Modeling relations between early life interpersonal stress, neural response to social reward, and depressive symptoms in adolescent girls

by

Esther E. Palacios-Barrios

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This dissertation was presented

by

Esther E. Palacios-Barrios

It was defended on

May 31, 2023

and approved by

Jennifer S. Silk, Ph.D., Professor, Department of Psychology

Kathryn A. Roecklein, Ph.D., Associate Professor, Department of Psychology

Lauren M. Bylsma, Ph.D., Associate Professor, Department Psychiatry

Luis E. Flores Jr., Ph.D., Assistant Professor, Department of Psychology

Dissertation Director: Jamie L. Hanson, Ph.D., Assistant Professor, Department of Psychology

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Esther E. Palacios-Barrios, Ph.D.

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Experiencing stressful events early in life is very common and widespread across the globe. Despite strong links between experiencing such stress and developing depression, the factors that drive this association remain unclear. Recent evidence suggests that interpersonal stressors (e.g., maltreatment), compared to impersonal stressors (e.g., poverty), uniquely relate to depression. Therefore, a focus on early life interpersonal stress (ELIS) may be critical for our understanding of the factors that contribute to stress-related depression. Prior work demonstrates that youth who experience ELIS exhibit altered neural response to social reward (e.g., positive social stimuli/ feedback) in reward-related brain regions (e.g., striatum, anterior cingulate cortex). Similar disruptions in neural response to social reward are also noted in studies of youth with depression. However, limited work has examined relations between ELIS, neural response to social reward, and depression all in one study. The present dissertation aimed to synthesize these separate, yet related, bodies of literature by investigating whether 1) ELIS related to altered neural response to social reward, 2) disruptions in neural response to social reward related to depression, and 3) altered neural response to social reward moderated links between ELIS and depression. An exploratory aim further tested whether developmentally relevant interpersonal stress vs. impersonal stress differentially associated with neural response to social reward. Notably, these aims were examined in a sample of adolescent girls (N = 31, M/SD age = 15.94/1.44), which is particularly important given the increases in interpersonal stressors, sensitivity to reward, and risk for depression that occur during this time, especially for girls compared to boys. The participants completed self-report measures of ELIS and depressive symptoms, a clinical interview measuring interpersonal stress vs. impersonal stress, and the fMRI Chatroom Interact Task. Neural response to the peer acceptance > control feedback contrast was examined in regions implicated in reward processing. Unfortunately, multiple regression and moderation analyses did not find significant associations between ELIS, neural response to social reward, and depression. Nevertheless, the present dissertation still provides novel contributions that positions future work to better understand the potential central role of social reward processing in the link between ELIS and depression.

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1.0 Introduction

Early life stress is an umbrella term used to describe stressful events occurring during development that exceed one's ability to cope and which produce frequent or chronic activation of the body's physiological stress response. Such stressors include poverty, natural disasters, community violence, or maltreatment, to name just a few. Exposure to stressful events early in life is lamentably very common and widespread across the globe. In the United States alone, an estimated 1 in 6 youth live in poverty, 1 in 7 youth experience maltreatment, and 3 in 5 adults report having lived through at least one type of adversity before the age of 18 (Fortson et al., 2016; Merrick, 2019).

Experiencing early life stress is largely associated with poorer physical and mental health outcomes later in life (Merrick, 2019; Middlebrooks & Audage, 2008). Among these outcomes, the development of depression is substantially evidenced to be one of the most prevalent (Dube et al., 2003; Lippard & Nemeroff, 2020; Teicher & Samson, 2013). Despite the strong association between early life stress and the onset and maintenance of depression, the factors underlying this link have yet to be determined. Existing research suggests that neural disruptions in reward processing may be central for understanding the emergence of depression following stress exposure (Auerbach et al., 2015; Pizzagalli, 2014). However, limited work to date has comprehensively examined relations between stress, reward processing, and depression all in a single study. Moreover, extant findings are largely based on studies utilizing 1) varying definitions of early life stress, 2) neural responses to either monetary reward (e.g., winning money) or negative social stimuli/ feedback (e.g., angry, sad, fear faces; rejection, exclusion feedback), and 3) samples of adults. The present dissertation sought to advance a better understanding of the link between

stress and depression through a specific focus on 1) early life interpersonal stress, 2) neural response to social reward (e.g., positive social stimuli/feedback), and 3) a homogenous population (i.e., adolescent girls).

1.1 Defining and Focusing on Early Life Interpersonal Stress

Across the expansive literature connecting stress exposure to depression, early life stress is often broadly, variably, and vaguely defined. For instance, poverty and maltreatment are both often used as measures of early life stress, yet there are a multitude of stressors embedded into each (Evans et al., 2013). This not only makes it difficult to interpret results across studies, but by grouping different forms of stress together, researchers make an implicit assumption that all types of adversity shape development and confer risk for depression through the same underlying processes. This limits the identification and understanding of how specific forms of stress impact development and contribute to the onset and maintenance of depression. Research aiming to elucidate the factors underlying the link between stress and depression necessitates models that more distinctly conceptualize the construct of early life stress in order to inform greater mechanistic specificity.

Recent models in the adversity literature theorize that different "dimensions" of environmental experience may drive distinct alterations in neurodevelopment. One such model proposes that "deprivation" (the absence of expected sensory and psychosocial inputs) vs. "threat" (the expectation or presence of harm) differentially shape neurodevelopment (McLaughlin et al., 2014; McLaughlin & Sheridan, 2016). There is support for some, but not all, of these neurobiological predictions. As reward processing is posited to play a significant role in the emergence of stress-related depression, it is essential for current models of adversity to discern the specific types of stress that may exert unique influences on reward-related brain activation. Critically, when it comes to applying the "deprivation vs. threat" model to neural response to reward, specifically in the striatum, the findings are mixed (McLaughlin et al., 2019). Conflicting findings may emerge because dimensional models consider different types of stress but do not account for context. For example, both sexual abuse and community violence are threat exposures, but they differ considerably in the level of direct victimization experienced. By assuming that all exposures within a dimension similarly impact neurobehavioral development, dimensional models are unable to disentangle how such contextually defined differences may contribute to neurobehavioral alterations, as well as risk for depression.

Leveraging frameworks from developmental psychology provides one approach to more clearly operationalizing early life stress in terms of subject-oriented perspectives. Literature from this area of work offers a "*person-centered*" approach, emphasizing the importance of a child's perspective on developmental outcomes (Berk, 2000; Brofenbrenner, 1989; Härkönen, 2001). Within this framework, early relationships are thought to be the initial blueprint for social information processing (e.g., identifying and encoding socioemotional cues). These skills pave the way for social learning as the child develops, which is critical for appropriately responding to social stimuli in social contexts and adaptively navigating social relationships later in life, particularly in adolescence (e.g., with peers). When identifying stressors that could impede these social learning processes, it may be crucial to consider how proximal stressful events are to the child and whether they are directed at the youth. Moreover, research in this domain posits that the closest interpersonal relationships with which a child maintains direct contact (e.g., caregivers, peers) have the strongest influence on the child's development. Drawing from this person-centered

approach, the present dissertation focused on experiences of early life interpersonal stress (ELIS), as social relationships critical for shaping child development. Adopting this person-centered perspective allows for a more meaningful understanding of the development of stress-related depression. The present dissertation sought to operationalize ELIS in ways that capture a range of stressful experiences that are developmentally relevant and occur within the context of a relationship where there is close, direct interaction with the youth. Specifically, the main aims examined maltreatment as a severe form of ELIS, as maltreatment is inherently interpersonal in nature. Additionally, the exploratory aim measured ELIS using conflict with parents and peers, as these are interpersonal stressors that have increased developmental relevance to adolescents. By focusing on ELIS specifically, researchers may gain a clearer and more precise understanding of the underlying factors that link stress and depression.

1.2 ELIS and Depression: Drawing Connections to Social Reward Processing

The connections between ELIS and depression have been well established (Björkenstam et al., 2017; Infurna et al., 2016; Kisely et al., 2018; Mandelli et al., 2015). Youth who experience ELIS are twice as likely to develop depression later in life compared to those without such experiences (Nanni et al., 2012). There is also evidence indicating a dose response relationship, such that those who have experienced multiple forms of ELIS are increasingly likely to develop depression with each additional stressor (Felitti et al., 1998). Moreover, ELIS is associated with a more severe and chronic course of depression, as well as less favorable response and remission outcomes for the treatment of this disorder (Carr et al., 2013; Grant et al., 2004; Williams et al., 2016). Critically, interpersonal stressors (e.g., maltreatment) have been shown to uniquely predict

depression compared to impersonal stressors (e.g., poverty) (LeMoult et al., 2019; Vrshek-Schallhorn et al., 2015).

Growing research indicates that experiencing ELIS disrupts neural responses to social reward (e.g., positive social stimuli/ feedback). For instance, youth with a history of ELIS consistently exhibit hypoactivation in the striatum in response to social reward (Hanson et al., 2021; Herzberg & Gunnar, 2020; Novick et al., 2018; Pechtel & Pizzagalli, 2011). Research in the broader depression literature echo these findings, showing similar disruptions in neural response to social reward (e.g., hypoactivation in the striatum) in youth with depression and depressive symptoms (Forbes & Dahl, 2012; Kwon et al., 2019; Olino et al., 2015). Indeed, alterations in neural response to reward is thought to play a key role in the development and maintenance of depression (Alloy et al., 2016; Davey et al., 2008; Forbes & Dahl, 2012; Treadway & Zald, 2013). Thus, disruptions in social reward processing may be a critical potential factor in elucidating the connection between ELIS and depression.

