Neural Substrates of Emotion Dysregulation and Self Injury in Adolescent Girls

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Abstract

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Self-inflicted injury (SII) in adolescence is a significant risk factor for later psychopathology and suicide, and may be a developmental precursor of borderline personality disorder (BPD). Research indicates that like adults with BPD, adolescents self-injure to regulate intensely negative emotions. Extensive neuroimaging research implicates the ventromedial prefrontal cortex (vmPFC), the amygdala, the anterior cingulate cortex (ACC), and their interconnections in the generation and regulation of emotional experience and expression. However, very little imaging research has been conducted with samples selected for SII, and only one functional imaging study with a small sample size has been conducted with self-injurying adolescents. In the present study, we used functional magnetic resonance to examine neural reactivity during presentation of facial exoressions of emotion among adolescent girls, ages 13-19, who engage in SII (n=21), compared with normal controls (n=21). An event-related design was implemented in which participants viewed angry, fearful, and neutral facial expressions during a gender typing task. Regions of interest analyses were performed for the amygdala, subgenual ACC and vmPFC/orbital PFC. Although study hyoptheses were not supported, this research marks an important step towards a more developmental approach to studying BPD. Further developmental considerations for null findings are discussed.

Suicide is an alarmingly prevalent international health concern. According to the World Health Organization (2012), nearly one million people die by suicide each year—more than those who die by war and homicide. Suicide and suicide-related behaviors affect people across cultures, ethnicities, and sexes, and are especially common among those with mood disorders, personality disorders, and other forms of psychopathology (for a review see Crowell, Derbidge, Beauchaine, in press). Since suicide is not specific to any psychiatric disorder, it is difficult to address without focusing squarely on the behavior itself.

The number of deaths by suicide among teens—which has remained stable for over a decade—is especially alarming. In 1999, 1796 youth ages 13-19 died by suicide in the US, accounting for 11.4% of all deaths in that age range. These data led the Surgeon General to release a report calling for improved prevention and intervention programs (U.S. Public Health Service, 1999). This report was followed in 2001 by a strategy for prevention from the US Department of Health and Human Services Center for Mental Health Division. Yet despite such calls to action, in 2008 suicide remained the third leading cause of death for youth ages 13-19, accounting for 12.7% of all mortalities (Centers for Disease Control and Prevention). Government reports and research publications have since reemphasized the importance of increasing our understanding of biological and psychological vulnerabilities to, and environmental risk and protective factors for, suicide and suicide-related behaviors.

Suicide ideation and attempts are often precursors to suicide, as are nonfatal self-inflicted injuries with and without intent to die (Briere, & Gil, 1998; Caspi et al., 2003). Estimated prevalence rates of self-inflicted injury (SII) among community samples of adolescents range from 13-46% (Lloyd-Richardson, Perrine, Dierker, & Kelly, 2007; Madge et al., 2008; Ross &

Heath, 2002). This wide range may derive from differences in ways questions are posed across studies (open-ended questions and interviews tend to provide lower estimates than checklists of self-injurious behaviors; Lloyd-Richardson et al., 2007; Madge et al., 2008). Although sex ratios change across the lifespan, women are overall 1.5 times more likely to self-inflict injury than men (Hawton & Harris, 2008). In adolescence, girls are three times more likely to self inflict injury than boys, although boys are more likely to die by suicide.

Suicide-Related Behaviors: Definitions

Consistent with previous research, we conceptualize self-injury across a spectrum of thoughts and behaviors (see e.g., Crowell, Beauchaine, & Linehan, 2009; Nock, Joiner, Gordon, Lloyd-Richardson, & Prinstein, 2006), including suicidal ideation, non-suicidal SII, and suicidal SII or suicide attempts (Crowell et al., in press). Self-inflected injury refers to all purposeful acts of self-injury enacted with the intent to cause bodily harm or death. Such behaviors can be subdivided into (1) suicidal SII, including all deliberate acts of bodily harm enacted with some degree of suicidal intent, including ambivalent or unequivocal; and (2) non-suicidal SII, including all deliberate acts of bodily harm enacted without any degree of suicidal intent. We consider these overt acts separately from the covert cognitive process of suicidal ideation.

Some have argued that relations between these suicide related behaviors may be more complex than previously thought (Brown, Comtois, & Linehan, 2002; Nock et al., 2006), yet examining them in aggregate has many conceptual advantages. Although large discrepancies between rates of suicide completion and SII exist, a history of self injury remains the single best predictor of later suicide across all ages—regardless of whether self-injury was associated with intent to die (Asarnow, 2011; Wilkinson Kelvin, Roberts, Dubicka, & Goodyer, 2011; Joiner, Conwell, et al., 2005; Nordström, Samuelsson, & Asberg, 1995; Shaw-Welch, 2001). In turn,

conservative estimates indicate the eventual rate of suicide completion among suicide attempters is about 15% (Bongar, 2002). Furthermore, among depressed samples of teens, past non-suicidal SII predicts suicide attempts more strongly than past suicide attempts (Asarnow, 2011; Wilkinson et al., 2011). This relationship is not accounted for by depression severity.

In addition, biological vulnerabilities to and environmental risk factors for suicidal thoughts and behaviors overlap considerably (see Joiner, Brown, & Wingate, 2005). Such data have led our research group and others to propose a developmental progression that, among vulnerable individuals, begins with ideation or mild self-injury (e.g., scratching self, picking at wounds) and progresses to behaviors that increase in lethality and degree of suicidal intent (Crowell et al., 2009; Crowell et al., in press). Hence, many researchers conceptualize a spectrum of suicide related thoughts and behaviors, including ideation, non-suicidal self-injury (NSSI), and suicide attempts (Brent et al., 1988; Stanley, Winchel, Molcho, Simeon, & Stanley, 1992). Identifying individuals early in this high-risk trajectory is an urgent public health concern (Crowell et al., in press).

A Developmental Psychopathology Perspective on Suicide

One influential approach to studying the onset and course of psychopathology is the developmental psychopathology perspective, which has only recently been applied to understanding suicide risk (Beauchaine et al., 2009; Crowell et al., 2009; Crowell et al., in press). Developmental psychopathologists examine relationships among biological (e.g., genetic, neural, hormonal), psychological (e.g., cognitive, affective), and social (e.g., familial, cultural, contextual) factors that potentiate or attenuate risk for psychopathology across development (Sroufe & Rutter, 1984). In recent years, vulnerabilities have come to refer to pre-existing *biologically based* traits or predispositions that confer risk for psychopathology, whereas risk

factors have come to refer to *environmental* influences that increase the likelihood of psychopathology, either alone or in combination with vulnerabilities (see e.g., Rutter & Sroufe, 2000). For example, trait impulsivity, which is highly heritable (see Beauchaine & Neuhaus, 2008) may render young males vulnerable to developing externalizing psychopathology only in neighborhoods high in violence and criminality (e.g., Lynam et al., 2000).

Our research group has recently proposed a developmental model of self-injury and borderline personality disorder (Beauchaine et al., 2009; Crowell et al., 2009; Crowell et al., in press). Although not all self-injuring adolescents develop BPD, an assumption of our model is that SII marks significant risk for the disorder. In brief, we propose that trait impulsivity, present very early in life, is a principle predisposing vulnerability to BPD. Trait impulsivity, marked behaviorally by difficulty planning ahead and a propensity to act without forethought, derives from heritable compromises in central dopaminergic and serotonergic function (for recent reviews see Beauchaine & Gatzke-Kopp, press; Beauchaine, Neuhaus, Zalewski, Crowell, & Potapova, 2011; Sagvolden, Johansen, Aase, & Russell, 2005). This vulnerability may be potentiated by and transact with high risk family environments through repeated intermittent reinforcement of emotional lability and aggression via coercive interaction patterns (Beauchaine, Gatzke-Kopp, & Mead, 2007; Snyder, Edwards, McGraw, & Kilgore, 1994; Snyder, Schrepferman, & St. Peter, 1997). In these interactions, the aggressiveness and high level of arousal displayed by the child is met or exceeded by the parent in response and the conflict escalates from there. Eventually, the escalation terminates the aversive interaction, reinforcing aggression, heightened autonomic arousal, and emotional lability in both parties (Patterson, Chamberlain, & Reid, 1982; Patterson, DeBaryshe, & Ramsey, 1989; Patterson, Degarmo, & Knutson, 2000; Patterson, Dishion, & Bank, 1984). In turn, impulsive and dysregulated

individuals are likely to affiliate with deviant peer groups, within which contagion effects (Prinstein, Boergers, Spirito, Little, & Grapentine, 2000) and social reinforcement (Nock & Prinstein, 2004, 2005) act as mechanisms through which SII is acquired and maintained as a maladaptive emotion regulation strategy. Over time, SII and related behaviors become canalized, contributing to the development of BPD and related forms of psychopathology such as antisocial personality disorder (Beauchaine et al., 2009). In this model, emotion dysregulation moderates trait impulsivity (see e.g., Beauchaine, 2012).

In the present study, we seek to better characterize the emotion dysregulation component of SII among self injuring adolescent girls. We propose that by adolescence, emotion dysregulation will be evidenced by abnormal neural processing of emotional information, consistent with research reported in the literature on adults with BPD. This is an important step toward (1) identifying biological vulnerability to self injury in younger participants than recruited to date, and (2) verifying the assumption that self-injury and BPD share overlapping vulnerability. Almost all research conducted with teens has been conducted at the behavioral level of analysis (e.g., Hilt, Cha, Nolen-Hoeksema, 2008; Lloyd–Richardson et al., 2007; Nixon, Cloutier, & Aggarwal, 2002; Zlotnick, Donaldson, Spirito, & Pearlsteig, 1997). In this study, I examine whether similar neurobiological responses to emotion characterize adolescents with SII, compared with findings from studies of adults with BPD.

Emotion regulation comprises all processes through which emotional experience (e.g., sadness) and expression (e.g., crying) are shaped in the service of adaptive functioning (Thompson, 1994). Some of these are automatic whereas others are volitional (see e.g., Goldsmith & Davidson, 2004). In contrast, emotion dysregulation refers to patterns of emotional experience and/or expression that interfere with adaptive functioning and appropriate goal-

directed behavior. Dysregulated emotions are evident in many if not most forms of psychopathology (Beauchaine, 2001; Beauchaine et al., 2007). Hence, in our developmental model, emotion dysregulation moderates heritable trait impulsivity to potentiate risk for self-injury (see above).

