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Prone to excitement: Adolescent females with non-suicidal self-injury (NSSI) show altered cortical pattern to emotional and NSS-related material

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ABSTRACT

Emotion-regulation difficulties have been identified as one of the core components in Non-suicidal self-injury (NSSI), a behaviour often beginning in adolescence. This pilot study evaluated differences in emotion processing between 18 female adolescents with and without NSSI by using verbal responses and functional magnetic resonance imaging (fMRI). Responses to pictures taken from the International Affective Picture System and slides with reference to NSSI were recorded both by verbal rating of valence and arousal and by fMRI. The NSSI group rated pictures with self-injurious reference as significantly more arousing than controls. For emotional pictures, the NSSI group showed a significantly stronger brain response in the amygdala, hippocampus and anterior cingulate cortex bilaterally. Depression explained differences between groups in the limbic area. Furthermore, the NSSI group also showed increased activity in the middle orbitofrontal cortex, and inferior and middle frontal cortex when viewing NSSI picture material. Participants with NSSI showed decreased activity in correlation to arousal in the occipital cortex and to valence in inferior frontal cortex when watching emotional pictures. The fMRI data support the notion that individuals with NSSI show an altered neural pattern for emotional and NSSI pictures. Behavioural data highlight proneness to excitement regarding NSSI topics. This fMRI study provides evidence for emotion-regulation deficits in the developing brain of adolescents with NSSI.

1. Introduction

Non-suicidal self-injury (NSSI) is defined as repetitive, deliberate destruction of one's own body tissue, without suicidal intent, that is not socially accepted (Lloyd-Richardson et al., 2007). Among adolescents, lifetime prevalence rates between 15 and 30% are reported in community samples from many nations (for review on prevalence rates, see Plener et al., 2010). Among psychiatric patients, NSSI is the most frequent reason for visits to medical emergency departments (Ballard et al., 2010). NSSI is not defined as a mental health disorder in the classification systems of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the International Classification of Diseases (ICD-10), but is mentioned as a symptom of borderline personality disorder (BPD). Thus, research about NSSI has often involved individuals with this personality disorder. However, NSSI – especially in adolescence – is not restricted to individuals with BPD but can be detected, for example, in depression, substance use disorders, eating disorders and also in teenagers without any further psychopathology (Jacobson and Gould, 2007; Stanford and Jones, 2009). Nock et al. (2006) showed in a sample of 89 adolescent inpatients with NSSI that only about half of the patients (51.7%) met criteria for BPD, while 59.6% met criteria for substance use disorder, 62.8% for externalizing and 51.7% for internalizing disorders. Thus, NSSI in adolescence does not seem to be specifically related to BPD. Recently, attempts have been made to propose the addition of a NSSI syndrome to the DSM-V (Shaffer and Jacobson, 2009).

Neuroimaging studies involving individuals with NSSI have so far been confined to studies in adults and older adolescents with BPD (and NSSI). One of the first functional magnetic resonance imaging (fMRI) studies compared 12 adult females with BPD and NSSI to 12 healthy controls when administering pain using heat stimuli (Schmahl et al., 2006). Patients with BPD showed an increased activity in the dorsolateral prefrontal cortex and a decrease in the posterior parietal cortex; individually adjusted pain stimuli led to a decreased activity in the perigenual anterior cingulate gyrus and the amygdala. Another study in 11 adult BPD patients and 10 healthy controls using an audio-script design (reporting a situation leading to NSSI) showed a decrease of activation in the right mid-cingulate and the left fusiform gyrus in the BPD group while imaging an act of NSSI (Kraus et al., 2010). Furthermore, studies on emotion processing in adult BPD patients often employed pictures from the International Affective Picture System (IAPS) (Lang et al., 2008). Herpertz et al. (2001) reported an elevated

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blood oxygenation level dependent (BOLD) fMRI signal in the amygdala bilaterally when comparing six female adult BPD patients with six healthy controls who viewed 12 emotionally aversive IAPS pictures. In another recent study, 20 BPD patients with a history of NSSI were compared to 23 healthy controls when IAPS pictures were presented in combination with warm or painful stimuli; it has been repeatedly shown that pain perception is altered in individuals with BPD (e.g. Cárdenas-Morales et al., 2011). The adult BPD patients with a history of NSSI demonstrated increased activity in the amygdala, insula and anterior cingulate cortex (ACC) when watching both neutral and negative IAPS pictures. Enhanced amygdala activity was positively correlated with self-perceived deficits in emotion regulation (Niedtfeld et al., 2010).

