research findings, a possible explanation for my surprising findings comes from animal models of reward processing, which have found that repeated
exposure to social stressors can actually increase reward salience (Chaijale, Snyder, Arner, Curtis, & Valentino, 2015). In our sample, emotional and physical maltreatment were experienced as social stressors that endured chronically over the course of participants’ childhood. In contrast, sexual abuse, which failed to show a significant relation to the PRT parameters, was, in our sample, typically perpetrated as an isolated event (e.g., a single incident of rape perpetrated by an acquaintance or romantic partner). It is still unclear why chronic childhood stress would be related to increased reward learning only in the context of clinical depression, however. Therefore, future research replicating the current findings in a larger sample of clinically diagnosed participants with exposure to different types and chronicity of lifetime stress is required before firm conclusions can be made.

Also of note is that most of the previous research studies using the PRT did not specifically look at childhood maltreatment and reward responsivity within a clinically depressed group, where inclusion in that group required meeting diagnostic criteria for MDD (Pizzagalli et al., 2005; Bogdan & Pizzagalli, 2006; Pechtel et al., 2013). Instead, these studies examined depression symptoms continuously in general community samples. When looking at the associations between maltreatment, depression severity, anhedonia, and PRT performance in a continuous sample, we did actually obtain findings that were comparable to previous research. Therefore, it is possible that within the depressed group, important individual differences relevant to response bias exist that are masked when conducting analyses in a continuous sample, and there may be other unexamined variables that are relevant in predicting response bias within depressed individuals. It is also possible that having a history of childhood maltreatment can be associated with different reward-related outcomes in individuals with clinical MDD versus in controls. However, the mechanisms underlying this possible relation are unknown, and additional research is needed before conclusions can be made.
Hypothesis 2b: Childhood Maltreatment and Stress Reactivity

In both the full sample and the depressed group only, there were no significant associations between childhood maltreatment and stress reactivity or total cortisol output. However, although not statistically significant, a qualitative examination of effect sizes suggests that within the depressed group, both emotional and physical abuse had a moderate positive association with AUCi and emotional abuse was positively associated with cortisol reactivity (see Table 6). These findings, suggesting hypercortisolemia in the context of maltreatment and depression, are opposite to the hypothesized blunting effect (e.g., Suzuki et al., 2014; MacMillan et al., 2009; Peckins et al., 2012; Carpenter et al., 2010; Harkness et al., 2011). Despite several studies finding a relation of maltreatment to cortisol blunting, several other reports have provided evidence for significantly increased cortisol output in abused groups. For example, research has found that women who had experienced childhood maltreatment tended to show increased cortisol responses to a stress task, and this was especially true in depressed women (Heim, Newport, Bonsall, Miller, & Numeroff, 2001; Heim et al., 2002).

Additionally, Harkness et al. (2011) found that an important factor that should be taken into consideration is the interaction between childhood maltreatment and symptom severity. Their results indicated that mild/moderately depressed people with a history of maltreatment exhibited cortisol hyper-reactivity, whereas more severely depressed participants with childhood maltreatment exhibited cortisol hypo-reactivity. In the current sample I did not have the statistical power necessary to further stratify the depressed group by severity. Thus, future research that has a larger sample size can better investigate this relation. Additionally, future research should conduct prospective research that follows people from the onset of their childhood stress to the onset of depression in order to learn more about the developmental processes of HPA axis dysregulation.
Hypothesis 3a: Reward Responsivity and Anhedonia

Consistent with previous research, the depressed group demonstrated significantly blunted reward learning compared to controls, and, in the full sample, reward learning was negatively correlated with depression severity and with MASQ AD (but not SHAPS) scores. In contrast, in the full sample there was no evidence of a significant relation of depression group, overall depression severity, or scores on the anhedonia measures with response bias scores.

As mentioned previously, response bias scores indicate how good a participant was at the PRT and is similar to their average score across the three trials. On the other hand, reward learning indicates the extent to which a participant was able to improve throughout the task. The finding that depression and anhedonia were associated with reward learning only may suggest that depressed individuals and controls do not significantly differ in their overall ability to exhibit a bias towards rewarding stimuli, but do differ in their ability to develop this bias based on reward history. In other words, compared to controls, depressed individuals have a reduced ability to use reward history to modify subsequent reward-related decisions and to modulate behaviour to achieve rewards. Additionally, although we had hypothesized that response bias would be negatively associated with the SHAPS and the MASQ AD, Bogdan and Pizzagalli (2006) did find that in healthy adults, MASQ AD scores were only significantly associated with response bias in conditions where participants were faced with threat-of-shock or performance evaluation. This may suggest that other variables interact with anhedonia in order to produce blunted response bias scores.