Neural Circuitry of ER

Neuroanatomical models of emotion regulation implicate the amygdala, the ventromedial prefrontal cortex (vmPFC), the anterior cingulate cortex (ACC), and their interconnected brain regions (Esposito, Spirito, Boergers, & Donaldson, 2003; Phillips, Ladouceur, & Drevets, 2008; Goldsmith, Pollak, & Davidson, 2008). This circuitry is involved in the generation of emotions, automatic responses to those emotions (i.e., automatic/unrestricted emotion regulation), and volitional regulation of emotions (for a review, see e.g., Phillips, Drevets, Rauch, & Lane, 2003; Phillips et al., 2008).

Neuroimaging studies demonstrate amygdala activation in response to several types of negatively valenced or unpleasant stimuli (Calder, Lawrence, & Young, 2001). Damage to the amygdala impairs generation of appropriate emotional experience in response to emotionally salient stimuli (Calder et al., 2001; Phillips et al., 2003, 2008). This includes impairments in identification of the emotional significance of stimuli (Adolphs, Baron-Cohen, & Tranel, 2002; Shaw et al., 2005). Neuroimaging studies demonstrate that the vmPFC is active during responses to various emotional stimuli, including mood induction and recall of personal memories and emotional information (Drevets, 2000; Phillips et al., 2008). Lesions to the vmPFC in rats impair autonomic nervous system responses to emotional stimuli (Verberne & Owens, 1998). Finally, neuroimaging studies evidence increased activation of the subgenual anterior cingulate cortex (sgACC) in response to several types of emotion eliciting stimuli (e.g., Elliot, Rubinsztein,

Sahakian, & Dolan, 2000; George, Ketter, Parekh, Horwitz, Herscovitch, Post, 1995; Mayberg et al., 1999). Damage to the sgACC impairs visceral and neuroendocrine responses to emotional and rewarding stimuli (for a review, see Drevets, Ongur, & Price, 1998). Extensive anatomical connections with neural circuitry involved in ER (amygdala and vmPFC), autonomic (brainstem nuclei), neuroendocrine (hypothalamus), and reward (ventral striatum) functions support the likely modulation role the sgACC has on these functions (Drevets, Savtiz, & Trimble, 2008).

Using functional magnetic resonance imaging (fMRI), several researchers have demonstrated modulatory effects of the vmPFC on the amygdala during voluntary emotion regulation in healthy adults (e.g., Urry et al., 2006). The amygdala is densely connected to the vmPFC (Le Doux, 1992; Shaw et al., 2005), and its activation increases reliably during unrestricted viewing and up-regulation of negative emotion, and decreases during voluntary regulation while healthy (and sometimes unselected) adults view negatively valenced stimuli (e.g., Schaefer et al., 2002; Urry et al., 2006). Additionally, as amygdala activation increases, vmPFC activation (extending to the ventral ACC) decreases (and vice versa), as revealed in several coactivation and functional connectivity analyses (Kim et al., 2004; Heinz et al., 2005; Schmitz & Johnson, 2006; Das et al., 2005; Pezawas et al., 2005; Williams et al., 2006) suggesting an inhibitory role of the vmPFC on the amygdala. Moreover, the degree of coactivation between the amygdala and vmPFC during and immediately following instructions to regulate emotion predicts successful ER on among healthy adults (Banks, Eddy, Angstadt, Nathan, & Phan, 2007).

Although much attention has been paid to neural processing of emotion regulation in adults, very little is known about how these processes develop in adolescents. The majority of findings to date suggest that adolescents process emotions similar to adults (Killgore & Yurgelun-Todd, 2006; Killgore & Yurgelun-Todd, 2007; Todd, Evans, Morris, Lewis, & Taylor, 2011), with

some evidence of broader neural activation in frontal regions (for a review see Monk, 2008), and perhaps a positive bias in the evaluation of the meaning of faces that decreases with age (Schepman, Weyandt, Schlect, & Swentosky, 2012). Activations in the PFC, amygdala, and ACC with perhaps more diffuse activation in frontal regions, have also been related to volitional and automatic emotion regulation in adolescents (McRae et al., 2012; Joormann, Cooney, Henry, & Gotlib, 2012).

Neural Circuitry of ER and BPD

Neuroimaging studies of adults with BPD support the presence underlying dysfunction in the neural circuitry of ER (e.g., Donegan et al., 2003; Herpertz et al., 2001; Minzenberg, Fan, New, Tang, & Siever, 2007; Driessen et al., 2004; Schmahl et al., 2003; Schnell, Dietrich, Schnitker, Daumann, & Herpertz, 2007; Silbersweig et al., 2007; Beblo et al., 2006). Across several emotion eliciting paradigms, dysfunction in the rostral/subgenual ACC, vmPFC, and amygdala are most commonly noted. Increased activity in the amygdala relative to controls during automatic/unrestricted responding to negative simuli is particularly robust among individuals with BPD (see Goodman, New, Triebwasser, Collins, & Siever, 2010). Although examination of volitional ER among those with BPD has provided intriguing new evidence of altered function of vmPFC and amygdala activity relative to controls (e.g., Koenigsberg et al., 2009, Silbersweig et al., 2007), more basic evaluations of emotional responding are better replicated (e.g., Herpetz et al., 2001; Donegan et al., 2003; Minzenberg et al., 2007). Furthermore, pictures of facial affect represent a set of well standardized images that can be easily categorized according to specific emotions (e.g., fear and anger; Ekman & Friesen, 1976).

When comparing negative relative to neutral facial expressions, adults with BPD show increased amygdala activity and increased PFC activity, perhaps indicating hyper-sensitive and

reactive emotional responding coupled with less efficient neural communication between these regions (Donegan et al., 2003; Minzenberg et al., 2007). This functioning may modulated by the sgACC, which evidences substantial deactivation during negative relative to neutral faces in BPD. In contrast, preliminary examinations suggest that the pattern of activation in the amygdala and sgACC may be reversed when the emotion being examined is anger (Minzenberg et al., 2007). In addition, these changes in activation from negatively valenced to neutral stimuli are greater among individuals with BPD than among non-clinical controls. Notably, depressed adult males with a history of SII relative to depressed adult males without a history of SII also evidenced abnormal responding to anger (Jollant et al., 2008), with increased activity in the ventral PFC in response to angry versus neutral faces.

In sum, despite alarming rates of adolescent suicide (Grunbaum et al., 2002) and self-injury (Lloyd–Richardson et al., 2007; Madge et al., 2008; Ross & Heath, 2002), research on the pathophysiology of self-injury in adolescents is scarce (see e.g., Crowell et al., 2012). A promising line of research in adults has implicated neural functioning related to emotion dysregulation (e.g., Goldman et al., 2010). Emotion dysregulation is the most pursued and promising line of research in SII in adolescents (e.g., Crowell et al., 2011). One mechanism of emotion dysregulation and SII may be dysfunction in the neural processing of emotional information, similar to that of adults with BPD, a question well suited for examination with fMRI BOLD activation. To date, only one study has examined emotional responding to negatively valenced images in adolescents who engaged in nonsuicidal self-injurious behavior (n=9) and found increased activity in the amygdala, hippocampus, and anterior cingulate cortex compared to healthy controls (n=9), similar to results in adults with BPD (Plener, Bubalo, Fladung, Ludolph, & Lulé, 2012). Hence, we propose that self injuring adolescents will evidence

similar neural correlates of emotional responding as adults with BPD. In addition, we hypothesize that changes in activation from negatively-valenced (i.e., fear and angry faces) relative to neutral stimuli will be greater in SII adolescents than typically developing controls. Functional neuroimaging represents a new direction for this line of research. Understanding the neural bases of SII in adolescents may ultimately lead to improvements in diagnostic specificity, intervention targets, and prediction of treatment response among these distressed youth.

Method

Participants

Self-injuring (n = 22) and healthy control (n = 22) adolescent females between ages 13 and 19 years completed the study. Among these, one participant from the self-injuring group was excluded due to excessive motion (greater than 8 mm from middle volume). One participant from the control group was excluded because she was taking a SSRI for depression, even though she did not report a current or lifetime mood disorder. Therefore, 21 individuals per group were included in all analyses. Twenty-six participants identified as Caucasian, 6 as Hispanic Caucasian, and 7 as biracial (4 mixed African American and Caucasian, 1 Filipino and Caucasian, 1 Japanese/Korean/Caucasian, and 4 Hispanic/non-Caucasian). Males were not included given lower prevalence rates of self-injury, which would have made timely recruitment difficult. In addition, the targeted sample size was inadequate for evaluating sex effects. Among the self-injuring and control participants, 4 and 1, respectively, were recruited from samples who participated in previous research on self-injury in our lab and a neighboring research center. These participants provided consent to retain their contact information for future studies. The remaining participants were recruited through direct mailings to families, postings on Craigslist, city bus advertisements, and flyers, brochures, and letters that were sent to mental health

providers, community centers, pediatrician's offices, and public schools and libraries. Study procedures were approved by Seattle Children's Hospital Institutional Review Board. Preliminary screening interviews with a trained research assistant took place by phone. Interviews were conducted with all families, regardless of recruitment source.

Phone Screening Interview

Parents and youth were interviewed separately for confidentiality purposes. While describing limits to confidentiality, however, adolescents were informed that their parents would be made aware of reported self-injury. To our knowledge, this did not lead to any youths dropping. The phone interview comprised mostly of questions generated by the researcher toassess (1) lifetime and current self-injurious behavior(s); (2) known diagnosis for lifetime and current bipolar disorder and schizophrenia (for exclusion purposes); (3) current major depressive disorder based on the depression subscales of the Adolescent Symptom Inventory (ASI; Gadow & Sprafkin, 1997) and the Youth's Inventory (YI; Gadow et al., 2002); (4) possible mental retardation; (6) current medication(s) taken; (7) handedness; and (8) MRI safety screening. Controls were screened out if they reported any lifetime self-injury event or any current or lifetime psychiatric diagnosis on the measures used. Self-injury participants were screened out if they reported current or lifetime diagnosis of bipolar disorder, schizophrenia, or fewer than 3 self-injurious episodes in the last year or 5 self-injurious episodes in their lifetime.