1.3 Social Reward Processing During Development

Identifying, responding to, and learning from social reward is a complex and dynamic process that occurs throughout childhood and adolescence, making it susceptible to experiences of ELIS and creating vulnerability for depression. The early interactions between a child and their caregiver(s) impact how youth identify and respond to social cues in the environment (Smith & Pollak, 2021). For instance, when caregivers serve as a reliable source of positive interaction, children demonstrate better identification of and greater preference towards positive social stimuli (Pollak et al., 2000; Troller-Renfree et al., 2015, 2017). Importantly, how the child responds to

social cues may then shape the associations the youth learns between social cues and outcomes in their environment (Pollak, 2015). Across development, these previously learned associations are often generalized to novel social situations (e.g., peer relationships) to guide understanding of new experiences and inform behavioral responses. When child-caregiver relationships are set in the context of interpersonal stress, aberrant social signaling may distort how the child learns from their environment. For instance, physically abused children are more likely to believe adults get angry or sad following any kind of social interaction, even positive ones (Perlman et al., 2008). Further, inconsistent social cues in the context of interpersonal stress may alter a child's expectations of social interactions, promoting maladaptive social learning processes. For example, children whose caregivers use harsh parenting are more likely to interpret positive social interactions with parents and peers (e.g., being praised, making a new friend) as negative (Rodriguez, 2006, 2011). This may indicate that children who experience ELIS find positive social exchanges less pleasant or rewarding. Importantly, this downplaying of positive events significantly accounted for the association between harsh parenting and internalizing symptoms. Alterations in social reward processing may predispose a unique vulnerability for depression. Disruptions in how youth respond to and learn from social cues in the environment may lead to perceiving social interactions as less pleasurable, which may in turn reduce motivation to engage in social interactions. Such impairments in perceived pleasure and motivation to pursue social reward (anhedonia) characterize depression.

Studies examining neural responses to reward (e.g., measuring how different regions of the brain activate or deactivate in response to reward) have identified distinct neural hubs in the brain that are sensitive to reward (Barch et al., 2012; Berridge & Robinson, 2003; Haber & Knutson, 2009; Rappaport & Barch, 2020). This "reward system" in the brain is comprised of a network of

connected regions within the cortico-striatal circuit. This includes the striatum (i.e., nucleus accumbens, putamen, caudate) and anterior cingulate cortex (ACC), which is divided into the pregenual (pgACC) and subgenual (sgACC) subregions. The striatum and ACC regions have been shown to activate when anticipating and receiving rewards. The sgACC in particular has been implicated in tracking the value of rewards, while the pgACC is particularly sensitive to positive emotions (e.g., happiness) and involved in regulating emotional responses to rewarding stimuli (Berridge & Robinson, 2003; Haber & Knutson, 2009; Stevens et al., 2011). Blunted activation in the striatum and ACC have been linked to reduced pleasure and motivation to pursue rewards (Barch et al., 2012; Rappaport & Barch, 2020). Critically, youth with a history of either ELIS or depression demonstrate comparable altered neural response to social reward, revealing blunted activation in the striatum and ACC as findings warranting further investigation (Forbes & Dahl, 2012; Hanson et al., 2021).

1.4 ELIS and Social Reward Processing

A growing body of work provides evidence that impairments in social reward processing are a downstream effect of ELIS (Oltean et al., 2022). Children who experience ELIS (maltreatment, institutionalization) demonstrate lower accuracy in identifying positive social stimuli (i.e., happy faces) (Bick et al., 2017; Koizumi & Takagishi, 2014; Moulson et al., 2015; Pollak et al., 2000). This difficulty in identifying positive social stimuli may then decrease the likelihood that positive social stimuli become a social reward that feels pleasant to receive and therefore is sought after. Troller-Renfree and colleagues provide supporting evidence for this, finding that previously institutionalized children who received a foster care intervention prefer to look at positive social stimuli (happy faces) while still-institutionalized children do not (Troller-Renfree et al., 2015, 2017). Importantly, this preference for positive social stimuli was associated with greater social engagement and prosocial behavior, as well as less emotionally withdrawn behavior. This may indicate that children who experience ELIS have a reduced propensity towards positive social stimuli, perhaps finding it less rewarding. If youth who experience ELIS find positive social stimuli and interactions less rewarding, they may be less inclined or find it more difficult to initiate or engage in social interactions. Indeed, adolescents who experience higher parental negativity report lower parental acceptance and slower reaction times to peer acceptance feedback (Tan et al., 2014). Institutionalized children are also less accurate in identifying whom to befriend when deciding between happy vs. angry faces (Moulson et al., 2015). These behavioral studies collectively provide evidence that experiencing ELIS may alter how positive social stimuli are perceived and appraised, which may diminish the pleasantness or rewarding feeling of receiving such stimuli over time. This may translate to a decreased tendency to pursue social reward, as they are not valued as rewarding, which may lead to challenges in navigating social situations.

While very few fMRI studies have examined associations between ELIS and neural response to social reward, there is building neuroimaging evidence that supports the behavioral findings. Initial work indicates a compelling link between ELIS and hypoactivation in the striatum and ACC in adolescents. For instance, adolescents with a history of institutionalization demonstrate reduced striatal reactivity to happy faces (Goff et al., 2013). Adolescents with a history of social deprivation (neglect) also show decreased activation in the striatum in response to happy faces (Hein et al., 2020). Likewise, adolescents who experience greater maternal negativity (a form of negative parenting) exhibit blunted responsivity to peer acceptance feedback

in the striatum and sgACC (Tan et al., 2014). These findings provide preliminary support for the impact of ELIS on adolescent's neural response to positive social stimuli, particularly in the striatum and ACC. Of note, these results are not entirely consistent, as additional studies did not find significant differences in neural response to positive social stimuli in adolescents with either a history of maltreatment or peer verbal abuse (Lee et al., 2017; McLaughlin et al., 2015). However, it is possible that the positive stimuli used in both of these studies (i.e., positive words, social scenes) may not be as salient as positive facial expressions and social feedback in eliciting neural responses. Given that hypoactivation in the striatum and ACC have been linked to reduced pleasure and motivation to pursue rewards, this may indicate that adolescents who have experienced ELIS find positive social stimuli to be less rewarding, which may in turn reduce the motivation to seek out or engage in social interactions. The subsequent social withdrawal and isolation may then increase susceptibility to depression.

1.5 Social Reward Processing in Depression

Numerous studies have explored the link between social reward processing and depression, revealing disruptions in social reward processing that mirror those observed in studies of youth with a history of ELIS. Behaviorally, positive social stimuli (e.g., parental praise, peer acceptance feedback) is consistently rated as less positive and less rewarding among children and adolescents with depression and depressive symptoms (Aupperle et al., 2016; Davey et al., 2011; Vandermeer et al., 2021). Even being confronted with social reward (e.g., positive parental clips, peer acceptance feedback) worsens depressed mood in adolescents with depression and depressive symptoms (Silk et al., 2014; Whittle et al., 2012). Blunted response to social reward may then

translate to reduced motivation to pursue social reward and interactions with others. Indeed, children with a preference for positive social stimuli (happy faces) demonstrate lower withdrawal and internalizing symptoms, and greater social engagement (Troller-Renfree et al., 2015, 2017). Children and adolescents with greater depressive symptoms report being less engaged in peer interaction tasks, and demonstrate significant impairments in task performance such as being less likely to accept other players during the task or working less to receive positive peer feedback (Belleau et al., 2021; Fussner et al., 2018; Kujawa et al., 2017; Kwon et al., 2019). This evidence indicates that, similar to ELIS, depression is associated with finding positive social stimuli less rewarding, having lower mood in response to social reward, and having decreased motivation to pursue social reward.

In another interesting parallel to ELIS research, fMRI studies similarly find that hypoactivation in the striatum and ACC in response to positive social stimuli relates to depression. Children and adolescents at high risk for depression have been shown repeatedly to exhibit blunted striatal response to happy faces and positive peer feedback (Kerestes et al., 2016; Monk et al., 2008; Morgan et al., 2019; Olino et al., 2015; Sequeira et al., 2021). Youth with depression and higher depressive symptoms also demonstrate reduced striatal response to positive social stimuli, including happy faces and parental praise (Goff et al., 2013; Silk et al., 2017; Whittle et al., 2012). In terms of the ACC, familial risk for depression and depressive symptoms have been separately linked to blunted activation in this region in response to social reward (e.g., happy faces, parental praise, and peer acceptance) in adolescents (Henderson et al., 2014; Olino et al., 2015; Whittle et al., 2012). Examining these studies at a broad level, there appears to be compelling support for blunted striatal and ACC response to social reward in youth with depression, indicating that they may find positive social stimuli to be less rewarding.

Despite the emerging evidence linking reduced social reward processing and depression, this finding is not definitive by any means. Many behavioral and neuroimaging studies in samples of older adolescents/ emerging adults do not find this association (He et al., 2019; Healey et al., 2014; Stretton et al., 2021; Wang et al., 2020). Moreover, some studies of adolescents even find that increased, not decreased, striatal activation in response to social reward is related to depressive symptoms (Quarmley et al., 2019; Sequeira et al., 2019). Interestingly, many of these studies involve the use of different types of positive social stimuli/feedback including being evaluated by a peer or being liked by a peer. This is in direct contrast to studies examining the relation between ELIS and social reward processing, as many of those studies widely rely on happy faces as the social stimuli used. So, while the connection between disrupted social reward processing and depression is still supported, the link may be more modest or may vary by how social reward is measured (e.g., happy faces vs. peer acceptance). This emphasizes the importance of further studies that use social stimuli/ feedback beyond what is typically used (e.g., happy faces) in order to increase our understanding of how alterations in social reward processing are related to depression.

1.6 Examining Social Reward Processing as a Moderator

Extensive research has documented the clear association between experiencing ELIS and susceptibility to depression. However, while ELIS is common, not all youth with a history of ELIS subsequently develop depression. Indeed, even though experiencing ELIS significantly impacts the likelihood of depression, the majority of youth with a history of ELIS (as high as 60-70%) exhibit resiliency and do not go on to develop depression (Collishaw et al., 2007; Tsehay et al.,

2020). A growing area of research has been dedicated to identifying biological markers of risk and resiliency to better understand the etiology of stress-related depression. Burgeoning work has demonstrated the moderating role of neural response to reward on the association between ELIS and depression. Specific alterations in neural response to reward (e.g., hypoactivation vs. hyperactivation in the striatum) have been differentially linked to vulnerability vs. resilience to depression following ELIS (Miller et al., 2022). These divergent findings highlight the potential importance of further examining neural response to reward as a moderating factor on the relation between ELIS and depression, such that youth who experience ELIS and exhibit distinct variations in neural response to reward are either protection from or at risk for depression.