However, given that NSSI often starts around the age of 13 (Lloyd-Richardson et al., 2007), it seems necessary to assess younger adolescents given the differences in neurobiological alterations. Only a few studies involved adolescents with NSSI. In a study comparing 15 adolescent female BPD patients (mean age: 17.4, S.D.: 1.2) with "parasuicide episodes" to 15 adolescent and young adult females (mean age: 19.7, S.D.: 2.2), decreased volume of the ACC was found in BPD patients, which was correlated with the number of "parasuicide episodes" (Whittle et al., 2009). As parasuicide episodes were defined as "suicide attempts and non-suicidal self-injury", findings about NSSI alone cannot be extracted from this study. In addition the age difference between patients and healthy controls must be considered as a possible limitation because brain maturation is not completed at this age. In another study of 20 adolescent BPD patients (mean age: 17.3, S.D.: 1.1 years), it was shown that greater numbers of "parasuicidal behaviours" were associated with an increased pituitary gland volume (PGV). Again, the authors did not differ between behaviours with and without suicidal intent (with 16 out of 20 who cut themselves), which – according to them – limited their findings (Jovev et al., 2008). To the best of our knowledge, no neuroimaging study has so far specifically investigated NSSI in adolescents by using an fMRI paradigm.

The regulation of both social situations and affective states has been suggested to be implicated in NSSI (Nock and Prinstein, 2004, 2005; Klonsky, 2007; Nock, 2010). In one of the few studies specifically addressing adolescents with NSSI, higher physiological reactivity (as measured by skin conductance) was observed in a distress task in subjects with NSSI (Nock and Mendes, 2008), a finding that is in line with poor distress tolerance, which is assumed to be an important factor in NSSI (Chapman et al., 2006). Another recent study showed an attenuated cortisol response to a social stress task in adolescent females with NSSI (Kaess et al., 2012). Based on the assumption that NSSI in adolescence is often used to regulate emotions, we hypothesized that alterations in emotion processing could be detected using fMRI in female adolescents with NSSI compared with healthy controls. As studies on adult BPD patients with NSSI showed a limbic hyperarousal when watching IAPS pictures (Niedtfeld et al., 2010) and pain can lead to decreased functional activity in the ACC and the amygdala (Schmahl et al., 2006), we hypothesized, that adolescents with NSSI would show limbic hyperarousal when watching IAPS pictures in comparison to findings in healthy controls. Furthermore, as NSSI often serves as an emotion-regulation strategy (Nock, 2010) and BPD can be seen as a "prototype of emotion dysregulation" (New et al., 2007), we hypothesized a dysfunctional prefrontal regulation mechanism in adolescents with NSSI, based on findings in BPD patients (New et al., 2007; Silbersweig et al., 2007). We further hypothesized, that adolescents with NSSI would find NSSI-related picture material more arousing than would healthy controls.

2. Methods

2.1. Participants

Nine adolescent females with NSSI (mean age 15.2 ± 1.5 years, range 14–18) were included in the study. Affected females had self-injured at least once within the past 6 months according to self-reports (see Table 1). Diagnoses of the NSSI group were defined according to clinical criteria and NSSI was assessed by using standardized instruments such as the Ottawa Self-injury Inventory (OSI; Nixon et al., 2002), the Self-Harm Behaviour Questionnaire (SHBQ; Gutierrez et al., 2001) and the Functional Assessment of Self-Mutilation (FASM; Lloyd et al., 1997; for synopsis, see Table 1). German version of assessment tools have been validated in previous studies (Plener et al., 2009, 2011).