These results also indicate that reward learning is more strongly associated with the construct of anhedonia that is measured by the MASQ AD than the SHAPS. This suggests that anhedonia as a whole is not necessarily predictive of blunted reward learning, and that the non-hedonic constructs of anhedonia (e.g., anticipation and motivation) are more relevant to reward learning than hedonic capacity. Although there is significant evidence that performance on the PRT is associated with MDD and anhedonia, it remains largely unclear if performance deficits are driven by problems with anticipation, motivation,
hedonic capacity, or a combination of the three (Treadway & Zald, 2011). Our finding that different parameters from the PRT are associated with different measures of anhedonia may help to address this issue and can help guide future research on the topic.

In direct contrast, within the depressed group, greater depression severity and higher SHAPS (but not AD) scores were associated with higher response bias scores. In general samples (both in my study and others; e.g., Pizzagalli et al., 2005; Bogdan & Pizzagalli, 2006), higher depression severity tends to be associated with blunted reward responsivity on one or both PRT parameters. However, within MDD, I found that higher severity of depression symptoms and higher anhedonia was associated with heightened response bias (but not reward learning). As indicated previously, research with animals has suggested that chronic social stress is associated with heightened reward salience. It is possible that experiences of childhood maltreatment and other chronic stressors may be partially driving this association in the depressed group. For example, if I examine partial correlations between SHAPS scores and response bias while controlling for physical abuse, the association is no longer statistically significant. It may also be the case that proximal social stress was an important factor, and although we have collected data on participants’ recent stressful life events, that data was not used in the present study. Research also shows that depressed individuals tend to experience more proximal stressors than non-depressed individuals (Monroe & Harkness, 2005; Monroe & Reid, 2009), which may help explain why the observed results were specific to the depressed group. Despite this, as indicated when discussing the positive relation between childhood maltreatment and response bias, it remains largely unclear why response bias would be positively correlated with MADRS and SHAPS scores exclusively in the depressed group. Additional research is needed before any conclusions can be drawn from these results.

**Hypothesis 3b: Stress Reactivity and Anhedonia**

Contrary to hypotheses, there were no significant associations between stress reactivity and anhedonia in either the full sample or in the depressed group. However, the $r$ values obtained for the
positive relation between AUCi and both the SHAPS and MASQ AD in the depressed group would likely be statistically significant in a larger sample. The direction of this relation in the depressed group, however, was contrary to our hypotheses. As mentioned previously, the small sample size made it difficult to account for a variety of factors that may have impacted these results (e.g., depression severity, menopausal status, medications, etc.). To the best of my knowledge, there has been no prior research that specifically examined the relation of anhedonia with cortisol reactivity to a social stress task. Further, while meta-analytic results suggest that depression, in general, is associated with cortisol blunting, to date no studies have been conducted examining the specific trajectory associated with an anhedonic symptom presentation in depression. Indeed, in studies that use other HPA axis paradigms (e.g., the DST), melancholic depression, which is characterized primarily by anhedonia, has been preferentially associated with cortisol hyper-secretion. Therefore, future studies using the TSST are needed use to examine the relation of anhedonia and HPA axis response to acute situational stressors.

**Hypothesis 4: Relation Between Reward Responsivity and Stress Reactivity**

Consistent with hypotheses, in the full sample, cortisol reactivity was significantly positively correlated with reward learning, indicating that individuals with a blunted cortisol reactivity to the TSST also tended to demonstrate blunted reward learning on the PRT. This is the first time that a study in humans has found evidence of an association between stress reactivity and a behavioural operationalization of reward responsivity, and my results further support the hypothesis that reward responsivity and stress reactivity are correlated endophenotypes (Matthews & Robbins, 2003; Pohl, Olmstead, Wynne-Edwards, Harkness, & Menard, 2007; Willner, 2005; Bogdan & Pizzagalli, 2006; Bogdan et al., 2011).