In terms of potential biological markers of resiliency to stress-related depression, there is some evidence to suggest that increased neural response to positive stimuli/ feedback in the striatum buffers the negative impacts of stress (Feder et al., 2009). For instance, in a large sample of over 800 young adults (ages 18-22), those with greater ELIS (maltreatment) who had increased reward-related activation in the striatum were protected from anhedonic symptoms (Corral-Frías et al., 2015). Specifically, those with greater ELIS and markedly higher than average striatal activation in response to reward (1 standard deviation above the mean) had lower anhedonic symptoms. These findings were replicated in another sizeable sample of 200 young adults (mean age 19), such that those with higher levels of stress and increased striatal activation in response to positive feedback were buffered against anhedonic symptoms (Nikolova et al., 2012). Relatedly, a study of almost 200 young girls between the ages of 8 and 14 found that experiencing positive events was associated with lower depressive symptoms but only for those with increased reward-related activation in the striatum (Luking et al., 2018). Young girls who experienced positive events and demonstrated significantly higher than average striatal activation in response to reward

(1 standard deviation above the mean) reported much lower depressive symptoms. These studies provide initial supporting evidence that increased neural response to reward may be an indicator of resiliency to the development of depression following ELIS. Specifically, these results suggest that youth who experience ELIS and demonstrate hyperactivity in the striatum in response to reward have lower depressive and anhedonic symptoms.

Regarding neural markers of risk for stress-related depression, a small body of literature has further demonstrated that blunted neural response to reward may be a risk factor for depression following ELIS. In one study, adolescents with and without a history of ELIS (physical or sexual abuse) viewed positive images during an fMRI scan and completed a clinical interview to assess symptoms of depression (Dennison et al., 2016). In this work, when looking across all participants (adolescents with vs. without a history of ELIS), striatal activation was not significantly associated with depressive symptoms. But, when examining the group separately, blunted striatal activation was related to symptoms of depression in the ELIS group. This relation was notably not found in adolescents without a history of ELIS. Additional supporting evidence comes from an EEG study of over 200 emerging adults (Pegg et al., 2019). Participants completed measures of lifetime interpersonal stress exposure and symptoms of depression, as well as an EEG task measuring neural response to social reward (peer acceptance). Reward positivity (RewP), an event-related potential that is associated with striatal activation, was measured in response to social reward. The study found that experiencing greater interpersonal stress and having reduced neural response to social reward was a notable risk for depression. Specifically, those with greater lifetime interpersonal stress and significantly lower than average neural response to social reward (1) standard deviation below the mean) reported greater depressive symptoms. A similar EEG study from the same research group found that emerging adults with high (but not low) sensitivity to

interpersonal stress and reduced RewP to peer acceptance report greater depressive symptoms (Pegg et al., 2021). These studies offer preliminary support that decreased neural response to reward may signify a unique vulnerability to depression following ELIS. The use of both fMRI and EEG neuroimaging techniques particularly demonstrates that youth who experience ELIS and exhibit hypoactivity in the striatum in response to social reward have greater symptoms of depression.

Additional research on the moderating effects of neural response to reward on the association between ELIS and depression would advance our understanding of the development of stress-related depression, as well as greatly inform identification and treatment methods. For instance, in a sample of over 300 young girls aged 8 to 14, reduced RewP to reward was found to predict increased depressive symptoms but only for those who experience high levels of stress, not average or low levels of stress (Burani et al., 2021). Moreover, variations in neural response to reward have been found to predict response to the treatment of stress-related depression, including neurostimulation therapy and antidepressants (Drysdale et al., 2017; Goldstein-Piekarski et al., 2016). However, most studies examining connections between ELIS, neural response to reward, and depression have largely focused on adult populations and tasks that use nonsocial reward (e.g., monetary reward). A specific focus on the adolescent population and neural response to social reward in particular is still clearly needed to better understand the development of stress-related depression. Importantly, a focus on adolescents and social reward could greatly improve specificity, as adolescence is a time when interpersonal stressors, sensitivity to reward, and risk for depression all increase substantially.

1.7 Adolescence as a Critical Developmental Period

Adolescence is a developmental epoch marked by a host of psychosocial and biological changes, increasing sensitivity to ELIS and vulnerability to depression. Adolescence acts as a secondary period of plasticity in social and motivational processing and designates a critical shift in the social realm as peer relationships increase in saliency (Dahl & Forbes, 2010). Indeed, adolescence is characterized by heightened responsiveness to incentives and positive stimuli, and greater reward-seeking behavior (Smith et al., 2012; Steinberg et al., 2008). During this time, adolescents become hypersensitive to peer feedback, making susceptibility to peer influence higher than ever (Andrews et al., 2021).

In concurrence with these behavioral alterations, this period is marked by dramatic neurodevelopment of reward-related structures. For example, reactivity in the striatum and ACC increase during this developmental stage (Casey, 2015; Giedd et al., 2015; Larsen & Luna, 2018; Luna et al., 2010). Changes in the structure and function of the reward circuit during adolescence is thought to underlie the heightened reward-driven behavior during this time period (Galvan, 2010; Schreuders et al., 2018; Somerville et al., 2009). For instance, adolescents show increased activation in reward-related brain regions, including the striatum, in response to being liked by peers (Davey et al., 2010).

Given the protracted neurodevelopment of reward-related structures, these still-developing systems may be influenced by stressful events, such as ELIS (Teicher et al., 2003). For instance, increases in social interactions during this time may generate greater opportunities for interpersonal stress (e.g., conflict in peer relationships). Adolescents, particularly adolescent girls, experience greater levels of interpersonal stress compared to children, adults, and even adolescent boys (Compas & Wagner, 2017; Shih et al., 2006). Critically, a recent meta-analysis has reported

that while interpersonal stress and impersonal stress shape brain development differently in childhood, interpersonal stress is associated with additional notable changes in brain development that occurs during adolescence (Vannucci et al., 2023). These documented impacts of interpersonal stress on brain development may have important implications for depression (Goddings et al., 2014). Depressive symptoms and episodes increase substantially during adolescence, particularly for girls more so than boys (Costello et al., 2003; Kessler, 1994; Kessler et al., 2001). The coinciding reward-related alterations that occur during adolescence may render youth especially vulnerable to developing depression (Davey et al., 2008). For example, alterations in reward-related circuitry, such as hypoactivity in the striatum and ACC, predict depression during adolescence (Auerbach et al., 2015; Forbes & Dahl, 2012). The unique combination of changing social landscapes and brain physiology may make adolescents, particularly girls, especially vulnerable to stress-related alterations in social reward processing that may confer risk for depression.

1.8 Enduring Limitations in the Field

Prior research suggests that disruptions in social reward processing are an important factor in understanding the relation between ELIS and depression. Analogous findings regarding neural response to social reward arise amongst ELIS and depression work. The striatum is reliably found to be deactivated in response to social reward in studies of youth with a history of ELIS or depression. A limited amount of work also suggests blunted ACC activity in response to social reward in youth who experience ELIS and youth with depression. However, major limitations still exist among studies seeking to understand the role of social reward processing on the association between ELIS and depression. Namely, 1) limited studies on ELIS and neural response to social reward, 2) the use of happy faces as the predominant form of positive social stimuli, and 3) operationalizing stress.

One clear limitation is that there is a dearth of studies investigating associations between ELIS and neural response to social reward. Additional investigations between ELIS and social reward processing are critical for furthering our understanding of this association and helping to strengthen links to depression. Another important limitation lies in how social reward is measured in stimuli and tasks. In studies examining ELIS and social reward, the positive social stimulus most commonly used is happy faces. Work examining social reward processing in depression uses more diverse social stimuli and tasks, including peer feedback and evaluation tasks. This highlights a crucial need for studies to look beyond happy faces and employ different types of social stimuli and tasks to better understand the impact of ELIS on social reward processing, which will help inform connections to depression. Finally, recent work suggests that interpersonal stressors more strongly relate to depression compared to impersonal stressors. However, almost all studies of interpersonal stress and social reward processing operationalized ELIS by the experience of institutionalization or maltreatment (specifically, neglect). While these are clear examples of directly experiencing targeted interpersonal stress, they capture more extreme forms of stress. It would be beneficial to not only examine the differential impacts of interpersonal stress vs. impersonal stress on social reward processing but also investigate the impact of other types of interpersonal stressors on neural responses to social reward. Limited studies to date have looked at how other developmentally relevant interpersonal stressors, such as relationship conflict with parents and peers, impact social reward processing. This may help elucidate whether the relation between stress and social reward processing is unique to severe forms of interpersonal stress (e.g.,

maltreatment), inclusive of interpersonal stressors more broadly (e.g., conflict with parents and peers), or generalized to impersonal stressors as well. The present dissertation aimed to address these outlined limitations by 1) contributing to our understanding of the impacts of ELIS on neural response to social reward, 2) using positive social stimuli beyond happy faces (i.e., peer acceptance feedback), and 3) examining the potential differential impacts of interpersonal stress vs. impersonal stress on social reward processing, as well as conceptualizing ELIS in ways that include both severe (i.e., maltreatment) and developmentally relevant (i.e., conflict with parents and peers) interpersonal stressors.