Nine age-matched adolescent females without NSSI and without a psychiatric axis I or II disorder (mean age 15.0 ± 0.9 years, range 14–16; $F = 0.15$, $p = 0.70$) were assessed to provide comparison data. All participants still attended school and were of Caucasian origin with the exception of one healthy control who was of mixed Afro-American/Caucasian origin. Participants were all right-handed. Exclusion criteria were substance abuse or dependence and a history of a mental health disorder for healthy controls. All participants were free of central nervous system medication apart from one patient (#4) who received medication (fluoxetine, 40 mg).

2.2. General procedure

Females with NSSI were patients of the Department of Child and Adolescent Psychiatry and Psychotherapy at the University Hospital of Ulm. Females without NSSI were recruited by providing announcements in public schools, via announcements in local Internet chat-rooms and by word of mouth. Following a telephone screening, participants were invited together with their parents to be personally informed about the research project. Within the next 2 weeks, participants were tested for NSSI and psychological parameters. Consecutively, fMRI scanning and verbal rating of stimuli were performed. All participants received morphological pictures of their brain on CD-ROM and a gift voucher of € 30.00 as reimbursement. The study was approved by the Institutional Review Board (IRB) of the University of Ulm. All participants provided written informed assent and their caregivers gave written informed consent for the study.

2.3. fMRI procedure

During fMRI scanning, stimuli were shown via video goggles. Participants were instructed not to suppress any upcoming emotion. After the scan, participants were asked to name the pictures they remembered as worst, and the pictures they liked the best to assure that they had kept their eyes open during fMRI scanning. Pictures of the International Picture System (IAPS) were used (Lang et al., 2008). Pictures varied according to their degree of emotional valence and arousal according to the standardized rating of the pictures (Lang et al., 2008). In addition, pictures depicting self-injury or themes related to self-injury (e.g. pictures of cutting oneself, razor blades, burning candles, shattered glass, and bandages around wrists) that had been taken by our study team were used. Pictures were presented in a pseudo-randomized order with respect to the emotional categories of valence and arousal (both based on standardised rating; Lang et al., 2008) and interleaved by pictures with self-injury picture content. The material used in this study can be obtained by contacting the corresponding author.

An event-related design optimized for maximal BOLD signal amplitude was used (Robinson et al., 2006). Stimuli were shown in the following mode: three stimuli (each 1 s, similar picture content; see supplemental data Table 1) interleaved by rest periods (1 s) and followed by a rest period of 13 to 18 s (interstimulus intervals, ISI, synchronized by the scanner) (Dale, 1999). Three sessions were done, with 26 triplets of pictures, adding up to 78 pictures per session. Each session took about 7 min. Each

Table 1
Patient characteristics.

Patient ID	Age	Diagnosis	Age of NSSI onset	Number of NSSI methods	History of suicide attempts	6-month prevalence of NSSI
1	14	MDD	12	8	Yes	4
2	18	MDD	12	6	No	3
3	16	PTSD, Combined personality disorder	15	7	Yes	3
4	14	MDD	13	4	No	3
5	14	MDD	12	3	Yes	3
6	15	MDD	13	3	No	3
7	14	BPD, Dysthymia	12	5	Yes	3
8	15	BPD, MDD	9	10	Yes	4
9	17	Mild depressive episode	13	4	Yes	1

Diagnosis according to ICD-10.
Age of onset: age at which patients injured themselves first.
Number of methods: number of different methods of NSSI according to FASM.
Suicide attempts: lifetime prevalence of suicide attempts according to SHBQ.
6-month prevalence of NSSI: according to OSI: "How often in the past 6 months have you: Actually injured yourself, without the intention to kill yourself? 0: not at all, 1: 1–5 times, 2: monthly, 3: weekly, 4: daily".
BPD: Borderline personality disorder.
MDD: Major depressive disorder.