Given our primary objective of assessing group differences in regional BOLD activation in the amygdala, subgenual region of the ACC, and vmPFC, anyone who reported contraindications to MRI scanning (e.g., braces, permanent metal retainers, implanted metal devices, physical anomalies such as a history of seizures and severe head injuries, claustrophobia) was excluded. Left-handed participants were also excluded, which allowed for comparisons in neural correlates

without a brain lateralization confound. In addition, those taking mood stabilizers, antipsychotics, and/or tricyclic antidepressants were excluded given widespread effects of these substances on brain function. Self-injuring adolescents who were taking SSRIs (n = 5) were allowed to participate[1]. Given the large number of self-injuring individuals who are prescribed SSRIs, excluding such individuals could have compromised external validity. Qualifying families were invited to participate in a more comprehensive lab visit screen to assess their eligibility more fully.

Lab Visit 1: Parent and Adolescent Interviews

Following written informed consent, participants completed a series of questionnaires and interviews. If, based on these interviews and questionnaires, all eligibility criteria were met, a mock scanning session was conducted to train participants on the behavioral tasks (described below), and to assess their comfort level and ability to remain still during scanning. Adolescents were paid $25 for participation during this visit. If eligible, families were invited to participate in a final visit including neuroimaging. Another $25 monetary incentive was provided for attendance.

As mentioned previously, inclusion in the SII group required at least 3 self-injury episodes in the preceding year or at least 5 lifetime. Self injury episodes were defined as any instance of intentional self-injury with or without intent to die. Participants who indicated SII during the phone screen were evaluated further at the lab visit using the Lifetime Suicide Attempt and Self-Injury Interview (L-SASI Count; Linehan & Comtois, 1996). Current disorders, including conduct, generalized anxiety, panic, obsessive-compulsive, posttraumatic stress, social phobia, schizophrenia, dysthymia, bipolar, anorexia, and bulimia were assessed using screening cut-offs established for the Youth's Inventory (YI; Gadow et al., 2002), a child self-report measure, and

the Adolescent Symptom Inventory (ASI; Gadow & Sprafkin, 1997a), a parent-report measure. We used a simple or algorithm. Lifetime histories of psychiatric disorder were assessed using questions from the whole life module of the computerized Diagnostic Interview for Children (C-DISC-IV; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). Participants who screened positive for current or lifetime diagnosis of schizophrenia or bipolar mood disorder were excluded. Controls were excluded for meeting any screening cut-off for current or lifetime history of DSM-IV diagnosis with the exception of simple phobia, somatic disorders, and ADHD, based on the ASI or YI. In each case, participants were not receiving any psychiatric treatment. Finally, SII adolescents who met criteria for substance dependence based on the C-DISC-IV (with the exception of nicotine and marijuana) interview were also excluded. Parent and adolescent interview measures included the following:

Computerized Diagnostic Interview Schedule for Children (C-DISC; Shaffer et al., 2000). The DISC is a commonly used, highly structured and reliable interview that assesses a wide range of DSM-IV-TR (APA, 2000) psychiatric disorders. We used the computerized version for ease of administration and scoring. This included both parent and youth reports. Although concerns over the validity of self-report diagnosis among children have been raised (see e.g., Renou, Hergueta, Flament, Mouren-Simeoni, & Lecrubier, 2004), the highly structured nature of the interview allows for a convenient administration due to minimal training requirements for interviews and reliable responses (Shaffer et al., 2000) with moderate internal consistency (κ = .60 parent, .10 youth, .48 parent and youth; Pelham, Fablano, & Massetti, 2005). In the validation sample, one year test-retest reliabilities ranged from .43 to .96 parent (n=84), .25 to .92 youth (n=82), and .48 to .86 parent and youth combined. Notably, reliability for major

depressive disorder diagnosis was .65 parent (*n*=84), .92 youth (*n*=82), and .65 parent and youth combined.

Structured Clinical Interview for DSM-IV Axis II (SCID-II; First, Gibbon, Spitzer, Williams, & Benjamin, 1997). The SCID-II is a widely used semi-structured interview that assesses Axis II psychopathology. We used it to assess BPD symptoms. The 15-items from the BPD section evidence strong inter-rater reliability (κ = .91; Lobbestael, Leurgans, Arntz, 2010; Maffei et al., 1997) and internal consistency (α = .71-.94; Maffei et al., 1997).

Lifetime - Suicide Attempt Self-Injury Count (L-SASI; Linehan & Comtois, 1996). This instrument assesses lifetime history of self-injury, including detailed information such as intent and severity for the first, most recent and most severe incidents. It was designed for use with adults, but has since been used with adolescents. No psychometric data on the L-SASI have been published.

Kaufman Brief Intelligence Test, 2nd ed. (KBIT-2; Kaufman & Kaufman, 2004). Adolescent IQ was assessed using the KBIT-2, a brief measure of verbal and nonverbal cognitive ability with excellent psychometric properties. Test-retest reliabilities range from .88 to .92, with strong internal consistencies for composite IQ scores (α = .89 to .96). Potential participants with composite IQ scores less than 85 (*n* = 0) were excluded.

MRI Safety Screening Form. Participants were interviewed in person to determine MRI eligibility, as a follow up and update to the phone interview.

Youth's Inventory (YI; Gadow et al., 2002). The YI is a 120-item checklist of DSM-IV symptoms that yields both dimensional scores and diagnostic cut-offs. Items are rated on a 4-point scale (0 = never, 1 = sometimes, 2 = often, and 4 = very often). In the validation sample,

internal consistencies ranged from .66 to .87, and two week test-retest reliabilities ranged from .54 to .92. Specificity and sensitivity for the scores range from adequate to excellent**.**

Youth Self-Report (YSR; Achenbach, 1991). The YSR is a 112-item self-report measure of child behavior problems, including several psychopathology subscales and broadband externalizing and internalizing factors. It is a well-validated measure with excellent psychometric properties. In a large validation sample, internal consistencies ranged from .71 to .95, and test-retest reliabilities ranged from .47 to .79.

Suicide Ideation Questionnaire (SIQ; Reynolds, 1987). Using the SIQ, adolescents were screened at each study visit for levels of suicide ideation. There are two versions of this measure based on grade level. The SIQ is comprised of 30-items and is used for students in adolescents in Grades 10-12. The SIQ-JR is comprised of 15 items and is designed for Grades 7-9. Both versions are scored on a 7-point scale, scored by summing scores from each item (0 = *I never had this thought* and 6 = *I had this thought every day*). Internal consistency is high for both the SIQ (α = .97) and the SIQ-JR (α =.93-.94). SIQ and SIQ-JR scores correlate moderately with constructs such as depression and hopelessness (.52-.70), indicating predictive validity. Test-retest reliability for the SIQ-JR is .89 (Reynolds & Mazza, 1999).

Adolescent Symptom Inventory (ASI; Gadow & Sprafkin, 1997). Like the YI, the ASI is a 120-item checklist of DSM-IV symptoms that yields both dimensional scores and diagnostic cut-offs. Items are rated on a 4-point scale (0 = never, 1 = sometimes, 2 = often, and 4 = very often). However, it is a parent-report version. Need internal consistency and test-retest reliabilities here. Concurrent validity with the CBCL has also been established, with correlations ranging from r = .41 to r = .80 for similar emotional and behavioral problems.

Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001). The CBCL is a well validated parent-report measure of child behavior problems, including both internalizing and externalizing subscales and broadband scores . Internal consistency estimates for the 2001 version range from .95 to 1.00, Inter-rater reliability estimates range from .93 to .96 and Internal consistencies range from .78 to .97.

Family demographics questionnaire: This is a brief 20-item questionnaire designed to capture basic demographic information about the parent and adolescent.

Lab Visit 2

Prior to neuroimaging, adolescents were assessed for current use of any psychoactive substances. None reported such use. Adolescents were also administered a urine pregnancy test and none were positive for pregnancy. The MRI safety screening form was also again reviewed to ensure safety before starting the imaging protocol. Following scanning, adolescents completed several measures (described in detail below).

Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004). The DERS is a 41-item measure of adolescent difficulties in regulating emotions across multiple dimensions and contexts, which was completed by both the parent and adolescent. Individual items are rated on a 5-point scale (1 = *almost never* and 5 = *almost always*), with higher scores indicative of dysregulated emotion. The DERS includes six subscales, including *non-acceptance* of emotions, difficulties engaging in *goal-directed* behavior, poor *impulse* control, lack of emotional *awareness*, limited emotion regulation *strategies*, and lack of emotional *clarity*. Although developed with adults, it has been validated among children and adolescents, and predicts physiological reactivity when teens are dysregulated emotionally (Vasilev et al., 2009).

Variable Manipulation Task. Using items from the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988), we asked participants to rate their mood after viewing one of four subsets of the fMRI paradigm stimuli. The PANAS is a 20-item measure consisting of two 10-item mood scales, one of positive and the other of negative emotions. We used selected three items (angry, afraid, and calm) for the purposes of a manipulation check, to assess mood after viewing one of six randomized subsets of the fMRI paradigm stimuli. Participants were randomly assigned to rate one of the 6 subsets of stimuli at the end of their scanning session. Participants were assigned which subset to rate based on a randomly generated series of numbers created using the Rand function in SPSS 14.0.

Dissociation State Scale-Short Form (DSS; Stiglmayr et al., 2001). The DSS is a 21-item measure of acute psychological and somatic dissociation and will be assessed following participation in the fMRI paradigm, as a potential covariate. Preliminary results indicate good test-retest reliability and high internal consistency.