1.9 Current Study

The present dissertation examined 1) associations between ELIS and alterations in neural response to social reward; 2) connections between variations in neural response to social reward and depressive symptoms; and 3) whether neural response to social reward moderates the relation between ELIS and depressive symptoms. An exploratory aim further investigated whether developmentally relevant interpersonal stress vs. impersonal stress similarly impacted neural response to social reward. Notably, the current study focused on adolescent girls aged 14-18. This sample is particularly important given the increases in interpersonal stressors, sensitivity to reward, and risk for depression that occur during this time, particularly for girls compared to boys. The participants in the current study completed the well-validated fMRI Chatroom Interact Task assessing neural reactivity to social feedback (Silk et al., 2012). Given the focus on social reward, neural activation during the fMRI task in response to positive social stimuli (i.e., peer acceptance feedback > control feedback) was examined in regions implicated in reward processing (e.g.,

striatum, ACC). The main aims used maltreatment as a measure of severe ELIS, self-reported retrospectively using the Childhood Trauma Questionnaire (Bernstein & Fink, 1998a). Additionally, current depressive symptoms were obtained using the Mood and Feelings Questionnaire, a self-report depression inventory (Angold & Costello, 1987). The exploratory aims employed developmentally relevant measures of interpersonal stress (parent-child conflict, peer conflict) and impersonal stress (academic, health) derived from the well-validated Child Episodic Life Stress Interview (Adrian & Hammen, 1993).

The following main aims and related hypotheses were tested (as shown in Figure 1):

<u>Aim 1:</u> Examine relations between ELIS and alterations in neural response to social reward.

• Hypothesis 1: Greater ELIS (maltreatment) will be associated with alterations in neural response to social reward (e.g., hypoactivity in the striatum and ACC).

<u>Aim 2:</u> Investigate associations between alterations in neural response to social reward and symptoms of depression.

• Hypothesis 2: Alterations in neural response to social reward (e.g., hypoactivity in the striatum and ACC) will be related to increased depressive symptoms.

<u>Aim 3:</u> Test whether alterations in neural response to social reward moderate the link between ELIS and depressive symptoms.

• Hypothesis 3: Neural response to social reward will moderate the association between ELIS and depressive symptoms, such that those with greater ELIS (maltreatment) and neural disruptions in social reward processing (e.g., hypoactivity in the striatum and ACC) will report increased symptoms of depression.

The following exploratory aim and hypothesis was also tested (as shown in Figure 2):

Exploratory Aim: Explore associations between interpersonal stress vs. impersonal stress and alterations in neural response to social reward.

• Hypothesis: Interpersonal stress (parent-child, peer conflict), but not impersonal stress (academic, health stress), will be associated with neural response to social reward (e.g., hypoactivity in the striatum and ACC).

2.0 Methods

2.1 Participants

The current study included a sample of adolescent girls ages 14-18 originally recruited as a part of a larger study examining how interpersonal vulnerabilities may increase risk for depression and suicidality, particularly in sexual minority girls (girls who endorse same-sex romantic or sexual attractions or behavior, or sexual orientation/identity). The original recruitment goal was 60 participants. However, due to the ongoing COVID-19 pandemic, recruitment was halted at 48 participants, of which 2 were excluded for missing questionnaire/ clinical interview data, 9 were excluded for not completing the fMRI task, and 6 were excluded for excessive movement during the fMRI task. Participants with completed questionnaire/ clinical interview data and usable fMRI data were included in the final sample (N = 31). The final sample was 61% White, 13% Black, 13% Hispanic/ Latino, 10% Mixed Race, and 3% Asian. While the aim of the original study sought to oversample for sexual minority girls, the final sample in the current study was predominately heterosexual/ straight (84%). See Table 1 for descriptive statistics and intercorrelations between study variables.

2.2 Procedures

Participants were recruited through a primary health care clinic at the Children's Hospital of Pittsburgh, study registries, as well as community, internet, and social media advertisements.

Interested youth completed a screener assessing: demographic information (including biological sex, age, ethnicity, sexual orientation, and gender identity), depressive symptoms (Short Form of the Mood and Feelings Questionnaire, SMFQ; Angold et al., 1995), handedness, medication use, serious medical conditions (e.g., concussions), other criteria to determine eligibility for fMRI scan (e.g., metal in body, pregnancy), and previous participation in research studies to determine whether participants had already completed the Chatroom Interact Task. Participants were included in the study if they met the following inclusion criteria: female, ages 14-18, elevated depressive symptoms (raw score of 5 or higher out of 26 on the SMFQ), parent or legal guardian between the ages of 25 to 85, and fluent in English. Participants were excluded from the study if they met one of the following exclusion criteria: presence of neurological disorder or serious medical condition, pregnancy (as assessed by urine screen on day of scan), positive urine drug test on day of scan, left handedness, uncorrected visual disturbance, taking medication that affects the central nervous or endocrine systems (stimulants permitted if not required 36 hours before the scan, presence of other MRI contraindications (e.g., braces), and prior completion of Chatroom Interact Task. Assessments were conducted across two days. On Day 1, participants completed self-report questionnaires and clinical interviews. On Day 2, which occurred within 2 weeks of Day 1, participants completed an fMRI scan at the University of Pittsburgh Magnetic Resonance Research Center.

2.3 Measures

2.3.1 Early Life Interpersonal Stress

The main aims of the current study used maltreatment, as assessed by the Childhood Trauma Questionnaire (CTQ), as a measure of ELIS. The CTQ is a well-validated 28-item self-report retrospective inventory of abuse and neglect (Bernstein & Fink, 1998a). The CTQ contains five subscales each comprised of five items: Emotional Abuse, Physical Abuse, Sexual Abuse, Emotional Neglect, Physical Neglect. Each question on the inventory uses a 5-point Likert scale ranging from never true = 1 to very often true = 5, producing scores of 5 to 25 for each trauma subscale. Consistent with prior studies, total scores were calculated for each participant, with a minimum total score of 25 and a maximum total score of 125 (Bernstein & Fink, 1998b). The CTQ has demonstrated high internal consistency (Cronbach's α = 0.95) and good test-retest reliability (ICC = .88) (Bernstein et al., 1994, 1997).

The exploratory aim of the current study measured ELIS using the overall severity of interpersonal stress and impersonal stress in the past year, as assessed by the Child Episodic Life Stress Interview (CELS) (Adrian & Hammen, 1993; Rudolph & Hammen, 1999). The CELS is a semi-structured contextual threat interview. This interview involves eliciting from the participant detailed information about the stressors they have faced in the past year. Interviewers began by asking a global question about the participant's experience of stressful events using the following prompt: "Has anything happened in the past year that has upset you, or caused you trouble, or have there been any big changes in your family or in your life?" Follow-up inquiries pertaining to specific, developmentally relevant, life domains (e.g., family, friends, school, health) were then made. Interviewers subsequently used detailed questions to elicit information about the context in

which the event occurred, including whether it was expected, prior experience, objective consequences, and emotional and instrumental support available for and used by the participant. Following the interview, an independent rating team, blind to the participant's symptoms and subjective reactions to the events, reviewed the contextual information obtained in the interview. The coders categorized the stressors into domain-specific content areas (e.g., parent-child conflict, peer conflict, academic stress, health stress). For each domain, the coders assigned an overall severity rating referring to how severe the stressor would be for the typical person under the same circumstances. Specifically, the rating represents the severity of threat entailed by the stressor, the coping demand imposed by the stressor, or the amount of readjustment required by the stressor, as would occur to any person of similar age and circumstances. The overall severity rating for each domain ranges from 1 (minimal threat) to 5 (severe threat). High interrater reliability of domains and severity ratings (ICC = .85), and good validity have been reported by users of this interview (Hammen et al., 1999). The current study summed the overall severity scores from the "parentchild conflict" and "peer conflict" domains as a measure of interpersonal stress. Examples of stressors in these domains include conflict between the participant and their parents or peers such as frequent arguments with parent or being isolated/rejected from peers. The current study summed the overall severity scores from the "academic stress" and "health stress" domains as a measure of impersonal stress. Examples of stressors in these domains include academic or health concerns such as failing multiple classes or being injured in an accident.

2.3.2 Depressive Symptoms

The Mood and Feelings Questionnaire (MFQ) Child Version (Angold & Costello, 1987) is a 33-item self-report questionnaire assessing symptoms of depression in youth ages 8 to 18. Youth rate their depressive symptoms (e.g., mood, appetite, sleep, psychomotor functioning, inappropriate guilt and feelings of worthlessness, suicidal ideation) within the past two weeks. Each item is rated on a three-point Likert scale (0 = "not true," 1 = "sometimes," 2 = "true") and summed to create a total score. Scores range from 0-66, with higher scores indicating greater depressive symptoms. Total MFQ scores were used to assess current depressive symptoms. The MFQ Child Version has demonstrated excellent internal consistency (Cronbach's α = .95) and good test-retest reliability (ICC = .80) (Burleson Daviss et al., 2006).

2.3.3 Social Reward Task

The well-validated Chatroom Interact Task (Silk et al., 2012) was used to assess neural response to peer acceptance feedback (example trial shown in Figure 3). The task has been shown to reliably activate reward-related brain regions, including the striatum and ACC. This is an event-related fMRI task that takes the form of a structured online interaction, rather than a free-form "chat," in order to give the impression that subjects and virtual peers are interacting in real time while maintaining sufficient standardization across subjects and repetition across trials for analysis. Participants were told that they would participate in a "chat game" with other girls their age over the internet during the upcoming fMRI visit, although in reality these were "virtual peers" with computer-generated responses. Participants were not led to believe that there would be any interaction beyond the structured games. Participants were asked to choose the top 5 girls that they would be interested in interacting with online at the next visit. They had their own photos taken and provided their own biographical profile, which ostensibly would be viewed by the virtual peers before the fMRI visit.