Much of the previous research on the association between stress reactivity and reward responsivity in humans has used neuroimaging methodology to assess reward responsivity. This study provides insight into the reward-related behaviours that are associated with stress responses. Additionally,
the specificity of this relation to cortisol reactivity and reward learning suggests that certain sub-
components of the stress and reward systems may be more highly related to one another than other
components, and that the stress and reward systems are not simply globally related to one another. The
reason why this relation is specific to reward learning and cortisol reactivity is largely unclear at this
point, but both involve attempted adaptation immediately after encountering an environmental stimulus.
This is unlike response bias, which assesses the ability to respond to rewards in general but does not
examine how one quickly changes their behaviour because of rewards; and AUCi, which does not provide
information on the strength of the immediate response of the HPA axis to a stressor. The finding that
reward learning is preferentially associated with cortisol reactivity may imply that these systems are
linked by underlying mechanisms relevant to our ability to quickly process and respond to incoming
information. However, since this study is the first to examine this relation in humans, these explanations
are purely speculative and further research is needed. This finding can also aid in focusing future research
on the neurobiological mechanisms that underlie associations between stress and reward and in guiding
research on why these specific components of the stress and reward systems are related.

**Hypothesis 5: Mediation Analyses**

Based on preliminary results, two mediation models met our required assumptions. The first
model examined if the association between emotional abuse and SHAPS scores was mediated by response
bias within the depressed group (see Figure 6), and the second model the second model examined if the
association between physical abuse and SHAPS scores was mediated by response bias within the
depressed group (see Figure 7). Neither model was significant, suggesting that response bias scores did
not partially account for the association between emotional/physical abuse and SHAPS scores. My results
suggest that although reward responsivity and stress reactivity may be associated with both childhood
maltreatment and anhedonia, they do not act as mediating mechanisms that partially account for the
relation between these variables. However, I did find many significant associations among these
variables. This suggests that even though my theoretical model needs revision, reward responsivity, stress reactivity, and anhedonia are important research targets for gaining a better understanding of how childhood maltreatment is associated with the etiology of depression. These findings also suggest that there are other mechanisms not looked at in my study that may mediate the association between childhood maltreatment and anhedonia. Future research should aim to replicate and expand on these findings in order to enhance and revise current theories about childhood maltreatment and depression, and should investigate other possible variables that may account for the relation between childhood maltreatment and anhedonic symptoms.

**Strengths and Limitations**

This study had a number of strengths. First, we were the first to investigate the relation between the reward system and the biological stress response system by using a behavioural measure of reward learning and a gold standard laboratory stress test. Additionally, instead of only looking at depressive symptoms, we had a control group and a group of participants who met diagnostic criteria for MDD. We also assessed childhood maltreatment using a contextual interview instead of using self-reports, which are more prone to retrospective errors, and we separated childhood maltreatment into emotional, physical, and sexual abuse in order to examine the differential effects of different abuse experiences.

Nevertheless, the results should be interpreted within the context of some limitations. First, the sample size was smaller than anticipated, which affected the power of statistical analyses, particularly involving the depressed group. I interpreted with caution the results for the depressed group based on effect sizes, but firmer conclusions will need to wait until data for our full sample has been collected. The small sample size also made it difficult to take some relevant factors into consideration for analyses, such as stratifying the depressed group based on severity for analyses using cortisol. Second, we used a community volunteer sample, and thus the results may not be generalizable to inpatient, outpatient, and epidemiological populations of depressed individuals. Third, although the CECA uses independent ratings
which helps to reduce depressive recollection biases, this measure still ultimately relies on retrospective self-reports and may not always be perfectly accurate.

Additionally, although the SHAPS specifically addressed the hedonic components of anhedonia, the MASQ AD assessed multiple constructs within anhedonia, which made it difficult to interpret some of the findings. In addition to items assessing hedonic capacity (e.g., “Felt like nothing was very enjoyable”), reward anticipation (e.g., “Looked forward to things with enjoyment”), and motivation difficulties (e.g., “Felt like it took extra effort to get started”), the MASQ AD also had multiple items that seem to assess self-esteem (e.g., “Felt unattractive”; “Felt really good about myself”) and suicidality (“Thought about death or suicide”). Additionally, other items were somewhat ambiguous with regards to what construct they were tapping into. For example, depending on participants’ interpretation, the item “Felt like there wasn’t anything interesting or fun to do” could be referring to their anticipation of upcoming activities or could be referring to their recent hedonic experiences with those activities, which is referring to two different types of anhedonia. Given our findings that different constructs within anhedonia may be preferentially related with different types of maltreatment and different parameters on the PRT, the use of measures that are more clearly associated with these different anhedonic constructs would have been very valuable.