State Trait Anxiety Inventory (STAI; Spielberger, Gorush, & Lushene, 1970). The STAI was also given following scanning. It is a 40-item questionnaire that assesses state and trait anxiety, both of which can affect respiration and consequently cerebral blood flow affecting the strength of the BOLD signal (Giardino, Friedman, & Dager, 2007). The measure has excellent reliability and validity (e.g., Spielberger, Ritterband, Sydeman, Reheiser, & Unger, 1995).

fMRI Data Acquisition

Structural and functional MRI scans were performed on a 3 Telsa Philips Achieva MR System (version 2.63, Philips Medical Systems, Best, The Netherlands) with dual Quasar gradients (80 mT/m at a slew rate of 110 mT/m/s; or 40 mT/m at a slew rate of 220 mT/m/s) and an 8-channel SENSE head coil. High resolution 3D FFE T1-weighted magnetization prepared-

rapid gradient echo (MPRAGE) fast imaging sequences generated 200 contiguous axial slices spanning the entire brain (TR = 7.7 ms; TE = 3.6 ms; flip angle = 8°; FOV = 220x220x200; matrix size = 220 x 205; voxel dimension = 1 × 1.07 × 1 mm; SENSE factor = 1). Total scan time for anatomical images was approximately 3 minutes. The structural data was used for image registration. Whole-brain T2*-weighted images were acquired using a single-shot gradient-recalled echo-planar imaging (EPI) sequence (TR = 2000 ms; TE = 21 ms; flip angle = 76°; FOV = 210 mm; matrix size = 72 × 72; in-plane resolution = 3 × 2.92 mm, slice thickness = 3 mm). Forty-seven or forty-eight contiguous 3 mm axial slices were collected per image volume using an ascending slice acquisition. Total scan time for functional images was approximately 24 minutes. A matching B0 field map using a fast field echo sequence was acquired to correct for distortions in the EPI data due to magnetic field inhomogeneities (TR = 563 ms; TE = 2.8; flip angle = 90degrees; FOV = 210 × 210 × 141; matrix size = 72 × 72; in-plane resolution = 3 × 2.92; slice thickness= 3 mm). Forty-seven or forty-eight contiguous 3 mm axial slices spanning the entire brain were collected per image.

fMRI Task. An event-related design was implemented with task procedures similar to those used in several previous studies of examined emotional face processing and ER (Donegan et al., 2003; Herpertz et al., 2001; Minzenberg et al., 2007). Stimuli were 24 digitized gray scale pictures of both men and women with fearful, angry, and neutral facial expressions from the Pictures of Facial Affect set (Ekman & Friesen, 1976). Modifications included standardization of image intensity and cropped out hair and clothing for final images showing only faces (Blair, Colledge, Murray, & Mitchell, 2001; Minzenberg et al., 2007). Pictures of facial affect successfully elicit emotion-induced BOLD responses in the PFC, ACC, and amygdala in normal and clinical samples (Breiter et al., 1996; Morris et al., 1996; Rauch et al., 2000).

During the scanning session, participants viewed the angry, neutral, and fearful faces separated by a fixation cross. Instructions were given to make right-handed button presses to discriminate the sex of each model, with equal emphasis on both speed and accuracy. All participants recruited were right-handed, allowing for comparisons in neural correlates without a task performance or brain lateralization confound. Behavioral performance measures included accuracy and reaction time (RT), with no hypotheses made regarding the performance between groups. Practice faces were not used in the actual imaging task.

E-prime and a back-projected mirror were used to present the imaging paradigm. The total task, including brief separations between runs, lasted approximately 24 min. Participants performed four runs, approximately 300 s long, consisting of 48 trials per run divided equally among four event types: anger, neutral, fear, and fixation cross. The fixation cross was included as an event type to improve the power of the design. Across the four runs, each picture of facial affect was presented six times. The stimuli were presented for approximately 0.5 s, followed by 5.5 s of fixation during each trial. An additional fixation cross was displayed at the beginning and end of each run, lasting approximately 6.0 s. During breaks between runs, participants were asked about their comfort level and reminded to remain still. Events presentations were triggered by the scanner, with a TR of 2 s. Randomization of event types followed the recommendations of Dale (1999) for optimizing fMRI designs. Efficiency was estimated for several thousand random number sequences of length 48 and four event types, and the four most efficient sequences were used for our four runs.

fMRI Data Processing and Statistical Analysis

Image data preprocessing. Data analysis procedures were performed using the Oxford Centre for Functional MRI of the Brain (FMRIB) Software Library version 5.0 (FSL;

http://www.fmrib.ox.ac.uk/fsl/). The following preprocessing steps were applied to the functional data: (1) removal of nonbrain structures using the Brain Extraction Tool (BET); (2) removal by regression of session-specific noise components using Multivariate Exploratory Linear Optimized Decomposition (MELODIC) on nonbrain areas; (3) motion correction conducted with Motion Correction using FMRIB's Linear Image Registration Tool (MCFLIRT), (4) temporal high-pass filtering using Gaussian-weighted least squares fitting with sigma = 66 s, (5) temporal spike identification and interpolation using AFNI's 3dDespike (http://afni.nimh.nih.gov/afni), (6) slice-timing correction to the middle volume using FSL's slicetimer, and (6) spatial smoothing using a Gaussian kernel of full width at half maximum = 5 mm.

Individual level analysis. Time series statistical analyses were carried out using FEAT (fMRI Expert Analysis Tool) version 6.00 in FSL. A voxelwise general linear model analysis was conducted for each participant by convolving a hemodynamic response function with onsets for each of the task regressors of interest: (i) correct trials for anger, (ii) correct trials for fear, and (iii) correct trials for neutral with a double γ hemodynamic response function. The temporal derivative of each regressor was included to account for slight variance in HRF. Incorrect trials were also modeled, but not analyzed. Motion parameters and their derivatives were modeled as regressors of noninterest. White matter and CSF regressors derived from segmentation of each participant's MPRAGE with FAST (FMRIB's Automated Segmentation Tool) were also modeled as regressors of noninterest. Condition effects were estimated at each voxel for the following contrasts: (1) fear vs. fixation, (2) anger vs. fixation, and (3) neutral vs. fixation. Resulting statistical images were transformed to MNI space for multi-session analyses based on concatenating matrices derived from a three-step process, including (1) registration of an example functional volume to the B0 magnitude image using an affine transformation with 6

degrees of freedom, (2) registration of the B0 magnitude image to the high-resolution T1 using an affine transformation with 6 degrees of freedom, and (3) registration of the high-resolution T1 to the MNI NIHPD atlas for 13-18.5 year olds (Fonov, 2011) in MNI space using an affine transformation with 12 degrees of freedom.

Statistical processing—group-level analysis. Using a region of interest approach, mean z-statistics were calculated for each a priori identified region and were included in analyses. The amygdala and ventromedial prefrontal cortex were identified with the Automated Anatomical Labeling atlas (Tzourio-Mazoyer et al., 2002). Because this preferred probability atlas does not identify the sgACC, the right sgACC was identified based on prior research with adolescents (Thomason, Hamilton, and Gotlib, 2011). A cube of 3x3x3 voxels was created around the peak and converted to MNI space. Next, a homologue was created for the left sgACC.

Results

Basic demographic information was collected to characterize groups and, in some cases, to use as possible covariates for later ROI analyses. The self-injury group (M=15.85, SD=1.98) did not differ from the control group (M = 15.81, SD = 1.83) in age, $F(1, 41) = 0.01$, $p = .95$, $\eta_p^2 = .00$. Nor did the self-injury group (M = 114.10, SD = 10.46) differ from the control group (M = 110.10, SD = 11.64) on full scale IQ, $F(1, 41) = 1.37$, $p = .25$, $\eta_p^2 = .03$. However, a significant difference in family income was observed, with the self-injuring (M = \$61,670, SD = \$7,540) teens living in families making substantially less per year than controls (M = \$81,670, SD = \$11,640), $F(1, 41) = 4.58$, $p = .039$ $\eta_p^2 = .10$. In addition, 5 self-injury participants were taking SSRI medication at the time of scanning, whereas no controls were. Therefore, SSRI status (yes = 1 and no = 0) was entered as a covariate in the ROI analyses. Group differences in psychopathology scores are summarized in Tables 2 and 3.

Behavioral Data

fMRI Task. Separate Group (control, SII) × Condition (fear, anger, neutral) repeated measures ANOVAs were conducted for reaction time and percent accuracy. In instances where the sphericity/compound symmetry assumption was violated, Greenhouse-Geisser corrected degrees of freedom were used, and associated epsilons are reported. Significant main effects of group were found for reaction time, $F(1,40) = 7.73$, $p = .008$, $\eta_p^2 = .16$, and accuracy, $F(1,40) = 10.32$, $p = .003$, $\eta_p^2 = .21$. Collapsed across conditions, the SII group responded more quickly ($M = 465.71$, $SD = 41.59$) and less accurately ($M = 0.71$, $SD = 0.13$) than the control group ($M = 495.51$, $SD = 29.16$ and $M = 0.82$, $SD = 0.08$) overall. The Group × Condition interactions were non-significant for both reaction time, $F(2,74) = 1.12$, $p = .33$, $\eta_p^2 = .027$, $\varepsilon = .87$, and accuracy, $F(2,80) = 0.48$, $p = .62$, $\eta_p^2 = .01$, $\varepsilon = .87$.

Emotion manipulation task. In order to evaluate group differences in patterns of self reported emotional rating (afraid, mad, calm) to the pictures of facial affect, a Group (control, SII) × Condition (fear, anger, neutral) × Rating (afraid, mad, calm) repeated measures ANOVA was conducted. There was a significant intercept effect, $F(1, 120) = 4135.53$, $p < .001$, $\eta_p^2 = .97$, and rating effect, $F(2, 120) = 301.05$, $p < .001$, $\eta_p^2 = .71$, $\varepsilon = .56$. Contrasts revealed that ratings of calm were significantly higher than ratings of afraid, $F(2, 120) = 288.91$, $p < .001$, $\eta_p^2 = .71$, and mad, $F(2, 120) = 339.88$, $p < .001$, $\eta_p^2 = .74$, respectively. There were no other significant within-subject effects, all Fs$(2, 120) \leq 3.49$, $p \geq .06$, η_p^2s $\leq .04$. There were no significant between-subject effects, all Fs$(2, 120) \leq 0.97$, all ps $\geq .50$, all η_p^2s $\leq .03$.

Imaging Data

Graphs of the averaged time series response for each group across each ROI in response to all emotion faces were created and reviewed visually to determine the presence of the expected

BOLD signal (Logothetis & Wendell, 2004). The amygdala was the only ROI that evidenced the expected signal and therefore was the only ROI interpreted as having a neural response correlated with the study stimuli. Repeated measures ANCOVAs were conducted to examine study hypotheses. In instances where the sphericity/compound symmetry assumption was violated, Greenhouse-Geisser corrected degrees of freedom were used, and associated epsilons are reported.