At the fMRI visit, participants were told that they were matched with 2 of the girls selected from the first visit to interact with during the task. They reviewed the photos and profiles for the selected peers. Pictures of the peers and participant were projected on the screen two at a time, as the subject and virtual peers took turns selecting who they would rather talk to about a series of teen interests (e.g., movies, music). The first block was a control condition in which a dot appeared over the picture of the person on the left or right, and the participant was asked to press a button indicating on which side the dot appeared. The chat game then proceeded in 3 blocks, each containing 15 trials in which a person was chosen (accepted) or not chosen (rejected) to discuss each topic. Topics were presented randomly and repeated in each block. In block 1, the subject chose among the virtual peers. Analyses focus on blocks 2-3, in which the subject was chosen/not chosen (accepted/rejected). The photo of the person making choices was shown at the bottom left corner of the screen and the photos of the other players were shown next to each other in the middle of the screen. At the beginning of each trial, the question "Who would you rather talk to about..." with the selected topic for that trial appeared on the screen for 3 seconds. The photo of the selected person was highlighted, and a line was placed through the photo of the rejected person. The participant pressed a button to indicate whether the person on the left or the right was chosen. Given the focus of the current study on the processing of social reward, only trials involving peer acceptance feedback (i.e., trials in which the participant was chosen by the virtual peer) compared to control feedback were analyzed in the present study.

2.3.3.1 fMRI Data Acquisition

Scanning took place on a Siemens 3T Prisma magnet with a 32-channel phased array coil. Anatomical images covering the entire brain were acquired first using a 3D magnetizationprepared rapid gradient-echo T1-weighted sequence [repetition time (TR) = 2,300 ms, echo time (TE) = 3.93 ms, flip angle = 9 degrees, inversion time (TI) = 900 ms, voxel size = 1 mm3]. Functional images were acquired using multi-band gradient echo-planar (EPI) sequences (60 slices, three-factor multiband) sensitive to Blood Oxygen Level Dependent (BOLD) contrast [T2*] (TR = 1,500 ms, TE = 30 ms, flip angle = 55 degrees, voxel size = $2.3 \times 2.3 \times 2.3$ mm). Field maps were acquired using gradient EPI imaging sequence for correction of field distortions in the functional images with the following parameters: TR = 590 ms, TE1 = 4.92 ms, TE2 = 7.38 ms, voxel size = $2.3 \times 2.3 \times 2.3 \times 2.3 \times 2.3$ mm, flip angle = 60 degrees.

2.3.3.2 fMRI Data Preprocessing and Restricted Voxel-Wise Analysis

Pre-processing was completed via fMRIprep and included the following steps: skullstripping, intra-subject realignment to the first BOLD acquisition volume in the time series, susceptibility distortion correction, co-registration with the anatomical reference via FSL's *bbregister*, spatially smoothing using a Gaussian filter set at 6-mm full-width at half-maximum, motion censoring, percent signal change normalization, and inter-subject registration to a standard stereotactic space (Montreal Neurological Institute-152 template) using a non-linear diffeomorphic registration algorithm and voxel resampling (2mm3).

Post this preprocessing, general linear models (GLM) were constructed using Analysis of Functional Neuroimages (AFNI; http://afni.nimh.nih.gov, Cox, 1996). First-level individual analyses for each participant were calculated by convolving the event timing with the canonical hemodynamic response function modeling the three conditions: peer acceptance, peer rejection, and control feedback. First-level models included nuisance covariates of the second-order polynomial used to model the baseline and slow signal drift, six motion estimate covariates and binary flags corresponding to neuroimaging frames with excessive motion (>2mm). Participants with >20% of total frames censored due to motion were excluded from all analyses (n = 6).
Region of interest (ROI) analyses were completed by combining data from an automated meta-analysis and a commonly used anatomical brain atlas (as shown in Figure 4). This involved combining voxel-wise maps of brain areas involved in reward processing using a mask derived from Neurosynth (Yarkoni et al., 2011), as well as the Harvard-Oxford anatomical atlas available in FSL. Neurosynth (neurosynth.org), is an automated brain-mapping application that uses textmining, meta-analysis, and machine-learning techniques to generate a large database of mappings between neural and behavioral/cognitive states. The current study focused on the term "reward" from Neurosynth's past studies database, which included 922 studies. The Harvard-Oxford Cortical and Subcortical Structural Atlases is a probabilistic atlas provided by the Harvard Center for Morphometric Analysis. Only clusters of > 50 voxels were included and explored in proceeding steps. Combining these data sources allowed for the isolation of brain areas related to reward that were anatomically distinct and did not span multiple areas. Such an approach may overcome issues with voxel-wise testing (e.g., clusters of interest spanning multiple discrete brain regions), as well as challenges with exact neural localization (e.g., portions of discrete brain regions not being involved with a candidate neurobehavioral process) (Woo et al., 2014). Derived ROIs included the left striatum, right striatum, sgACC, and pgACC (as shown in Figure 4). The mean activity for each ROI were extracted for the peer acceptance > control feedback contrast for use in analyses. After ROI extraction of mean parameter estimates, linear regression models were used to examine associations between ELIS, average activation for the peer acceptance > control feedback contrast in each ROI, and depressive symptoms. Analyses were conducted in SPSS Version 28 (IBM Corp., 2021).

3.0 Analytic Plan

The current study aimed to test three main hypotheses: 1) greater ELIS (maltreatment) will be associated with altered neural response to social reward (e.g., hypoactivation in the striatum and ACC), 2) alterations in neural response to social reward will be related to increased depressive symptoms, and 3) disrupted neural response to social reward will moderate the relation between ELIS and depressive symptoms (i.e., those with greater ELIS and neural disruptions in social reward will report increased depressive symptoms). An exploratory analysis also tested the hypothesis that interpersonal stress (parent-child, peer conflict), but not impersonal stress (academic, health stress), will be associated with alterations in neural response to social reward. Age was included as a covariate in all analyses.

To test Hypothesis 1, separate multiple regression analyses were conducted to examine the relations between ELIS (maltreatment measured by total CTQ score, entered as the independent variable) and neural response to the peer acceptance > control feedback contrast in reward-related ROIs derived using the methods described above (entered as the dependent variable, entered in separate models). To test Hypothesis 2, separate multiple regression analyses were performed to examine associations between neural response to the peer acceptance > control feedback contrast in reward-related ROIs (entered as the independent variable, entered in separate models) and adolescent depressive symptoms (measured by total MFQ score, entered as a dependent variable). For Hypothesis 3, separate moderation analyses tested the interaction effects of ELIS (maltreatment measured by total CTQ score, entered as the independent variable) and neural response to the peer acceptance > control feedback contrast is contrast in reward-related ROIs (entered as the independent variable, entered as a dependent variable).

(measured by total MFQ score, entered as the dependent variable). Related to the exploratory analysis, separate multiple regression analyses were performed to test associations between interpersonal stress (measured by summing the severity ratings for parent-child conflict and peer conflict, entered as the independent variable) vs. impersonal stress (measured by summing the severity ratings for academic stress and health stress, entered as the independent variable) and neural response to the peer acceptance > control feedback contrast in reward-related ROIs (entered as the dependent variable, entered in separate models). Formal tests were conducted to assess whether the relations between interpersonal stress vs. impersonal stress and neural response to social reward in the reward-related ROIs were statistically significantly different from each other using an extension of the Fisher z transformation that is formulated to test the difference between two dependent correlations while considering the correlations between the variables of interest (r between interpersonal stress vs. impersonal stress) (Meng et al., 1992). To reduce Type I error, for analyses conducted under each aim, the p-values were adjusted based on the Benjamini & Hochberg False Discovery Rate Correction (Benjamini & Hochberg, 1995).

4.0 Results

4.1 Aim 1: Examining Relations Between ELIS and Neural Response to Social Reward

Using the methods described above, four anatomically distinct reward-related ROIs were derived and used for analyses: left striatum, right striatum, sgACC, and pgACC. Associations between ELIS (maltreatment) and neural response to social reward in each ROI were examined separately (as shown in Table 2). Multiple regression analyses did not indicate significant relations between total CTQ scores and neural response to the peer acceptance > control feedback contrast in the left striatum ($\beta = .08$, SE = .02, p = .70), right striatum ($\beta = .26$, SE = .02, p = .17), sgACC ($\beta = -0.003$, SE = .02, p = .99), or pgACC ($\beta = .27$, SE = .01, p = .14), when controlling for age.

4.2 Aim 2: Investigating Associations Between Neural Response to Social Reward and Depressive Symptoms

Associations between neural response to social reward in each of the derived rewardrelated ROIs and depressive symptoms were examined (as shown in Table 3). Multiple regression analyses did not show significant relations between neural response to the peer acceptance > control feedback contrast in the left striatum ($\beta = .003$, SE = 2.79, p = .99), right striatum ($\beta = .13$, SE = 3.05, p = .48), sgACC ($\beta = -0.29$, SE = 4.11, p = .12), or pgACC ($\beta = .37$, SE = 4.39, p = .06), and total MFQ scores when controlling for age.

4.3 Aim 3: Testing the Moderating Effects of Neural Response to Social Reward on the Link Between ELIS and Depressive Symptoms

Separate moderation analyses were conducted to investigate the moderating effects of each of the derived reward-related ROIs on the relation between ELIS and depressive symptoms (as shown in Table 4). For each moderation analysis, the predictor variable was the total CTQ score, and the outcome variable was the total MFQ score. Separate moderation analyses were performed with neural response to the peer acceptance > control feedback contrast in the left striatum, right striatum, sgACC, and pgACC as the moderator variable. There were no significant moderating effects of neural response to the peer acceptance > control feedback contrast in the left striatum (B = -0.25, SE = .53, p = .65), right striatum (B = .08, SE = .52, p = .87), sgACC (B = -0.22, SE = .54, p = .68), or pgACC (B = -0.46, SE = .84, p = .58), on the relation between total CTQ score and total MFQ score when controlling for age.