Conclusions and Future Directions

There are three major take-home findings from this study. First, we found that there was a positive association between reward learning on a behavioural reward task and cortisol reactivity to a psychosocial stressor. This is important because it is the first time that this relation has been investigated in humans and it provides support for the hypothesis that blunted reward responsivity and blunted stress reactivity are correlated endophenotypes. Further, this finding implies that these systems are not globally related and that certain sub-systems have a preferential association with one another. Future research can
further investigate this through imaging studies, which will help provide information on the neural time course and neural activation associated with these behavioural and hormonal outcomes.

Second, I found that within the depressed group, response bias on the PRT was positively correlated with emotional and physical maltreatment, depression severity, and anhedonic symptoms. The direction of these associations were opposite to what I had initially hypothesized, and this finding is important because it suggests that our theoretical models surrounding anhedonia and response bias within depression may need revision. Future research with a larger depressed group should examine sources of heterogeneity within the group that may be differentially associated with response bias. Additionally, a larger sample of depressed individuals will allow for examination of the interaction of variables that may be relevant to response bias (e.g., different forms of chronic stress, other symptom profiles in MDD, etc.).

Finally, I found that different types of childhood maltreatment were associated with different constructs within anhedonia. To my knowledge, this is the first study that has examined the association between anhedonia and different forms of maltreatment, and our results imply that different experiences abuse may be important in the development of different anhedonia-related deficits. This finding is important in understanding of the etiology of MDD and anhedonia. Future research should use methodology that can more accurately assess the different constructs within anhedonia through both self-reports and behavioural tasks. For example, in order to behaviourally assess the motivational aspects of anhedonia, we could use the Effort Expenditure for Rewards Task (EEfRT; Treadway, Buckholtz, Schwartzman, Lambert, & Zald, 2009). Additionally, a larger sample of maltreated participants would allow for additional features of abuse to be considered in analyses (e.g., frequency of abuse, the perpetrator(s), interactions between forms of abuse, etc.)

In conclusion, anhedonia and its underlying mechanisms remain an important research target for understanding of the pathology of MDD. This study provides evidence that the reward and stress systems are related, and also suggests that within a clinically depressed group, childhood maltreatment and
depression severity may actually be associated with increased response biases towards reward. Finally, the finding that different forms of maltreatment are associated with different types of anhedonia helps to shed light on the negative outcomes associated with childhood adversity.
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Appendix A
Consent Form

Stress sensitization and reward responsivity in major depression

Information/Consent Form

Background
You are invited to participate in a research project conducted by Dr. Kate Harkness (Principal Investigator), Department of Psychology; Dr. Roumen Milev, Department of Psychiatry; Dr. Linda Booij, Department of Psychology; and Alina Marin, Department of Psychiatry, all at Queen’s University; as well as Dr. Katherine Wynne-Edwards, Faculty of Veterinary Medicine at the University of Calgary. The goal of this project is to learn more about the different ways in which people process information that is stressful and rewarding, and how abnormalities in these two processes are related to depression. This study is supported by a grant from the Ontario Mental Health Foundation.

This study has been reviewed for ethical compliance by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.

What is involved?
You will be asked to participate in two 2.5-hour sessions separated by a week at either Providence Care, Mental Health Services, or Hotel Dieu Hospital. At the first session you will be asked to complete a packet of questionnaires about your mood and to take part in an interview about your mood, medications, drug use, and any other symptoms, as well as an interview about your relationships with your parents and any experiences of abuse. At the second session you will be asked to give a brief speech about yourself and to complete a brief arithmetic test. The speech and arithmetic test will take approximately 10-15 minutes. The purpose of them is to allow us to measure a hormone called cortisol that is secreted during stress. Therefore, over the course of this second session (the speech, test, and a recovery period of relaxation) you will be asked to provide eight saliva samples. For each sample you will be given a small sterilized test tube into which you will spit a small amount of saliva. At the end of the session you will also be asked to complete a task on the computer that involves looking at cartoon faces and making decisions about them. You will receive $50 for your participation to compensate you for your time in attending the sessions.