Aim 1: Characterizing the SII group. First, we hypothesized that (a) self-injuring adolescents would show neural correlates of emotion processing similar to those observed among adults with BPD. More specifically, when comparing fearful relative to neutral facial expressions, we hypothesized that SII adolescents would show (1) increased amygdala activity, (2) deactivation in the subgenual/rostral region of the ACC, and (3) increased activation in the vmPFC. A contrast of angry relative to neutral facial expressions was hypothesized to result in increased activation of the subgenual/rostral region of the ACC. Upon review of the time series, the BOLD signal was not observed in response to any facial expression relative to fixation in the sgACC or vmPFC. To evaluate the amygdala hypothesis, patterns of activation across the three ROIs in the SII group were assessed using one-way ANOVAs (see Figure 1). One Way ANOVAs were performed to determine whether neural activity during the viewing of any facial expressions vs. fixation was significantly different than zero. Indeed, each condition for each hemisphere was statistically different than zero, all Fs$(1, 20) \geq 13.99$, all ps $\leq .001$. However, when comparing emotion vs. neutral faces, the change did not differ from zero, all Fs$(1,20) \leq 2.34$, all ps $\geq .14$. This suggests no difference in activity between emotional and neutral expressions. Because nonzero increases relative to fixation were observed, however, results of regional activation were still compared according to a priori hypotheses using a full factorial Condition (anger vs. fix, fear

vs. fix, neutral vs. fix) × Hemisphere (left, right) repeated measures analyses of variance for the SII group. SSRI use (0 = no, 1 = yes) was entered as a between-subjects covariate. Additional covariates included age and average reaction time for all facial expressions accurately identified. Mauchley's test indicated that the assumption of sphericity had not been violated for the main effect of Condition nor for the interaction effect, $\chi^2(2) < 3.50$, $p > .05$. No significant between subject effects, all Fs$(1,17) < 1.73$, all ps $> .20$, all η_p^2s $< .10$, all εs $< .24$, or within-subject effects, all Fs$(2,34) < 0.87$, all ps $> .40$, all η_p^2s $< .05$, all εs $< .19$, were found. This indicates there were no differences in neural activity between emotional expressions, hemispheres, nor interactions between them within the SII group.

Aim 2: Group comparisons. Next, we hypothesized that changes in activation by expression (netural, fear, anger) relative to fixation stimuli would be greater among SII adolescents than controls. To evaluate this hypothesis, results of regional activation during faces relative to fixation conditions were evaluated in a full factorial Group (SII, control) × Hemisphere repeated measures ANOVA. Significant Group × Region interactions were hypothesized with significant group effects for each region. Current use of SSRIs (0 = no, 1 = yes), reaction time, and age were entered as covariates. Neither reaction time nor use of SSRIs contributed to significant between group or within group effects and so were removed from the model in a step-wise fashion (reaction time, then SSRI use). Mauchley's test indicated that the assumption of sphericity had not been violated for the main effect of Condition nor for the interaction effect, $\chi^2(2) \leq 3.53$, $p > .05$. No within subjects effects were observed, including all Fs$(2,78) < 0.51$, all ps $> .60$, all η_p^2s $< .01$, all εs $< .14$. A significant between subjects interaction for age was observed, $F(1,38) = 4.54$, $p < .04$, $\eta_p^2 = .10$, $\varepsilon = .55$. The relationship between age and change in activity for all faces versus fixation was evaluated by calculating the bivariate correlation with a two-tailed Pearson's

r test, $r = -.33$, $p = .03$. This indicated that with increasing age, amygdala activity decreased during the viewing of facial expressions, regardless of the expression.

One-way ANOVAs indicated that the control group also exhibited nonzero increases in neural activity across both hemispheres and all emotional expressions relative to fixation, all Fs ≥ 16.33, ps $\leq .001$, consistent with our findings for the SII group (see Figure 2). However, when comparing emotion vs. neutral faces, the change did not differ from zero, all Fs$(1,20) \leq 1.07$, all ps $\geq .31$.

Discussion

As mentioned previously, this study is the one of the first to examine neural correlates of emotion dysregulation and self-injury in adolescent girls and incorporates the largest sample size to date (e.g., Plener et al., 2012). Thus, it represents a significant step forward in characterizing affective processing correlates of SII. Consistent with our developmental model (Beauchaine et al., 2009; Crowell et al., 2009), we propose that self-injury marks risk for later development of BPD. Thus, we proposed that self-injuring teens would evidence similar neural activation patterns to emotional stimuli as adults with BPD. Results from our ROI analysis did not support this hypothesis. Indeed, a BOLD signal was not observed in two of three ROIs during the viewing of any facial expressions relative to fixation. A BOLD signal was observed in both hemispheres of the amygdala, but no group differences were observed in neural activity. Consistent with some prior reports, activity in the amygdala decreased with increasing age (Casey, Tottenham, Liston, & Durston, 2005). In light of the lack of support for hypotheses, a review of the behavioral findings may aid in the interpretation of null results. Namely, in the next section, we have considered whether the selected sample is representative of the intended population.

Implications of Behavioral Data

Evidence suggests the two groups were behaviorally distinct. The psychopathology data and behavioral data collected were highly consistent with the expectation of increased emotion dysregulation in the SII relative to the control group. Collapsed across conditions, adolescents in the SII group responded more quickly and less accurately to the emotion face paradigm than did the control group. This is consistent with our theory that SII is highly associated with impulsivity (Crowell et al., in press). Across all measures of youth behavior problems and difficulties in emotion regulation, parents and youth rated adolescents in the SII group as struggling significantly more than adolescents in the healthy control group. Therefore, the selected sample largely represented the intended population. However, neural differences were not found in response to the emotional face paradigm. The simplest interpretation of these null findings is that adolescents who self-injure are not similar to adults with BPD in neural responding and do not evidence neural vulnerabilities associated with deficits in emotion dysregulation. However, the sample could represent the intended population precisely and still not evidence aberrant neural responses to emotional information. Our theory suggests biologically based impulsivity is an initial distinguishing feature of SII (Crowell et al., in press). We theorize that dysregulation develops later through thousands of interactions with the environment. Therefore, aberrant neural response to emotional information may not be evident until late adolescence or early adulthood when neural development is much further along. Nevertheless, there are some limitations to the sample that warrant further consideration.

For scanning purposes, adolescents taking medications other than SSRIs were excluded, which may have excluded severity and obscured differences between groups. Furthermore, a history of SII and not current activity was required for the self-injury group. A more acutely self-

injuring or suicidal sample might have evidenced greater differences compared with a normal control group. Also, older adolescents tended to report more problems with increasing age in both groups, but more so in the SII group. This may have added unintended variance into the SII group and obscured differences between groups. Indeed, the range of ages in this study spanned all of adolescence, a period of dramatic neural maturation (e.g., Diamond, 2002).

Uncontrolled Developmental Factors

This study implemented a top-down approach to studying adolescent self-injury. We selected stimuli and created hypotheses based on the assumption of substantial similarities between adults and youth. However, there are several developmental considerations that may have affected the results. First, ROIs and their connections develop actively throughout adolescence into early adulthood (Bunge, Dudukovic, Thomasson, Vaidya & Gabrieli, 2002). Therefore, the large age range in the present study may have increased variability and reduced our power. Second, regional contribution to emotional control may not be consistent across age, even among normative samples. Unfortunately, research on the relationship between functional and structural changes as they related to cognition, emotion, and behavior is still in its infancy.

Emerging research suggests that adolescents process emotional information *similar* to adults (Killgore & Yurgelun-Todd, 2006; Killgore & Yurgelun-Todd, 2007; Todd, , Evans, Morris, Lewis, & Taylor, 2011). Activations in the PFC, amygdala, and ACC with more *diffuse* activation in frontal regions, have been related to volitional and automatic emotion regulation in adolescents (McRae et al., 2012; Joormann et al., 2012). However, the developmental course of each ROI and the relationships between them may prove to be more important than originally hypothesized. Therefore, we have reviewed each region and notable considerations next.

Development and vmPFC. It is widely understood that PFC development enhances children's and adolescents' abilities to self-regulate emotion, thoughts, action, and attention (Diamond, 2002). Furthermore, the PFC and its functions mature later than any others, reaching maturation in the early 20s (Bunge et al., 2002). Generally speaking, as children mature through adolescence, neural correlates of emotional response shift from more limbic structures like the amygdala to more frontal regions in the service of emotional control (Casey et al., 2005). We, too, observed decreased amygdala activity with increased age across both groups; however, there was no evidence of the expected corresponding increase in vmPFC activity. This shift towards frontal lobe specification over time helps explain findings of broader neural activation in frontal regions in adolescents relative to adults (for a review see Monk, 2008). For example, research has shown a linear age-related increase in activation in the left ventrolateral PFC, which has also been associated with effective emotion regulation via cognitive reappraisal (McRae et al., 2012). In fact, age related increases in functioning have also been reported within the dorsolateral and ventromedial PFC while participants viewed scenes where painful situations were intentionally inflicted (Decety & Michalska, 2010). In the same study, neural activity shifted with age from the more medial portions to the more lateral portions of the vmPFC. These data suggest the current study's analyses may have been prematurely limited to specific regions of interest. Future examinations may benefit from more exploratory approaches or may benefit from approaches examining connectivity rather than individual ROIs.

Development and sgACC. There was also no evidence of differential sgACC activity between groups, nor any sgACC response to the stimuli set. This finding is in contradiction to the widely held notion that the anterior cingulate cortex is an essential component of the brain's self-regulatory network (e.g., Amodio and Frith 2006). Moreover, the subgenual and perigenual

regions of the ACC are estimated to be the regions of the ACC most closely involved with cognitive, social, and emotional regulation. Like the PFC, these regions of the ACC have been found to be some of the last cerebral regions to fully mature, such that functional connectivity between the ACC and PFC follow a similar pattern as with the amygdala and PFC, with increased localized function shifted to the PFC with increased age (Kelly, et al., 2009).