4.4 Exploratory Aim: Exploring Connections Between Interpersonal Stress vs. Impersonal Stress and Neural Response to Social Reward

Associations between interpersonal stress vs. impersonal stress and neural response to social reward in each ROI were examined separately. Multiple regression analyses did not indicate significant relations between interpersonal stress and neural response to the peer acceptance > control feedback contrast in the left striatum ($\beta = -0.14$, SE = .13, p = .5), right striatum ($\beta = -0.3$, SE = .11, p = .15), sgACC ($\beta = .002$, SE = .08, p = .99), or pgACC ($\beta = -0.13$, SE = .08, p = .53), when controlling for age (as shown in Table 5). Multiple regression analyses did not show

significant relations between impersonal stress and neural response to the peer acceptance > control feedback contrast in the left striatum ($\beta = -0.07$, SE = .14, p = .74), right striatum ($\beta = .03$, SE = .12, p = .9), or pgACC ($\beta = .07$, SE = .08, p = .73), when controlling for age. However, there was a significant negative association between impersonal stress and neural response to the peer acceptance > control feedback contrast in the sgACC ($\beta = -0.45$, SE = .08, p = .02), when controlling for age (as shown in Table 6). In order to test whether the relations between interpersonal stress vs. impersonal stress and neural response to social reward in the reward-related ROIs were significantly different from each other, an extension of the Fisher z transformation test was performed (Meng et al., 1992). The relations between interpersonal stress vs. impersonal and neural response to social reward in the left striatum ($\Delta r = 0.04$, z = -0.16), right striatum ($\Delta r = 0.23$, z = -0.17), and pgACC ($\Delta r = 0.22$, z = -0.91) were not statistically different (p > .05). However, the relations between interpersonal stress and neural response to social reward in the sgACC ($\Delta r = .47$, z = -2.01) were statistically different from each other (p < .05).

5.0 Discussion

5.1 Summary

The present dissertation aimed to elucidate the potential factors that drive the wellestablished association between ELIS and depression. Motivated by prior research, neural response to social reward was examined as a central factor in understanding the link between ELIS and depression. Three main aims investigated whether: 1) ELIS related to alterations in neural response to social reward, 2) disruptions in neural response to social reward related to depressive symptoms, and 3) neural response to social reward moderated links between ELIS and depressive symptoms. An exploratory aim evaluated differential associations between developmentally relevant interpersonal stress vs. impersonal stress and neural response to social reward. In all of these aims, neural response to social reward in four reward-related brain regions were examined (right striatum, left striatum, sgACC, and pgACC ROIs). Regarding the main aims, no significant associations were found between ELIS and neural responses to social reward, nor between disruptions in neural response to social reward and depressive symptoms. There were no significant moderating effects of neural response to social reward on the relation between ELIS and depressive symptoms. Pertaining to the exploratory aim, while there were no significant associations between interpersonal stress and neural response to social reward, impersonal stress was significantly associated with reduced activation in response to social reward in the sgACC. Results notwithstanding, it is important to contextualize and discuss three discernable areas in which the methods and results of the current study differs from prior research: 1) operationalizing ELIS and its relations to social reward processing, 2) measuring neural response to social reward,

and 3) the potential links between hyperactivation in the pgACC and depression. Examining these differences in detail may facilitate a better understanding of the results and provide direction for future research.

Operationalizing ELIS

The main aims of the current study operationalized ELIS using total maltreatment, inclusive of all types of abuse and neglect experiences, which are considered severe forms of interpersonal stress. This approach was taken since maltreatment is the most commonly used measure of ELIS in studies of social reward processing. Interestingly, prior studies of ELIS and social reward processing have largely used samples with histories of neglect specifically, and found consistent associations between experiences of neglect and reduced striatal activation in response to social reward (Goff et al., 2013; Hein et al., 2020). Certain models of adversity use these findings to support the notion that distinct "dimensions" of stressful experiences may relate to specific neural alterations. One such model theorizes that deprivation (e.g., neglect) vs. threat (e.g., abuse) are associated with differentiated neural alterations in response to social rewards (McLaughlin et al., 2014; Sheridan & McLaughlin, 2014). Regarding neural response to social reward, this model contends that deprivation is associated with hypoactivation in the striatum while threat is associated with hyperactivation in this brain region (McLaughlin et al., 2019). However, empirical support for this notion remains to be seen. One study of abuse and neural response to the passive viewing of "social scenes and images" did not find neural differences between participants with a history of abuse and control participants (McLaughlin et al., 2015). Another study using the same stimuli found that while participants with a history of abuse did initially show hyperactivation in the striatum, a history of abuse was related to increased depressive symptoms only for those with hypoactivation in the striatum (Dennison et al., 2016). While there

is inconclusive evidence that neglect vs. abuse have differentiated neural alterations in response to social rewards, this may indicate a unique phenotype for vulnerability to depression following stress. Specifically, youth with a history of maltreatment, regardless of type, and hypoactivation in the striatum in response to social reward are particularly susceptible to depression. Indeed, blunted striatal response to reward has been identified as a potential marker of risk for depression following ELIS (Miller et al., 2022). This underscores the importance of continued investigations into the potential moderating role of social reward processing on the relation between ELIS and depression.

Pertaining to the exploratory aim, interpersonal stress, but not impersonal stress, was hypothesized to be related to disruptions in neural response to social reward. This hypothesis was motivated by recent work showing that, compared to impersonal stress, interpersonal stress is uniquely related to alterations in reward-related brain regions (Vannucci et al., 2023). Contrary to the hypothesis, no significant associations between interpersonal stress and neural response to social reward were found in the current study. Notably, the exploratory aim operationalized ELIS using developmentally relevant interpersonal stressors (conflict with parents and peers). As discussed, prior studies of ELIS and neural response to social rewards have largely focused on severe forms of ELIS, mainly neglect. The results of the current study may indicate that less severe forms of ELIS, such as conflict with parents and peers, do not have significant impacts on neural response to social reward. However, one study has found that adolescents who experience greater negative parenting exhibit blunted responsivity to social reward in the striatum and sgACC (Tan et al., 2014). Thus, continued investigations into the relations between developmentally relevant stressors and neural response to social rewards are still needed, as limited studies have assessed this to date.

Finally, the second part of the exploratory aim tested whether impersonal stress related to alterations in neural response to social reward, and it was hypothesized that it would not be. Unexpectedly, impersonal stress was found to be significantly associated with reduced activation in response to social reward in the sgACC. This may indicate that the impact of stress on social reward processing extends to all experiences of stress more generally, regardless of the interpersonal component. Yet, there is mounting evidence from the adversity literature detailing the unique impacts of interpersonal stress vs. impersonal stress on the development of distinct neural hubs. Specifically, interpersonal stressors (e.g., maltreatment) are linked to disruptions in brain networks that are central for emotional and social processing and learning (e.g., amygdala, ventral striatum), while impersonal stressors (e.g., poverty) are related to impairments in cognitive systems that are implicated in memory and executive functioning (e.g., hippocampus, subregions of the prefrontal cortex) (Bick & Nelson, 2016; Brito & Noble, 2014). These differences are thought to emerge due to the nature of the stressor, such that interpersonal stressors violate a child's expectations of safety and security, thereby altering how they respond to and learn from social cues, and thus activating or deactivating brain regions that are implicated in emotional and social processing and learning (Smith & Pollak, 2021). This notion is consistent with a recent theoretical framework positing that the primary goal of the human brain and other physiological systems (e.g., immune system) is to maintain social safety, thus boosting sensitivity to social cues and the enhancing the importance of social support and connection (Slavich et al., 2023). Taken together, there is growing evidence from prior work showing that interpersonal stress vs. impersonal stress have independent influences on brain development, and future work examining relations between ELIS and neural response to social reward should focus on brain regions implicated in emotional and social processing (e.g., amygdala, ventral striatum).

Measuring Neural Response to Social Reward

Even though aberrant reward processing is thought to be a key factor in the development of stress-related depression, extant findings are largely based on studies utilizing monetary reward (e.g., winning money). This is problematic for several reasons outlined in a recent review, including that the monetary reward tasks that are most commonly used in studies of reward processing (e.g., the monetary incentive delay task) lack behavioral output and correlate poorly with self-reports, leaving the interpretation of the results susceptible to bias (Nielson et al., 2021). A specific focus on social reward (i.e., positive social stimuli/ feedback) may better contribute to our understanding of the development of depression following stress, particularly in adolescence. During this developmental time period, reward-related brain regions undergo significant neurodevelopment, coinciding with increased sensitivity to social cues and feedback as well as increased risk for depression (Dahl & Forbes, 2010). Indeed, the saliency of social reward as opposed to monetary reward during adolescence is supported by a growing number of EEG studies in both the adversity and depression literatures finding that youth with a history of either ELIS or depression demonstrate disruptions in neural response to social, but not monetary, reward (Ait Oumeziane et al., 2019; Rappaport et al., 2019; Zhang et al., 2020). Therefore, it is important for studies examining neural alterations in reward processing in relation to ELIS and depression to move away from the use of only monetary rewards and employ social reward tasks.

That being said, only a few fMRI studies have examined relations between ELIS and neural response to social reward. While these studies have reported clear links between experiencing ELIS and having reduced striatal response to social reward, the stimuli largely used to measure social reward in these studies is happy faces. The use of happy faces as social stimuli has helped establish a reliable connection between the experience of ELIS and hypoactivation in the striatum.

Critically, studies investigating relations between social reward processing and depression have leveraged more diverse social stimuli, including peer acceptance and parental praise feedback. Tasks that use such social stimuli have reported associations between depression and altered neural responses to social rewards in regions beyond the striatum, including the ACC and other subregions of the prefrontal cortex (PFC) (Davey et al., 2011; Olino et al., 2015; Silk et al., 2017). Studies examining neural response to peer acceptance and parental praise feedback in samples of depression also find corresponding behavioral output and correlations to self-reports. For example, youth with depression rate peer acceptance and parental praise feedback as less rewarding, report worsened mood in response to these social rewards, and engage less with positive social feedback (Davey et al., 2011; Kujawa et al., 2017; Silk et al., 2014; Vandermeer et al., 2021). Nevertheless, it is important to note that the findings of reduced response to social reward in samples with depression are not conclusive or even perfectly uniform. Some studies do not find any significant associations between neural response to social reward and depression, while others actually report opposing results to those found in the ELIS literature, such that increased striatal response to social reward is linked to depression (Quarmley et al., 2019; Sequeira et al., 2019). The type of stimuli used to measure social reward may be one important factor driving these contradictory findings. As previously mentioned, studies of ELIS and social reward processing predominantly use happy faces, while studies of social reward processing and depression have pivoted to more complex social stimuli/ feedback including being evaluated by a peer or being liked by a peer. Crucially, neural response to social reward could differ as a function of the type of stimuli used. Not only could the neural response to *looking* at happy faces be different from the neural response to being accepted by a peer, but neural response to being accepted by a peer could further differ from neural response to being evaluated by a peer. There is an apparent need for studies of ELIS and social

reward processing to move beyond happy faces and use more innovative and ecologically valid measurements of social reward. There is additional need to clarify the relations between ELIS, depression, and neural response to varied types of social reward (e.g., peer acceptance, parental praise, peer evaluation).

