Psychiatry Research: Neuroimaging 254 (2016) 145–155

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

The neurobiology of self-knowledge in depressed and self-injurious youth

Karina Quevedo [a,*], Jodi Martin [b], Hannah Scott [a], Garry Smyda [c], Jennifer H. Pfeifer [d]

[a] Department of Psychiatry, University of Minnesota, Minneapolis, MN, USA
[b] Institute of Child Development, University of Minnesota, Minneapolis, MN, USA
[c] School of Public Health, University of Pittsburgh, Pittsburgh, PA, USA
[d] Department of Psychology, University of Oregon, Eugene, OR, USA

ARTICLE INFO

Article history:
Received 4 December 2015
Received in revised form
9 June 2016
Accepted 15 June 2016
Available online 25 June 2016

Keywords:
Neuroimaging
Non-suicidal self-injury
Self-knowledge
Depression
Adolescence
Limbic and cortical midline structures
Emotional invalidation

ABSTRACT

There is limited information regarding the neurobiology underlying non-suicidal self-injury (NSSI) in clinically-referred youth. However, the salience of disturbed interpersonal relationships and disrupted self-processing associated with NSSI suggests the neural basis of social processes as a key area for additional study. Adolescent participants ($N=123$; $M=14.75$ years, $SD=1.64$) were divided into three groups: NSSI plus depression diagnosis (NSSI), depression only (DEP), healthy controls (HC). In the scanner, participants completed an Interpersonal Self-Processing task by taking direct (own) and indirect (mothers', best friends', or classmates') perspectives regarding self-characteristics. Across all perspectives, NSSI showed higher BOLD activation in limbic areas, and anterior and posterior cortical midline structures versus DEP and HC, while HC showed greater activity in rostrolateral, frontal pole and occipital cortex than NSSI and DEP youth. Moreover, NSSI youth showed heightened responses in amygdala, hippocampus, parahippocampus, and fusiform when taking their mothers' perspective, which were negatively correlated with self-reports of the mother's support of adolescents' emotional distress in the NSSI group. NSSI youth also yielded greater precuneus and posterior cingulate cortex activity during indirect self-processing from their classmates' perspective. Findings suggest a role for disruptions in self- and emotion-processing, and conflicted social relationships in the neurobiology of NSSI among depressed adolescents.

1. Introduction

Non-suicidal self-injury (NSSI) is the self-inflicted destruction of body tissue without suicidal intent, using socially unsanctioned methods (Nixon and Heath, 2009). This behavior is common among clinically referred youth, with between 38% and 67% of adolescents with a psychiatric diagnosis reporting NSSI behavior (Brunner et al., 2014; Heath et al., 2009). NSSI is comorbid with both externalizing and internalizing disorders, including borderline personality (BPD), substance use, eating disorders, and depression (Nock et al., 2006). Understanding NSSI within its comorbid disorders is essential, as this behavior portends chronic mental illness (Barrocas et al., 2015), increased suicide risk (Dickstein et al., 2015; Klonsky et al., 2013), and lifetime impairment (Glenn and Klonsky, 2013; In-Albon et al., 2013). Identifying neural signatures distinguishing NSSI from comorbid disorders may elucidate unique neural signatures of higher risk trajectories. For instance, NSSI may facilitate severe negative outcomes such as suicide attempts (Whitlock et al., 2013a), and BPD diagnosis (Groschwitz et al., 2015), which is associated with high societal costs (Brettschneider et al., 2014).

Despite these justifications for examining NSSI behavior's associated neural signatures there is little neuroimaging research on NSSI in general; moreover, although NSSI's highest prevalence rates occur in adolescence (Moran et al., 2012) the lack of neuroimaging studies is especially notable within adolescent groups. The few existing imaging studies regarding self-injury show altered emotional processing sub-served by limbic hyperactivity. For instance, Davis et al. (2014) found that self-injurers demonstrate more amygdala activation following instructions to regulate emotional responses to negative stimuli compared to healthy controls, even though no such differences were evident in basic emotional reactivity to stimuli. Davis et al. (2014) also reported heightened activity in self-injurers versus depressed non-self-injuring controls in posterior cingulate cortex and prefrontal motor areas (BA8 and BA6) during regulation of negative emotions, perhaps suggestive of greater cognitive effort expended by self-injurers during emotion regulation. In the single neuroimaging

* Correspondence to: 2450 Riverside Avenue, Minneapolis, MN 55454, USA.
E-mail address: queve001@umn.edu (K. Quevedo).

http://dx.doi.org/10.1016/j.pscychresns.2016.06.015
0925-4927/

study of adolescent-specific NSSI, Plener et al. (2012) reported hyperactivation of the bilateral amygdala, hippocampus, anterior cingulate cortex (ACC), and cerebellum in 9 self-injurers versus 9 healthy controls in response to viewing negative images; however, controlling for depression accounted for these group differences, and this investigation is limited by its small sample size.

While vastly limited in scope, existing neuroimaging research of adult and adolescent NSSI has focused primarily on emotion dysregulation and corresponding limbic hyperactivity during processing of negative stimuli. Nonetheless, the scarcity of existing studies, small sample sizes, and absence of psychiatric, non-NSSI control groups suggest that additional study in this area is urgently needed. Past neuroimaging research has also typically employed methods which are remote from the individual's own inter- or intra-personal context (i.e., viewing negative images). Thus existing studies have overlooked two relevant and interrelated features of NSSI: interpersonal relationship difficulties and distorted self-processing, both of which are the focus of the present study.