Development and amygdala. Lastly, increased amygdala activity is so often observed in adults with BPD relative to controls that the lack of this finding in our youth sample deserves some special consideration (e.g., Lis et al., 2007). Again, development likely plays an important factor. Results for amygdala response have been mixed in youth (for a review, see Blakemore & Choudhury, 2006). In fact, teens do not exhibit the same indiscriminate amygdala response to negative emotional stimuli as adults and the stimuli set may have played a role in the null results for this investigation. Despite effectiveness with adults, the stimuli used in the current study may not have been perceived as negative by the youth scanned (e.g., Herpetz et al., 2001). Although individual physiological response is often dissociated from self report of emotion, participants rated minimal to no emotional response to viewing the negative stimuli during the manipulation check. Indeed, the stimuli may have little affective power relative to other images encountered in daily life, such as in violent video games. This is consistent with Todd and colleagues (2011) report of an amygdala preference for happy faces among children, something rarely observed in adult samples. Some researchers say that children have a positivity bias in which neutral and mildly negative expressions are viewed as positive (see e.g., Joorman et al., 2012). Thus, the amygdala in children is thought to still be involved in identifying emotionally salient information, but negative facial expressions are not automatically viewed as salient to the child. This may explain why the only other study of self-injury in teens found increased amygdala

activity using stimuli depicting negative emotional scenes (Plener et al., 2012). The context may have aided the child in attending to the negative aspects of the images. If this amygdala response to emotional information evolves over the course of adolescence so that negative emotional expressions become more recognizable and salient, the relatively large age span from 13 to 19 years in the present study may have substantially reduced our group's homogeneity without the needed increased sample size to tease out these nuanced developmental patterns. Consistent with these studies, Todd and colleagues (2011) found age related changes in the amygdala such that amygdala activity for angry faces increased with age.

When researchers have reported increased amygdala activation to negative emotional stimuli (relative to some baseline) among children and youth, they have typically provided more context in their stimuli or employed tasks that manipulate attention to the salience of the stimuli (for a review, see Blakemore & Choudhury, 2006). Unfortunately, the task in the current study, if anything, likely distracted youth from the emotional content of the image by asking them to attend to the sex of the person pictured. This may have affected results. These emerging developmental neuroscience data should be considered in future research in efforts to identify salient stimuli, and perhaps incorporate a real time manipulation check for accurate (or rather inaccurate) identification of negative emotions. Neural response based on such information may be more valuable than that based on accurate sex identification. Clearly, developmental considerations are necessary for this kind of research at each step of the study design, despite the likely additional complications. Developmental considerations for the current study, for example, suggest it may have benefited from additional piloting of stimuli in an adolescent sample prior to study inception, a more homogenous age group, and perhaps a less specific ROI analysis approach.

Summary

As previously mentioned, this research is the second and largest study known to the authors to examine neural correlates of emotion dysregulation and self-injury in adolescent girls (Plener et al., 2012). Thus, it represents a significant step forward in characterizing affective processing correlates of SII. Behavioral data suggest that the two groups in the current study were behaviorally distinct in ways that likely affect emotion regulation capabilities. However, neural vulnerabilities were not captured. There are several reasons this may have occurred. First, adolescents who self-injure may not share neural vulnerabilities in emotion regulation with adults with BPD. Second, the groups two may not be differ in their neural processing of emotional information. Third, the groups may represent adolescents on developmental paths leading to healthy adulthood and diagnoses of BPD respectively, but who have not yet developed different neural responses to emotional information at this age range. Our theory suggests impulsivity is the initial distinguishing feature of SII and emotion dysregulation develops later through interactions with the environment. Null findings, therefore, are not necessarily inconsistent with the theory because abnormal emotional responding may not be evident until late adolescents or early adulthood when neural development is much further along. Lastly, the stimuli used in this study may not properly capture the specific aspect of emotion dysregulation characteristic to both SII and BPD.

Limitations and Future Directions

Significant space has already been spent exhausting possible explanations for null hypothesized results. Therefore, this section includes a brief summary and a few notable limitations. The combination of large adolescent age range, limited sample size, and inclusion of participants taking SSRIs could have contributed to some null findings. In addition, allowing

teens with a history of, but not current, SII, may have contributed to null results. A more acutely self-injuring or suicidal sample may have evidenced differences compared with a normal control group. Furthermore, our results cannot be generalized to males, who are at higher risk of suicide than females, though not self-injury (e.g., Joiner, Conwell, et al., 2005). Adding a depressed clinical control group might also have helped to better characterize the neural correlates of self-injury.

Much like in early days of research on child psychopathology, we took a top-down, adult-centric approach to study hypotheses when identifying our regions of interest and stimuli. This was due in part to limited data on adolescent affective responses, even within normal control samples. Nevertheless, incorporating emerging research on childhood affective processing such as the aforementioned positivity bias, should lead to development of a more appropriate task paradigm. In addition, a theoretical task paradigm examining features of impulsivity, for example, could elucidate our developmental model further and more specifically than one focused generally on emotion dysregulation.

In addition, developmental considerations might suggest a less specific ROI approach. Indeed, there are multiple ways to approach fMRI analysis and each has pros and cons in terms of answering specific questions. While a review of these analytic methods is beyond the scope of this discussion, other more exploratory hypotheses and analytic approaches may be more successful in future work (for a review, see Poldrack, Mumford, & Nichols, 2011). There are also other ways to affect the signal-to-noise ratio in preprocessing that may be useful in future work. Lastly, controlling for region size in analyses may evidence group differences that could explain the null findings in this study such that the same amount of functional activity in both groups may have been driven by smaller amygdala in the SII group and, thus, still represent a

hyperactive and taxed amygdala in the SII group. Studies in adults with MDD have illustrated the utility of such an approach (e.g., Gotlib & Hamilton, 2008).

Finally, ours and other developmental models of emerging psychopathology will likely benefit from longitudinal research that incorporates examination of biological, psychological, and environmental factors at multiple levels of analysis (see Beauchaine et al., in press). For example, studies that examine neural processing as a mediator between relevant genes and parent-child interaction patterns over the course of development will likely be needed to fully contextualize the intricate relationship between these risk and vulnerability factors in the development of emotion dysregulation and SII.

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Table 1.

Self-Injurious Thoughts and Behaviors by Group

Characteristic/ Measures	Control (*n=21*) Mean (***SD***)	Self-injuring (*n=21*) Mean (***SD***)	***F***(1,41)	Partial η^2
SIQ-Jr (*n* = 18, df = 1, 17)	1.30 (1.89) *n = 10*	14.88 (15.72) *n* = 8	7.43*	.32
SIQ (*n* = 24, df = 1, 23)	2.55 (5.30) *n* = 11	46.77 (30.56) *n* = 13	22.33***	.50
Lifetime # of non-suicidal self-injurious episodes	0.0 (0.0)	175.10 (250.26)	-	-
Lifetime # of ambivalent suicide attempts	0.0 (0.0)	110.00 (19.67)	-	-
Lifetime # of high intent suicide attempts	0.0 (0.0)	1.29 (2.31)	-	-
Total # of suicide attempts	0.0 (0.0)	19.95 (36.74)	-	-
Lifetime # of ALL self-injurious episodes	0.0 (0.0)	195.05 (269.74)	-	-

Note. SIQ=Suicide Ideation Questionnaire (raw scores), standardized by grade level. SIQ-Jr (grades 7-9) raw scores ≥ 31 and SIQ (grades 10-12) raw scores ≥ 41 are indicative of significant clinical concern regarding suicide risk (Reynolds, 1987). LSASI= Lifetime Suicide Attempt Self-Injury Count (scales scored according Linehan and Comtois, 1996).

*$p \leq .05$, **$p \leq .01$, $p \leq .05$.

Table 2.

Diagnostic Interview Descriptive Statistics

Characteristic/Measures	Control (***n***=21) **Mean** (***SD***)	Self-injuring (***n***=21) **Mean** (***SD***)	***F***(1,41)	Partial η^2
major depressive disorder diagnosis (DISC youth report)	0	5 (past month) 4 (past year)	-	-
major depressive disorder diagnosis (DISC parent report)	0	4 (past month) 2 (past year)	-	-
nicotine dependence disorder (DISC youth report)	0	2	-	-
nicotine dependence disorder (DISC parent report)	0	0	-	-
marijuana abuse disorder (DISC youth report)	0	3	-	-
marijuana abuse disorder (DISC parent report)	0	1	-	-
marijuana dependence disorder (DISC youth report)	0	2	-	-
marijuana dependence disorder (DISC parent report)	0	0	-	-
alcohol abuse disorder (DISC youth report)	0	2	-	-
alcohol abuse disorder (DISC parent report)	0	0	-	-
other substance abuse disorder (DISC youth report)	0	1	-	-
other substance abuse disorder (DISC parent report)	0	0	-	-
borderline personality disorder symptoms (SCID-II youth report)	0.00 (0.00)	2.81 (1.72)	55.97***	.58
borderline personality disorder raw (youth report)	9.14 (0.36)	15.90 (3.75)	67.53***	.63
borderline personality disorder symptoms (SCID-II parent report)	0.15 (0.49)[a]	2.25 (1.65)	29.77***	.44
borderline personality disorder raw (SCID-II parent report)	9.50 (1.23)[a]	14.55 (3.49)	37.28***	.50

Note. DISC = Diagnostic Interview for Children (Shaffer et al., 2000); SCID-II = Structured Clinical Interview for DSM-IV Axis II (First et al., 1997).