Will the information be kept confidential?
All questionnaires and interviews you complete will be identified with a code number and your name will not be on any of this material. All information you provide at the interview and on the questionnaires is confidential and will not be shared with anyone. However, if you are in
treatment for depression this information may be shared with your treatment provider(s) with your consent. We may not be able to guarantee confidentiality under the following three conditions: 1) if you reveal that you have abused children or elderly people; 2) if you reveal that children under 16 have been physically or sexually abused or neglected by others; or 3) if you reveal threat to seriously harm yourself or others. In these conditions we may need to disclose information to the proper authorities.

The interviews will be audiotaped and your speech will be videotaped. This is to enable the interviewer to code your responses at a later time. There is a risk of re-identification from voiceprint and/or visual images from the tapes and, therefore, absolute confidentiality cannot be ensured. We will minimize this risk by ensuring that the tapes are only identified by a code number and your name will not be associated with the tapes. Further, all tapes will be stored digitally on a secure, password-protected computer server in the Principal Investigator’s locked lab at Queen’s University. Once we have coded the tapes they will be deleted from the server. The tapes will not be used for any purpose other than coding for data directly related to this study.

The saliva samples will be identified only by a code number. The saliva samples will be mailed from Kingston to Dr. Wynne-Edwards’ secure, locked lab at the University of Calgary for processing and will be stored there in a freezer. The stored hormone material will be kept until our research is finished. No samples will be kept for more than 24 months. No genetic testing will be done on the saliva samples.

Your name will be stored in a master file that matches it to your code number in a password protected computer file on a secure, password-protected server in Dr. Harkness’ secure, locked lab at Queen’s University.

Results from this study may be presented at meetings and may be published. Your name and identifying information will not be given out at these presentations or in any publications. Your study records may be reviewed by the investigators and/or their representatives, the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board for this study, or other regulatory authorities to verify that study procedures are carried out correctly and data is being managed correctly.

What are the risks?
There is a possibility that you may feel uncomfortable with the kind of information we ask for. You may also feel stress and/or psychological discomfort by participating in the speech and arithmetic test. You are free to stop participating at any time by letting the interviewer know. If you experience any psychological discomfort or distress from participating in this study you may let the interviewer know. If your psychological discomfort or distress continues or worsens after leaving the session you should contact your treatment provider or the 24-hour Crisis Line at 613-544-4229.
There are no risks to providing the saliva samples.

**Are there any benefits?**
Please be reminded that this project is strictly for research and will not include any treatment intervention. Therefore, we cannot guarantee that you will receive any personal benefit from participating in this study. However, your participation will be helpful in learning more about depression. You are free to stop participating at any time with no penalty.

**How will I be informed of the results?**
We will be happy to go over the results of the interviews and questionnaires with you. In addition, if you are currently in treatment for depression, with your signed consent, the results of the interviews and questionnaires will be shared with your clinician.

**What are my rights as a participant in this study?**
Your participation is voluntary. Your decision whether to participate or not participate will not affect your treatment in any way or affect your relationship with Queen’s University, Providence Care Mental Health Services, or Hotel Dieu Hospital. If you decide to participate you will be free to withdraw your consent and discontinue participation at any time. If you withdraw from the study, your interview and questionnaire material, as well as any samples you provided, will be destroyed to ensure your confidentiality.

**Who should I contact if I have questions?**
If you have any questions about your participation in this project at any time, please feel free to contact Dr. Kate Harkness at 613-533-2886, Dr. Roumen Milev at 613-546-1101, or the Head of the Department of Psychology, Queen’s University (613-533-2494). If you have questions regarding your rights as a research participant, please contact Dr. Albert Clark, Chair of the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board at (613) 533-6081. You will be given a copy of this form to keep.

Agreement to Participate

I, ______________________________, have read the consent form and all conditions of this study entitled “Stress sensitization and reward responsivity in major depression”. I give consent and I understand that I can withdraw my consent to participate in this study at any time.

I am voluntarily signing this form. By signing this form I agree to participate in this study. I will be given a copy of this form to keep.
Research participant

Signature: _______________________

Date: __________________________

Name: __________________________

Person Conducting the Consent Process:

Signature: _______________________

Date: __________________________

Name: __________________________

By signing below I agree to be contacted about future research studies conducted by the current study investigators that I may be eligible for. I understand that I am free to refuse participation in any study for which I am contacted.