The current study leveraged the well-validated Chatroom Interact task, an fMRI task measuring neural response to social feedback from peers. The present dissertation used the peer acceptance > control feedback contrast to assess neural response to positive social feedback as compared to a baseline. Although the use of this social reward task in relation to ELIS is relatively novel and addressed a needed gap in the literature, the current study did not find significant associations between ELIS and neural response to positive social feedback. Interestingly, many studies using this task report significant differences in neural response to the peer rejection > peer acceptance feedback contrast. For instance, one study using this task found that neural response to peer rejection > peer acceptance feedback in the sgACC was negatively associated with peer connectedness and predicted depressive symptoms (Silk et al., 2022). It could be that ELIS and depression are associated with both decreased neural response to peer acceptance and increased neural response to peer rejection, that when contrasted together, capture significant differences in neural response to social feedback.

It is imperative that future work continue developing and employing ecologically valid and reliable tasks that employ positive social stimuli/ feedback. This will help strengthen our understanding of how ELIS and depression influence neural response to social reward across different brain regions, as certain reward tasks and stimuli may activate different brain regions. For instance, one study has found that adolescents with depression showed blunted response to clips of maternal praise > neutral clips in reward-related brain regions, including the ventromedial

prefrontal cortex (vmPFC) and caudate (Silk et al., 2017). Moreover, reward processing involves separate phases including reward anticipation, receipt of reward, and reward learning (Barch et al., 2012; Berridge & Robinson, 2003). Developing and utilizing tasks that not only use different reward stimuli/ feedback, but also measure different phases of reward, could elucidate alterations across different brain regions in samples with a history of ELIS or depression. As mentioned, studies of ELIS and reward processing focus largely on either monetary reward or social reward measured by happy faces. Not surprisingly then, most of the findings center around the striatum. Scarcely any studies have reported on the associations between ELIS and subregions of the PFC. The subregions of the PFC are central for reward learning, and the vmPFC in particular is implicated in updating reward outcome expectancies and allowing for adaptive and flexible learning (Frank & Claus, 2006). Prior work has found that ELIS impairs associative learning and cognitive flexibility (Hanson et al., 2017; Harms et al., 2018). However, the relations between ELIS and social reward learning are still not fully understood.

Potential Role of pgACC in Depression

Evidence from previous studies show that youth with depression demonstrate blunted activation in the striatum and ACC in response to social rewards (Olino et al., 2015; Whittle et al., 2012). Based on this prior work, disruptions in neural response to social reward were hypothesized to be associated with increased depressive symptoms. While the current study did not find significant relations between neural response to social reward and depressive symptoms, the association between hyperactivation of the pgACC and increased depressive symptoms was trending towards significance (p = .06). Though formal conclusions from this finding cannot be drawn, as criteria for statistical significance were not met, this may point to the pgACC as a region of specific interest for further investigation. One other study has reported hyperactivation of the

pgACC in response to social reward in a sample of youth with depression (Davey et al., 2011). The pgACC is implicated in regulating emotional responses to rewarding stimuli, and this hyperactivity of the pgACC in response to positive social stimuli is thought to reflect inability to effectively regulate mood. Indeed, individuals with depression may need to expend extra effort to self-regulate in what is thought to be a compensatory process (Johnstone et al., 2007). This is supported by behavioral findings that youth with depression report worsened mood when faced with social reward (Davey et al., 2011). The potential association between hyperactivation of the pgACC in response to social reward and increased depressive symptoms could indicate a compensatory process in which youth with depression need to work harder to self-regulate their emotions when facing positive social stimuli/ feedback. Further research is needed to explore this potential compensatory process in the pgACC in response to social rewards and relations to depression. Furthermore, depression is a heterogeneous disorder with different phenotypes that may relate to different neural activity. For instance, some individuals with depression may exhibit hyperactivation of the pgACC, whereas others may demonstrate blunted activation in this region. Such heterogeneity might explain why some individuals respond better to certain treatments than others. Recent work highlights this by identifying increased activation in the pgACC as a predictor of treatment response (Godlewska et al., 2018).

5.2 Strengths and Limitations

The current study had several notable strengths that set it apart from prior research and positioned it to make a novel contribution to the literature on stress, reward processing, and depression. First, the present dissertation conceptualized ELIS using a person-centered approach. In other words, ELIS was operationalized in ways that captured a spectrum of stressful experiences that were both developmentally relevant and occurred within the context of a relationship where there is a close, direct interaction with the participant. Specifically, the main aims measured ELIS using maltreatment, a severe form of interpersonal stress, while the exploratory aim measured ELIS using conflict with parents and peers, a developmentally relevant form of interpersonal stress. Prior studies have largely focused on severe forms of ELIS, mainly neglect. Moreover, the current study captured experiences of ELIS using both self-reports and clinical interviews. This may be particularly important given recent work showing that youth's reported experiences of stress are more potently related to depression than objective reports like official records (Danese & Widom, 2020).

Second, the use of the well-validated Chatroom Interact task to assess neural response to social reward (peer acceptance feedback) was a particular strength. Prior studies of ELIS and social reward processing often use happy faces as the social stimuli, which may not stimulate reward-related brain regions beyond the striatum. Moreover, peer acceptance is a particularly salient social reward for adolescents. By using a social reward task that is more ecologically valid and therefore more closely reflects the social experiences of adolescents, the present dissertation was poised to shed light on how ELIS and depression relate to alterations in neural response to social reward.

Third, the recruited sample focused specifically on adolescent girls. Adolescence is a developmental time period marked by increases in interpersonal stress, sensitivity to rewards, neurodevelopment of reward-related brain regions, and depressive symptoms – increases that are more notable in girls compared to boys. This is in contrast to prior studies, which often focus on young adults or adults. A recent meta-analysis suggests that the impacts of interpersonal stress vs. impersonal stress on the brain differ depending on when events occur in development (Vannucci

et al., 2023). Specifically, interpersonal stress, but not impersonal stress, that occurs during adolescence impacts the development of reward-related brain regions. By using a sample of adolescent girls, the current study was positioned to offer important insights into the factors that contribute to stress-related depression in this population specifically.

Finally, although there was no statistically significant support for the main aims, the theory that social reward processing plays a central role in the relation between ELIS and depression is strongly supported by past studies. Moreover, the current study fills in major gaps in the existing literature in terms of the focus on social, as opposed to monetary, reward. Thus, the present study adds to a growing body of research and encourages future investigation of the role of social reward processing in the relation between ELIS and depression.

Despite the strengths of the current study, there were several limitations that should not be overlooked. First, the sample size was small due to recruitment challenges imposed by the COVID-19 pandemic. Only 31 participants completed the questionnaires/clinical interview and had usable fMRI imaging data. This limited the power to detect significant effects, particularly in the moderation analyses. In fact, it is suggested that a sample size of at least 250 subjects are needed for a moderation analysis (Schönbrodt & Perugini, 2013). This is a common issue amongst neuroimaging studies, with 25 subjects being the median sample size of most neuroimaging projects (Marek et al., 2022). Critically, multiple research groups are asserting that to capture reproducible brain-behavior associations, neuroimaging sample sizes should have thousands of participants.

Second, the present dissertation strived to operationalize ELIS using a person-centered approach, which is a novel and necessary endeavor. For the main aims, the participants selfreported their maltreatment history. This suitably assessed each participant's personal experiences with this severe type of interpersonal stressor. For the exploratory aim, the participants underwent a clinical interview to assess the severity of their experiences with developmentally relevant stressors (conflict with parents and peers). However, in line with previous studies, this severity score was calculated without considering the participant's subjective reactions to the stressor. To truly keep with a person-centered approach, future studies should measure subjective interpretations of developmentally relevant stressors in ways that truly capture the child's perspective (e.g., how severe are conflicts with parents and peers *to the child*).

Third, the current study focused on neural response to social reward in four reward-related brain regions: right striatum, left striatum, sgACC, and pgACC. The use of these constrained ROIs may have limited the ability to detect more subtle effects in brain regions outside of these predetermined ROIs. For instance, prior studies consistently find associations between ELIS and hypoactivation in the ventral striatum, as well as blunted activation in the caudate and putamen in samples with depression, specifically. Moreover, limited ELIS and depression work have reported on altered neural response to social reward in the subregions of the PFC, namely, the vmPFC. Future studies could use methods that do not constrain analyses, such as whole brain approaches. However, larger sample sizes are needed for such analyses.

Finally, while the CTQ and MFQ are widely used assessments of maltreatment and depressive symptoms respectively, there was limited variability in these measures within the sample. Only a small proportion of participants reported significant levels of maltreatment and clinically significant symptoms of depression. Moreover, a closer examination of the types of maltreatment reported showed that of those participants that reported experiencing maltreatment, the majority were experiences of emotional abuse and neglect, while only a handful of participants

reported physical abuse or neglect, or sexual abuse. Oversampling for experiences of maltreatment should be considered in future work.