[a]$n = 20$

***$p \leq .001$.

Table 3

Youth's Inventory (Self-Report) Scores by Group

Subscale	Control (***n***=20)[a]	Self-injury (***n***=21)	***F*(1, 40)**	Partial η^2
specific phobia raw	0.50 (0.61)	1.14 (0.79)	8.44**	.18
specific phobia symptoms	0.05 (0.22)	0.29 (0.46)	4.24*	.10
specific phobia diagnosis	1	6		
somatic raw	0.55 (0.94)	1.10 (1.34)	2.25	.06
somatic symptoms	0.10 (0.31)	0.24 (0.44)	1.36	.03
somatic disorder diagnosis	0			
ADHD Inattentive raw	5.35 (2.68)	11.76 (4.52)	30.17***	.44
ADHD Inattentive symptoms	0.35 (0.67)	3.05 (2.91)	16.38***	.30
ADHD Inattentive diagnosis	0	4		
ADHD Hyperactivity raw	5.10 (4.45)	6.33 (3.15)	1.06	.03
ADHD Hyperactivity symptoms	0.95 (1.61)	1.05 (1.02)	0.05	.001
ADHD Hyperactivity diagnosis	1	0		
ADHD Combined raw	10.45 (5.80)	18.10 (6.73)	9.63**	.28
ADHD Combined symptoms	1.30 (1.66)	4.10 (3.69)	15.12***	.20
ADHD Combined diagnosis	0	0		
CD raw	0.40 (0.75)	3.05 (2.62)	18.95***	.33
CD symptoms	0.05 (0.22)	0.52 (1.03)	4.04*	.09
CD diagnosis	0	3		
ODD raw	3.95 (3.17)	7.76 (3.63)	12.77**	.25
ODD symptoms	0.25 (0.64)	1.62 (1.88)	9.51**	.20
ODD diagnosis	0	2		
separation anxiety raw	0.10 (0.31)	1.24 (1.87)	7.23*	.16
separation anxiety symptoms	0.00 (0.00)	0.29 (0.72)	3.17	.08
separation anxiety diagnosis	0	1		
GAD raw	2.50 (2.01)	10.52 (5.77)	34.65***	.47
GAD symptoms	0.00 (0.00)	1.86 (3.04)	7.47**	.16
GAD diagnosis	0	6		
panic raw	0.00 (0.00)	0.67 (0.73)	16.65***	.30
panic symptoms	0.00 (0.00)	0.05 (0.22)	0.951	.02
panic diagnosis	0	1		
OCD raw	0.10 (0.31)	1.38 (1.50)	14.02**	.26
OCD symptoms	0.00 (0.00)	0.38 (0.67)	6.48*	.14
OCD diagnosis	0	6		

Subscale	Control (***n***=20)[a]	Self-injury (***n***=21)	***F*(1, 40)**	Partial η^2
PTSD raw	0.25 (0.55)	1.95 (1.75)	17.36***	.31
PTSD symptoms	0.00 (0.68)	0.48 (0.68)	9.81**	.20
PTSD diagnosis	0	2		
social phobia raw	0.80 (1.01)	2.05 (1.96)	6.47*	.14
social phobia symptoms	0.10 (0.31)	0.52 (0.75)	5.50*	.12
social phobia diagnosis	0	3		
schizoid personality raw	1.00 (0.92)	2.38 (1.12)	18.60***	.32
schizoid personality symptoms	0.05 (0.22)	0.57 (0.68)	10.76***	.22
schizoid personality diagnosis	0	2		
schizophrenia raw	0.85 (1.09)	3.10 (2.49)	13.76**	.26
schizophrenia symptoms	0.10 (0.31)	0.43 (0.75)	3.33	.08
schizophrenia diagnosis	0	0		
major depression raw	4.55 (3.28)	16.86 (8.77)	34.75***	.47
major depression symptoms	0.75 (0.79)	4.48 (2.86)	31.70***	.45
major depression diagnosis	0	8		
dysthymia raw	4.05 (3.03)	13.71 (7.19)	30.86***	.44
dysthymia symptoms	0.50 (0.76)	3.81 (2.66)	28.74***	.42
dysthymia diagnosis	0	12		
bipolar raw	9.15 (3.18)	8.10 (3.30)	1.083	.03
bipolar symptoms	2.55 (1.19)	1.76 (1.45)	3.61	.09
bipolar diagnosis	0	0		
anorexia raw	1.55 (1.99)	4.19 (1.99)	12.43***	.24
anorexia symptoms	0.20 (0.62)	1.24 (1.04)	14.84***	.28
anorexia diagnosis	0	3		
bulimia raw	0.55 (1.19)	3.00 (3.00)	11.59**	.23
bulimia symptoms	0.05 (0.22)	0.95 (1.12)	12.56***	.24
bulimia diagnosis	0	6		
substance abuse raw	0.25 (0.55)	1.67 (1.93)	9.97**	.20
substance abuse symptoms	0.05 (0.22)	0.48 (0.87)	4.48*	.10
substance abuse diagnosis	1[b]	6		

Note. ADHD=attention deficit hyperactivity disorder; CD=conduct disorder; ODD=oppositional defiant disorder; GAD=generalized anxiety disorder; OCD=obsessive compulsive disorder; PTSD=post traumatic stress disorder. Data taken from self report of Youth's Inventory (Gadow et al., 2002).

[a]Due to technical difficulties with the computerized questionnaire, data were lost for one participant who had already screened into the control group and participated in the study.

[b]Although one participant met screening threshold for substance abuse diagnosis, she did not meet criteria for dependence based on the Diagnostic Interview for Children (Shaffer et al., 2000). *$p \leq .05$. **$p \leq .01$, $p \leq .01$.

Table 4

Adolescent Symptom Inventory (Parent-Report) Scores by Group

Subscale	Control (***n***=21)	Self-injury (***n***=21)	***F***	Partial η^2
specific phobia raw	0.09 (0.30)	0.14 (0.36)	0.22	.01
specific phobia symptoms	0.09 (0.30)	0.14 (0.36)	0.22	.01
specific phobia diagnosis	2	3		
somatic raw	0.90 (1.22)	1.81 (1.57)	4.35*	.10
somatic symptoms	0.14 (0.48)	0.43 (0.60)	2.93	.07
somatic disorder diagnosis	2	8		
ADHD inattentive raw	5.62 (3.57)	11.81 (6.43)	14.87***	.27
ADHD inattentive symptoms	0.33 (0.58)	3.05 (3.06)	15.98***	.29
ADHD inattentive diagnosis	0	4		
ADHD hyperactivity raw	3.71 (4.08)	4.24 (4.15)	0.17	.004
ADHD hyperactivity symptoms	0.43 (1.33)	0.76 (1.34)	0.66	.02
ADHD hyperactivity diagnosis	1	0		
ADHD combined raw	9.33 (5.54)	16.06 (9.36)	8.00**	.17
ADHD combined symptoms	0.6 (1.41)	3.81 (3.71)	12.38***	.24
ADHD combined diagnosis	0	0		
CD raw	0.57 (0.87)	3.90 (3.46)	18.30***	.31
CD symptoms	0.00 (0.00)	0.62 (0.97)	8.49**	.18
CD diagnosis	0	2		
ODD raw	4.19 (2.94)	8.48 (5.92)	8.82**	.81
ODD symptoms	0.10 (0.30)	2.05 (2.82)	9.96**	.20
ODD diagnosis	0	6		
separation Anxiety raw	0.29 (0.64)	2.05 (4.76)	2.83	.07
separation Anxiety symptoms	0.00 (0.00)	0.57 (1.47)	3.18	.07
separation Anxiety diagnosis	0	2		
GAD raw	3.19 (2.34)	7.48 (4.32)	15.99***	.29
GAD symptoms	0.00 (0.00)	0.24 (1.09)	1.00	.02
GAD diagnosis	0	1		
panic raw	0.10 (0.30)	0.52 (0.81)	5.13**	.11
panic symptoms	0.00 (0.00)	0.10 (0.30)	2.10	.05
panic diagnosis	0	2		
OCD raw	0.14 (0.36)	0.62 (0.92)	4.88*	.11
OCD symptoms	0.00 (0.00)	0.10 (0.30)	2.10	.05
OCD diagnosis	0	2		

Subscale	Control (***n***=21)	Self-injury (***n***=21)	***F***	Partial η^2
PTSD raw	0.33 (0.73)	1.24 (1.34)	7.40*	.16
PTSD symptoms	0.00 (0.00)	0.24 (0.62)	3.05	.07
PTSD diagnosis	0	3		
social phobia raw	0.10 (0.30)	1.67 (2.20)	10.53**	.21
social phobia symptoms	0.00 (0.00)	0.43 (0.75)	6.92*	.01
social phobia diagnosis	0	3		
schizoid personality raw	0.62 (1.02)	1.00 (1.05)	1.42	.03
schizoid personality symptoms	0.05 (0.22)	0.05 (0.22)	0.00	.00
schizoid personality diagnosis	0	0		
schizophrenia raw	0.19 (0.40)	0.81 (0.98)	7.16*	.15
schizophrenia symptoms	0.00 (0.00)	0.05 (0.22)	1.00	.02
schizophrenia diagnosis	0	0		
major depression raw	1.38 (1.56)	8.05 (4.09)	48.62***	.55
major depression symptoms	0.14 (0.48)	1.90 (1.90)	17.53***	.30
major depression diagnosis	0	2		
dysthymia raw	1.29 (1.45)	6.24 (3.13)	43.26***	.52
dysthymia symptoms	0.00 (0.00)	0.90 (1.18)	12.36***	.24
dysthymia diagnosis	0	1		
dysthymia research raw	1.76 (1.64)	8.00 (4.23)	39.69***	.50
dysthymia research symptoms	0.00 (0.00)	0.90 (1.18)	12.36**	.24
dysthymia research diagnosis	0	0		
bipolar raw	2.57 (2.73)	4.10 (3.30)	2.66	.06
bipolar symptoms	0.05 (0.22)	0.38 (0.92)	2.61	.06
bipolar diagnosis	0	0		
anorexia raw	0.29 (0.72)	2.43 (2.80)	11.52**	.22
anorexia symptoms	0.00 (0.00)	0.57 (0.98)	7.16*	.15
anorexia diagnosis	0	5		
bulimia raw	0.38 (0.80)	1.81 (2.16)	8.07**	.17
bulimia symptoms	0.00 (0.00)	0.43 (0.81)	5.87*	.13
bulimia diagnosis	0	4		
substance abuse raw	0.00 (0.00)	1.19 (1.40)	15.17***	.28
substance abuse symptoms	0.00 (0.00)	0.05 (0.22)	1.00	.02
substance abuse diagnosis	0			

Note. ADHD=attention deficit hyperactivity disorder; CD=conduct disorder; ODD=oppositional defiant disorder; GAD=generalized anxiety disorder; OCD=obsessive compulsive disorder; PTSD=post traumatic stress disorder.

Data taken from parent report of the Adolescent Symptom Inventory (Gadow et al., 2002).

*$p \leq .05$. **$p \leq .01$, $p \leq .01$.