Signature: _______________________

Date: __________________________

Name: __________________________
## Appendix B

**Sample Section of SCID Scoresheet**

### MAJOR DEPRESSIVE EPISODE (Check here if past ___)

<table>
<thead>
<tr>
<th>A1</th>
<th>A. Five (or more) during same 2 weeks. At least one symptom is either A1 depressed mood or A2 loss of interest or pleasure</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2</td>
<td>(2) markedly diminished interest or pleasure</td>
</tr>
<tr>
<td>A3</td>
<td>(3) weight loss/gain; decreased/increased appetite</td>
</tr>
<tr>
<td>A4</td>
<td>(4) insomnia/hypersomnia</td>
</tr>
<tr>
<td>A5</td>
<td>(5) psychomotor agitation/retardation</td>
</tr>
<tr>
<td>A6</td>
<td>(6) fatigue or loss of energy</td>
</tr>
<tr>
<td>A7</td>
<td>(7) worthlessness or excessive guilt</td>
</tr>
<tr>
<td>A8</td>
<td>(8) diminished ability to think or indecisiveness</td>
</tr>
<tr>
<td>A9</td>
<td>(9) thoughts of death, suicidal ideation, attempt, plan</td>
</tr>
</tbody>
</table>

#### A10 MEETS SYMPTOM CRITERIA FOR MAJOR DEPRESSIVE EPISODE

#### A11 B. Clinically significant impairment or distress

#### A12 C. Not due to substance or general medical condition

#### A13 D. Not better accounted for by bereavement

#### A14 CRITERIA A, B, C, AND D ARE “+”

---

A29 Total number of Major Depressive Episodes ___

A30 Date of Onset of Current Episode ___/___/___

A31 Age of Onset of First Episode ___
Appendix C

Sample CECA Interview Questions

1. RELATIONSHIP WITH PARENT FIGURES

MOTHER  
How well did you get on with your mother?  
Were you close?

(AFFECTION)  
Was she affectionate towards you?  
How would she show it? Did you ever wish she were more affectionate?

(COMPARISON-SHIP)  
Did your mother spend much time with you when you were little?  
Did you enjoy this time?  
What sort of things did you do together? Were there any special activities or games?

Could you have a laugh together?

ANTIPATHY  
Was she hard to please?  
IF YES: In what sort of way?  
Was she very critical of you?  
Was she ever cold and distant?  
Did you ever feel she didn’t want you or didn’t like you?  
Did she ever say anything rejecting? What sorts of things would she say?  
How often would she say these things?  
Did she ever argue much with her? What about? How often?

Did she ever push/slap/hit you?  
How often did this happen?  
(Skip to physical abuse section if necessary)

Was your relationship the same when you were younger? Did it change at all over childhood?  
IF YES: When was that? In what way did it change? Why do you think that was?

FATHER  
What was the relationship with your father like?  
Were you close to him? Was it a different relationship from that with your mother?

Was he affectionate towards you?  
How did he show it? Did you ever wish he was more affectionate?

Did your father spend much time with you?  
What sort of things did you do together? What about times when he wasn't working?

ANTIPATHY  
Was he hard to please?  
IF YES: In what sort of way?  
Was he very critical of you?  
Was he ever cold and distant?  
Did you ever feel he didn’t want you around or didn’t like you?
Did he ever say anything rejecting? What sort of thing? How often?

Did you argue much with him?
What about? How often? When did that start?

Did he ever push/slap/hit you? (Skip to physical abuse section if necessary)

Was your relationship the same when you were younger? Did it change at all over childhood?
IF YES: When was that? In what way did it change? Why do you think that was?

RELATIONSHIP WITH SIBLINGS
How well did you get on with your brother(s) and sister(s)?
Did you enjoy spending time with them? What sort of things did you do together?

FAVOURITISM
Were there any favourites in the family?
IF YES; Who is that? In what way are they favoured? By mother or father?
Was that any different when you were younger? In what way?

SCAPEGOATING
Did any one of the children get picked on more than the others?
IF YES: Who? In what way? Which parent did that?

PARENTAL INDIFFERENCE
Did you feel your parents always have time for you and take an interest?
Could you go to them if you are upset or unhappy? Were they usually helpful?

Was that the same for your mother and father?
IF NOT: Which one took more interest? In what way?

(BIRTHDAY)
Did you parents always remember your birthday?
Did you celebrate it in some way?