Conflict with parents tends to increase during adolescence (Shanahan et al., 2007), and closeness and warmth within these relationships may decrease during this period (Marceau et al., 2015; Paikoff and Brooks-Gunn, 1991). Although self-injuring youth typically report conflict in both family and peer relationships (Lundh et al., 2009) researchers suggest that a history of conflict with caregivers may play a key role in the emergence of NSSI behavior through the development of poor emotion regulation skills, and that conflict with peers may serve to maintain existing NSSI behavior (Crowell et al., 2009). Specifically, caregiver emotional invalidation, conceptualized as parenting practices which imply the child's opinions and emotions are invalid, irrational or unimportant (Linehan, 1993), have been linked to emotion dysregulation and NSSI (Adrian et al., 2011; Sturrock and Mellor, 2014; Tan et al., 2014; Yurkowski et al., 2015). Indeed, when accounting for multiple interpersonal characteristics, retrospective self-reported experiences of maternal antipathy have been shown to be the sole significant predictor of NSSI behavior (Kaess et al., 2013), and observed maternal emotional invalidation and coerciveness have been linked to greater conflict in interactions between adolescent self-injurers and their mothers (Crowell et al., 2013). With respect to peers, conflict in peer relationships is also associated with youth NSSI behavior (e.g., Hilt et al., 2008), perhaps by placing continued stress on already dysregulated emotional processing systems, or by serving as distressing triggers for NSSI engagement. Consequently, the current study examined how indirect self-processing from both mothers' and peers' perspectives engages the neural basis of emotion and self-processing in self-injurers.

Self-processing is the ability to perceive, evaluate and judge one's states, traits and abilities. Toward the end of adolescence, self-referential processing results in global cognitive self-representations (self-knowledge) enabled by abstract thinking skills that emerge during this period (Harter, 1999). Researchers have shown that, in addition to dysfunctional interpersonal relationships, negatively biased self-knowledge and unresolved identity formation characterize youth who engage in NSSI. For example among eating disorder (ED) patients, NSSI is significantly and robustly related to greater identity confusion and to less identity coherence (Claes et al., 2015). Similarly, among self-injuring adolescents with ED, poor interoceptive awareness and high interpersonal ineffectiveness are both associated with NSSI (Ross et al., 2009). Lack of self-esteem and low self-efficacy have also each been linked with NSSI in student samples (Tatnell et al., 2014). High self-criticism has been shown to mediate associations between exposure to emotional abuse in childhood and NSSI behavior (Glassman et al., 2007), and is also linked with pain analgesia and higher pain endurance in self-injurers (Glenn et al., 2014; Hooley and Germain, 2014). Thus, it has been proposed that NSSI may represent a possible manifestation of one's painful, confused or disrupted self-processing (Claes et al., 2010b, 2015).

The neural substrates of self-processing implicate somewhat distinct systems compared to those involved in emotion processing and regulation (i.e., limbic regions, lateral prefrontal cortex [PFC]). Specifically, processing information regarding the self reliably engages both anterior and posterior cortical midline structures (CMS), including rostral and perigenual anterior cingulate cortex (ACC), posterior cingulate cortex (PCC), precuneus and medial PFC, particularly medial BA10 (Ichikawa et al., 2011; Kircher et al., 2000). Additionally, dorsal ACC recruitment has been noted during social rejection or negative evaluation (Rotge et al., 2015), and when healthy adolescents engage in both direct (self perspective) and indirect (important others' perspectives) self-referential processing (Jankowski et al., 2014; Pfeifer et al., 2009). Although limited in scope, existing research has shown that self-injuring youth and adults demonstrate hyperactivation of CMS regions (i.e., ACC, PCC) during emotionally distressing tasks (Davis et al., 2014; Plener et al., 2012), perhaps suggesting self-injurers' atypical processing of self-related information during heightened emotional demand. Hyperactive CMS during direct or indirect self-referential processing is also generally implicated for depressed individuals (Cooney et al., 2010; Ruiz et al., 2013; Zhang et al., 2013), a common comorbid diagnosis of NSSI (Lofthouse et al., 2009). Self-harming adults have also been shown to demonstrate even greater activation of the PCC than depressed (but non-self-harming) controls during emotion processing (Davis et al., 2014). It is also likely there are interactions among the neural systems engaged by self-processing and emotion processing. For example, self-criticism and negative self-concept, which both characterize self-injuring youth (Claes et al., 2010a; Glassman et al., 2007), are also each linked to greater limbic activity during exposure to adjectives of personally-relevant negative content versus exposure to neutral and negative non-self-referential adjectives (Doerig et al., 2014). Overall, the extant literature reviewed here lends support for studying the hypothesis that depressed youth with NSSI may show higher activity in *both* CMS and limbic areas when engaged in self-processing compared to depressed youth without NSSI and healthy controls.

Given NSSI's association to both chronic interpersonal difficulties and negatively biased self-processing, the current study sought to compare patterns of neural activation in depressed youth with and without NSSI and psychologically healthy controls during self-processing appraisals both indirectly (from the perspectives of key social others: mother, best friend and classmates), and from their own direct perspective. This research was guided by two overarching hypotheses. First, we hypothesized that NSSI youth would show the greatest hyperactivation of CMS during direct and indirect self-referential processing, regardless of perspective, followed by depressed youth without NSSI, and then psychologically healthy controls. Second, we predicted that self-processing from the mothers' perspective would elicit greater limbic activity in depressed youth with NSSI compared to both depressed and healthy controls; this hypothesis was based on theory (Linehan, 1993; Yates, 2009) and research (e.g., Kaess et al., 2013) suggesting the relevance of parental emotional invalidation on dysregulation of emotional processes in self-injuring youth. To further corroborate this putative explanation for variation in neural responses in the NSSI group, we also explored associations between observed neural activation during the mothers' perspective and mothers' reports of providing support to adolescents' experiences of sadness, anger, and fear; we expected that for self-injurers, greater limbic activity would be related to less maternal support of negative emotions.