Table 5

Parent and Youth Reports of Child Behavior Problems

T- Score	Control (***n***=21) Mean (***SD***)	Self-harm (***n***=21) Mean (***SD***)	***F***	Partial η^2
Youth's Self Reports				
Withdrawn	50.24 (1.09)	60.57 (9.05)	27.00***	.40
somatic complaints	50.76 (1.67)	55.33 (6.15)	10.80**	.21
anxious/depressed	50.14 (0.65)	64.38 (13.57)	23.05***	.37
social problems	52.43 (6.22)	58.90 (8.74)	7.66**	.16
thought problems	51.71 (3.16)	55.86 (7.16)	5.89*	.13
attention problems	51.52 (3.40)	61.76 (9.52)	21.53***	.35
delinquent behavior	51.81 (3.56)	64.85 (9.64)	33.67***	.46
aggressive behavior	52.00 (4.02)	56.24 (5.13)	8.88**	.18
externalizing	46.29 (8.19)	58.19 (9.38)	19.18***	.32
internalizing	39.00 (6.12)	59.05 (13.96)	36.33***	.48
Parent Reports				
Withdrawn	51.30 (3.67)	59.48 (9.76)	12.37***	.25
somatic complaints	57.40 (7.21)	61.00 (8.89)	2.02	.16
anxious/depressed	52.40 (4.68)	60.70 (10.76)	10.00**	.21
social problems	50.75 (1.83)	56.80 (7.11)	13.60***	.26
thought problems	51.00 (3.23)	54.29 (7.29)	3.42	.08
attention problems	51.50 (3.10)	59.05 (7.51)	17.27***	.31
internalizing scale	47.20 (10.38)	59.75 (11.39)	13.26***	.26

Note. Youth and Parent reports of child behavior and emotional problems were taken from the Youth's Self Report (Achenbach, 1991) and Child Behavior Checklist (Achenbach & Rescorla, 2001), respectively. All values represent T scores. Due an administrative error, 6 items from across the aggressive behavior, delinquent behavior, and externalizing scales were missing. Therefore, T scores were not interpreted for scales with missing items.

*$p \leq .05$. **$p \leq .01$, $p \leq .01$.

Table 6

Reports of Youth's Difficulties in Emotion Regulation Scale

Scale	Control (***n***=21) Mean (***SD***)	Self-injury (***n***=21) Mean (***SD***)	***F***	Partial η^2
Youth Self Reports				
non-acceptance	1.37 (0.54)	2.34 (1.24)	10.98**	.22
problems with goals	1.66 (0.51)	3.10 (1.18)	26.65**	.40
problems with impulse control	1.29 (0.35)	2.21 (1.01)	15.74**	.28
lack of emotional awareness	2.01 (0.57)	2.92 (1.10)	11.48**	.22
limited ER strategies	1.29 (0.35)	2.77 (0.94)	45.72**	.53
lack of emotional clarity	1.58 (0.44)	2.64 (0.88)	24.39**	.38
total difficulties in ER	**1.51 (0.29)**	**2.66 (0.79)**	**38.37****	**.49**
Parent Reports				
non-acceptance (*n*=20)	1.34 (0.37)	1.70 (0.55)	5.97*	.13
problems with goals	1.76 (0.86)	2.81 (1.06)	12.41**	.24
problems with impulse control	1.38 (0.58)	2.35 (0.97)	15.31**	.28
lack of emotional awareness	2.15 (0.65)	2.79 (0.88)	7.24*	.15
limited ER strategies	1.33 (0.58)	2.33 (0.68)	26.64**	.40
lack of emotional clarity	1.61 (0.53)	2.15 (0.72)	7.54*	.16
total difficulties in ER	**1.59 (1.59)**	**2.36 (0.60)**	**18.88****	**.32**

Note. ER = emotion regulation; These data represent scales from the Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004).

*$p \leq .05$. **$p \leq .01$.

Footnotes

[1]SSRIs are a class of drugs that act as agonists for serotonin and other monoamines in the brain and are commonly used to alleviate symptoms of anxiety and depression (see e.g., Barlow, & Durand, 2009). Serotonergic dysfunction in the prefrontal cortex has been consistently linked to suicidal behavior (see e.g., Currier & Mann, 2008). SSRI medication decreases metabolic activity in the amygdala and sgACC, an effect that is associated with treatment response (see e.g., Drevets et al., 2008). Moreover, SSRIs have also been associated with increased coupling of the amygdala and prefrontal and cingulate cortices among depressed patients. However, given the frequency with which these drugs are prescribed for affective disturbances, ranging from mild depression and anxiety to panic and severe mood lability, we elected to include participants taking them. Five members of our self-injury sample were medicated with SSRIs at the time of scanning. No members of the control sample were medicated.

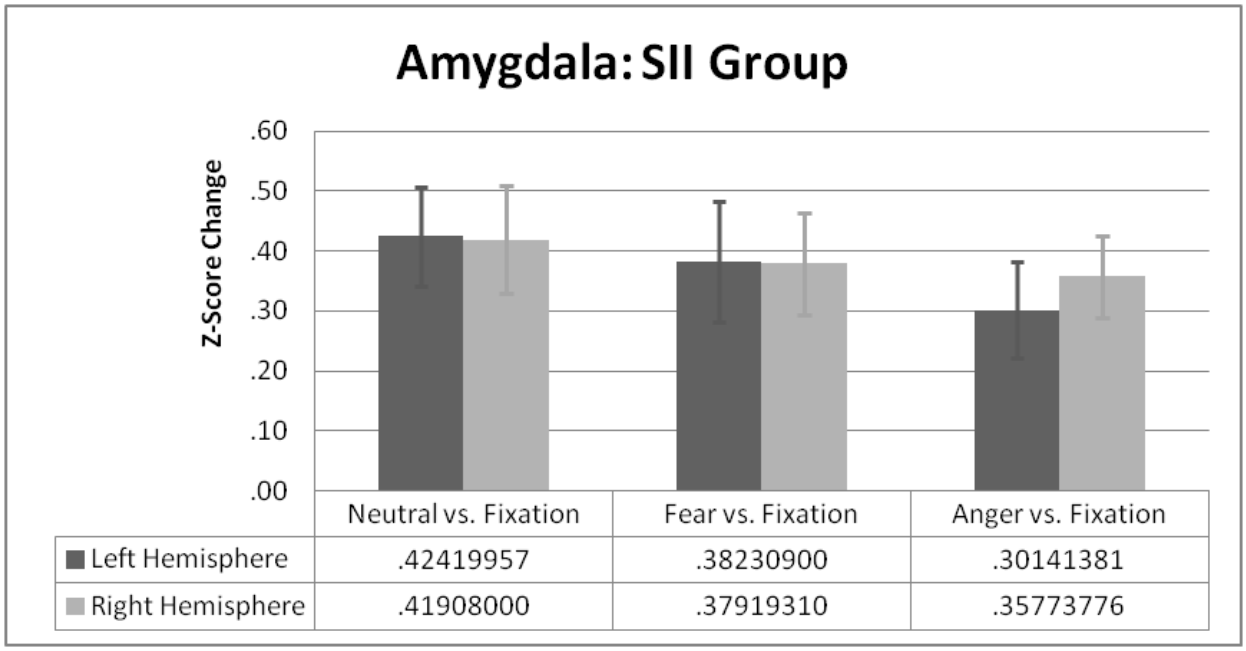
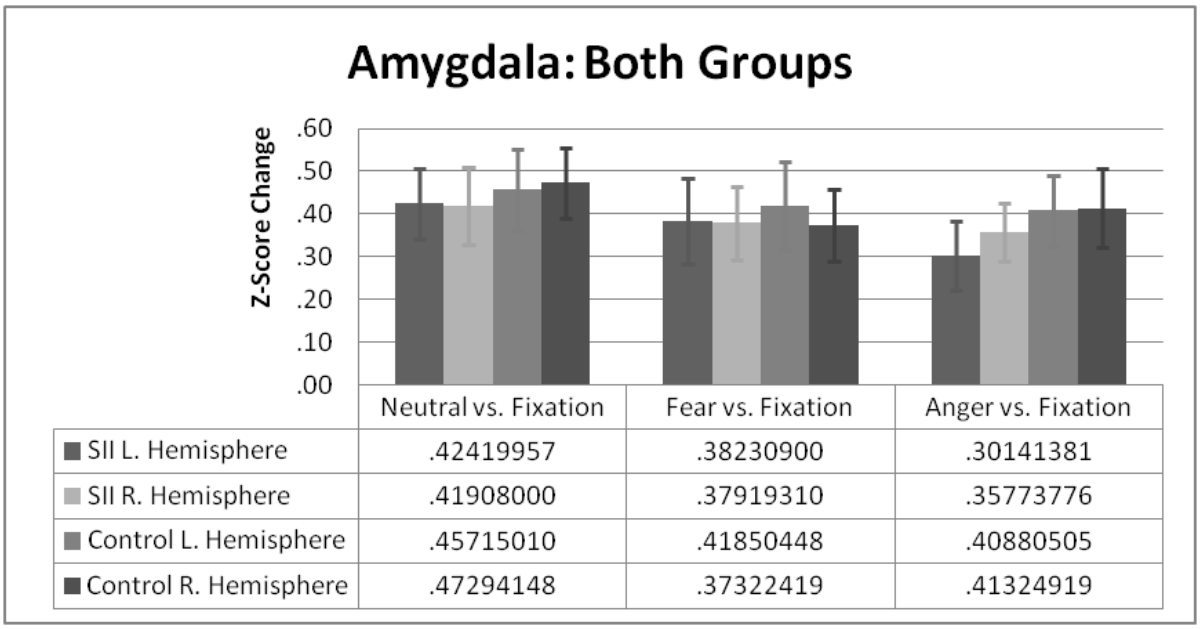


Figure 1. Pattern of fMRI BOLD response within the SII Group. One Way ANOVAs were performed to determine whether the neural activity correlated with facial expression vs. fixation conditions were significantly different than zero. Each condition relative to fixation for each hemisphere was statistically different than zero, all $Fs(1, 20) \geq 13.99$, all $ps \leq .001$, for the SII Group.



	Neutral vs. Fixation	Fear vs. Fixation	Anger vs. Fixation
SII L. Hemisphere	.42419957	.38230900	.30141381
SII R. Hemisphere	.41908000	.37919310	.35773776
Control L. Hemisphere	.45715010	.41850448	.40880505
Control R. Hemisphere	.47294148	.37322419	.41324919

Figure 2. Pattern of fMRI BOLD response within the SII Group and Control Groups. One-way ANOVAs indicated that both groups exhibited nonzero increases in neural activity across both hemispheres within the amygdala and across all emotional expressions relative to fixation, all Fs ≥ 13.99, ps $\leq .001$.