(MATERIAL CARE)
Did your parents take good care of your material needs?
For example washing your clothes and cooking your meals?
Were you expected to do any of that yourself as you got older?
Did you always have enough to eat?

(SCHOOL)
Were your parents keen for you to do well at school?
Did they give you guidance in choosing courses?
Were they satisfied with your achievements?

Did they take an interest in your choice of career?

(IllNESS)
If you were ill and had to take time off school who would look after you?
Were your parents particularly caring if you were ill? Was that both of them?
Did you get any special treatment if you were ill? What sort of thing?

CHANGES
Did your parents changed at all in the amount of interest they showed in you as you got older?
IF YES: In what way?
Appendix D
TSST Script

START STOPWATCH

Introduction: (Read by interviewer)
“This is [Ann] and [Katherine]. They are from the human resources department at the hospital and have been very generous in volunteering their time to help us with this part of the study. They’ll provide the instructions for this task.”

Instructions: (Read by panel member)
“Listen carefully to these instructions; you will not be given an opportunity to ask questions. Imagine that you are applying for a job in customer service. I am the Director of Customer Relations at the company where you are applying, and I have raised several concerns. The first is that you were fired from your last job and you will now have to convince me that you are still a good candidate. The second is that, based on a review of your application, I believe you may not have all the skills required to do this job. More specifically, I am skeptical about your level of experience. You must now convince me that you are the ideal candidate and I should hire you. At the end of these instructions, you will be given several minutes to prepare a statement to convince my colleague (gesture to colleague), who would be your direct supervisor, and me (slight pause) that you are the right person for the job. Following this preparation period, you will come back into the room to present your statement. My colleague and I will be using our experience to evaluate you in a number of ways, to help determine if you are the right person for the job. Further, we will be video recording your statement for later analysis in the study. The recording will be used to assess your ability to maintain a professional demeanor under stress, including analyzing body language. You will be given 5 minutes to speak, and you must utilize the full 5 minutes. I will tell you when this 5-minute period is over. Remember, you must be as convincing as possible in order to be hired. We also ask that you maintain eye contact with us throughout the task.

The interviewer will be here in the room to make sure everything goes smoothly, but please do not talk to anyone during the preparation period, and please do not ask any questions during your statement. Also, keep in mind that we will not provide you with any feedback during the task. You may feel the urge to use your hands when you begin to speak, but again, please bear in mind your body language will be analyzed. You now have several minutes to prepare your statement.”

[Interviewer escorts the participant out of the room to prep]
10:00 TSST:  [Participant re-enters the room]

[Panel turns on the video camera]
“You will now deliver your statement. Please remember to remain as still as possible. Please go ahead.”

Prompts:
• If there are prolonged pauses in speech, use: “Please continue, you still have time remaining” or “Please continue with your statement” or “Please go on.” [1
  time: 10 seconds; 2
  time: 20 seconds; 3
  time: go straight to questions]
• If participant fails to maintain eye contact, use: “Please maintain eye contact.” [10 seconds]

15:00: say, “You may stop; this task is over.”
Arithmetic Task

(Read by panel member)

“You will now participate in a mental arithmetic task. For this challenge, you will be given a number from which you must continuously subtract 13 as quickly and accurately as possible. If you make a mistake, we will point it out and ask you to start again. I will let you know when this task is over. Please count aloud backwards from 2083 in steps of 13. You may begin now.”

2083  1927  1771  1615
2070  1914  1758*  1602
2057  1901  1745  1589*
2044  1888*  1732  1576
2031  1875  1719*  1563
2018  1862  1706  1550
2005  1849*  1693  1537
1992  1836  1680  1524
1979  1823  1667  1511
1966  1810  1654  1498*
1953  1797  1641  1485
1940  1784  1628*  1472

Prompts:

- If participant says any calculations aloud, say, “Please perform all calculations in your head and say only the number.”
- If participant fails to maintain eye contact, use: “Please maintain eye contact.”
- If participant is taking too long to calculate, say, “Please calculate more quickly” or “Faster please.” (faster than 1 answer per 5 seconds)
- If participant is doing well with the task, say, “Please hurry” or “You’ve made a mistake. Please start again from 2083.” Note: Asterisks (*) represent good places to tell a participant she has messed up and needs to start again.
- If a participant has memorized first numbers (1 answer per second), start at stuck point.

When the timer reads 20:00, say, “You may stop; this task is over.”