5.3 Future Directions and Conclusions

Studies aiming to elucidate connections between ELIS, neural response to social reward, and depression would benefit greatly from expanding on the present project. First, it is recommended that future studies utilize longitudinal study designs, starting in childhood and following participants through adolescence. This would help identify the developmental trajectory of altered neural responses to social reward following experiences of stress and improve our ability to make connections with adolescent depression. Second, prior studies of ELIS and social reward processing operationalize ELIS using maltreatment, with a specific focus on neglect. Dimensional models posit differences in neurodevelopment based on stressful events related to either deprivation (e.g., neglect) or threat (e.g., abuse). However, there are limited studies testing this theory in regard to social reward processing. Oversampling for children with documented experiences of neglect vs. abuse may help ascertain whether maltreatment overall, regardless of type, or whether neglect vs. abuse specifically, are associated with altered neural response to social reward. Third, investigating associations between developmentally relevant interpersonal stressors, such as conflict with parents and peers, and social reward processing is still needed. This will help speak to how different types of stress relate to altered neural circuitry involved in social reward processing. Finally, it is imperative that future work on the relations between ELIS, reward processing, and depression transition from the use of monetary reward tasks and employ social reward tasks. Additionally, social reward tasks should evolve beyond the use of happy faces, which

seem to only show neural disruptions in the striatum. The use ecologically valid measures of positive social stimuli, such as peer acceptance and parental praise feedback, could expand our knowledge of how ELIS and depression relate to neural responses to positive social stimuli in other reward-related brain regions (e.g., ACC). Moreover, there is an enduring need for the development of other social reward tasks that capture different phases of reward (i.e., anticipation, receipt, learning, reversal learning). Such tasks would activate other reward-related brain regions (e.g., subregions of the PFC) and deepen our understanding of how ELIS and depression may relate to disruptions in these regions.

In conclusion, the present dissertation endeavored to better understand the factors underlying the strong association between ELIS and depression. The role of social reward processing was motivated by prior work, yet limited work to date has tested associations between ELIS, neural response to social reward, and depression. The current study addressed critical gaps in the literature by operationalizing ELIS to capture a spectrum of interpersonal stressors, employing a social reward task, and focusing on a sample of adolescent girls. Nonsignificant results notwithstanding, the current study offers important considerations and strengths that highlight avenues for future research into the role of social reward processing in our understanding of stress-related depression.

6.0 Figures and Tables

6.1 Figures





Figure 1. Main Aims

Aim 1 tested the relations between ELIS (maltreatment) and alterations in neural response to social reward. Aim 2 tested the association between alterations in neural response to social reward and depressive symptoms. Aim 3 tested whether neural response to social reward moderated the association between ELIS (maltreatment) and depressive symptoms.



Figure 2. Exploratory Aim

Exploratory aim tested the relations between interpersonal stress (conflict with parents and peers) vs. impersonal stress (academic stress and health stress) and alterations in neural response to social reward. Exploratory aim tested the relations between interpersonal stress (conflict with parents and peers) vs. impersonal stress (academic stress and health stress) and alterations in neural response to social reward.



Figure 3. Social Reward Task

Example trial of peer acceptance feedback in the Chatroom Interact Task (Silk et al., 2012). The photo of the "virtual peer" making the choice is shown at the bottom left corner of the screen and the photos of the other players (including the subject) are shown next to each other in the middle of the screen. At the beginning of each trial, the question "Who would you rather talk to about..." with the selected topic for that trial appears. The photo of the selected subject is highlighted (indicating a peer acceptance trial), and a line is placed through the photo of the rejected player.



Figure 4. Regions of Interest

Region of interest (ROI) analyses were completed by combining data from an automated meta-analysis mask of the term "reward" derived from Neurosynth (top left) and the commonly used Harvard-Oxford Cortical and Subcortical Structural Atlases (top right). Combining these data sources allows for the isolation of brain areas related to reward that were anatomically distinct and did not span multiple areas. Adapted from "Anatomy of the Brain", by BioRender.com (2022). Retrieved from <u>https://app.biorender.com/biorendertemplates</u>

6.2 Tables

	1	2	3	4	5	6	7	8	9
1. Age	1								
2. CTQ Total	.34	1							
3. Interpersonal Stress	.44*	.34	1						
4. Impersonal Stress	.27	.23	.17	1					
5. MFQ Total	.17	.49*	.17	.2	1				
6. Left Striatum	.12	.1	07	03	.02	1			
7. Right Striatum	.18	.3	16	.07	.16	.9**	1		
8. sgACC	08	03	03	44*	3	.31	.13	1	
9. pgACC	.35	.35	06	.16	.39*	.35	.53**	18	1
Mean	15.94	33.52	4.73	3.58	20.39	-0.46	-0.37	-0.44	0.23
SD	1.44	7.16	1.4	1.2	12.57	0.85	0.77	0.55	0.53
Range	14-18	25-54	2.5-7.5	2-7	4-46	-2.87- 1.77	-2.39- 1.14	-1.55- 0.4	-1.06- 1.65

Table 1. Descriptive Statistics and Intercorrelations Between Study Variables

Bolded values indicate statistically significant at * = p < .05, ** = p < .01; activity for all brain regions is for peer acceptance > control feedback contrast; CTQ = Childhood Trauma Questionnaire, MFQ = Mood and Feelings Questionnaire, sgACC = subgenual anterior cingulate cortex, pgACC = pregenual anterior cingulate cortex, SD = standard deviation.

Model DV	Predictor	β	В	SE(B)	<i>p</i> -value (B)	
T 0.04	T ()		1.52	1 70	4	
Left Striatum	Intercept		-1.53	1./8	.4	
	Age	.08	.05	.12	.68	
	CTQ Total	.08	.01	.02	.7	
Right Striatum	Intercept		-2.21	1.56	.17	
	Age	.1	.06	.1	.59	
	CTQ Total	.26	.03	.02	.17	
sgACC	Intercept		.02	1.16	.99	
	Age	07	03	.08	.71	
	CTQ Total	003	.000	.02	.99	
	-		• • •		. .	
pgACC	Intercept		-2.06	1.02	.05	
	Age	.27	.1	.07	.14	
	CTQ Total	.27	.02	.01	.14	

Table 2. Associations Between ELIS (Total CTQ Score) and Neural Responses to Social Reward (Peer

Acceptance > Control Feedback) in Derived ROIs

Model DV	Predictor	β	В	SE(B)	<i>p</i> -value (B)	
MFO Total	Intercent		-2.93	26.4	91	
	Age	.17	1.47	1.64	.38	
	Left Striatum	.003	.04	2.79	.99	
MFQ Total	Intercept		1.25	26.52	.96	
	Age	.14	1.25	1.64	.45	
	Right Striatum	.13	2.18	3.05	.48	
MFQ Total	Intercept		-2.86	24.96	.91	
-	Age	.15	1.28	1.57	.42	
	sgACC	29	-6.61	4.11	.12	
MFQ Total	Intercept		13.47	25.74	.61	
-	Age	.35	.31	1.63	.85	
	pgACC	.37	8.8	4.39	.06	

Table 3. Associations Between Neural Responses to Social Reward (Peer Acceptance > Control Feedback) in

Derived ROIs and Depressive Symptoms (Total MFQ Score)

 Table 4. The Moderating Effects of Neural Responses to Social Reward (Peer Acceptance > Control

 Feedback) in Derived ROIs on the Association Between ELIS (Total CTQ Score) and Depressive Symptoms

Model DV	Predictor	В	SE(B)	<i>p</i> -value (B)	
MFO Total	Intercept	-6.4	26.81	.81	
	CTO Total	.78	.35	.03*	
	Left Striatum	7.51	17.58	.67	
	CTQ Total x Left Striatum	-0.25	.53	.65	
	Age	.04	1.62	.98	
MFO Total	Intercept	-10.77	25.24	.67	
	CTQ Total	.84	.33	.02*	
	Right Striatum	-2.5	17.39	.89	
	CTQ Total x	.08	.52	.87	
	Right Striatum				
	Age	.2	1.59	.9	
MFO Total	Intercept	-5.11	26.39	.85	
	CTQ Total	.73	.4	.08	
	sgACC	1.24	19.15	.95	
	CTQ Total x	-0.22	.54	.68	
	Age	-0.11	1.51	.95	
MFQ Total	Intercept	-4.45	27.19	.87	
	CTQ Total	.88	.43	.05	
	pgACC	21.6	28.22	.45	
	CTQ Total x	-0.46	.83	.58	
	Age	-0.34	1.58	.83	

(Total MFQ Score)

	Table 5. A	ssociations	Between	Interpersona	l Stress and	Neural Res	sponses to S	Social Re	ward (Pee	r Acce	otance
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Model DV	Predictor	β	В	SE(B)	<i>p</i> -value (B)	
Left Striatum	Intercent		-1.63	1 77	37	
Lett Sulatum	Age	17	-1.05	1.77	.57	
	Interpersonal Stress	-0.14	-0.09	.12	.5	
Right Striatum	Intercept		-2.29	1.56	.16	
-	Age	.31	.17	.11	.13	
	Interpersonal Stress	-0.29	-0.16	.11	.15	
sgACC	Intercept		.02	1.16	.99	
C	Age	-0.08	-0.03	.08	.72	
	Interpersonal Stress	.002	.001	.08	.99	
pgACC	Intercept		-1.97	1.05	.07	
	Age	.41	.15	.07	.05	
	Interpersonal Stress	-0.13	-0.05	.08	.53	

> Control Feedback) in Derived ROIs

Model DV	Predictor	β	В	SE(B)	<i>p</i> -value (B)	
Left Striatum	Intercept		-1.45	1.77	.42	
	Age	.12	.07	.12	.53	
	Impersonal	-0.07	-0.05	.14	.74	
	Stress					
Right Striatum	Intercept		-1.95	1.6	.24	
C	Age	.18	.1	.1	.37	
	Impersonal	.03	.02	.12	.9	
	Stress					
sgACC	Intercent		01	1.03	99	
55/100		05	.01	07	70	
	Impersonal	-0.45	-0.2	.07	.72	
	Stress	-0.45	-0.2	.08	.02	
pgACC	Intercept		-1.87	1.05	.09	
ro	Age	.34	.13	.07	.08	
	Impersonal	07	03	.08	73	
	Stress	.07	.05	.00		

Table 6. Associations Between Impersonal Stress and Neural Responses to Social Reward (Peer Acceptance >

Control Feedback) in Derived ROIs

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