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Commentary

The Neural Basis of Social Evaluation in Adolescents with Non-Suicidal Self-Injury

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Non-suicidal self-injurious behavior (NSSI) is common in adolescents, with rising prevalence in recent decades. NSSI is associated with future suicide attempts [1], underscoring the need to develop new interventions. NSSI episodes are often triggered by interpersonal stress; individuals with NSSI have enhanced rejection sensitivity [2], often feeling they do not belong, even when they are included [3]. Therefore, investigation of the neural systems underlying self/other perceptions is a promising area for NSSI research.

In the current issue, Perini et al. examined behavioral and neural correlates of self/other evaluation using a within-scanner rejection sensitivity paradigm in 30 adolescents with NSSI and 30 healthy controls [4]. Participants judged others, were informed how others judged them, and reported their perceptions and feelings during the procedure. Compared to controls, the NSSI group felt rejected more frequently, felt more upset during perceived rejection, disliked seeing their own face more, and (at a trend) disliked others more frequently. Both groups enjoyed being liked by others. Replicating this team's prior work using this paradigm in healthy adolescents [5], both groups demonstrated activation in the anterior cingulate cortex and insula during social evaluation (no group differences). However, a multivariate machine learning analysis was capable of classifying groups with 68% accuracy, 74% sensitivity and 59% specificity. Post-hoc analysis of the classification results showed that while awaiting peer evaluation, activation in the subgenual cingulate cortex, dorsomedial prefrontal cortex, and posterior cingulate cortex was lower in the NSSI group than controls. Validating the construct, classification scores correlated with rejection sensitivity scores.

A key strength of this study is the application of a novel, ecologically-valid behavioral paradigm to assess social rejection in adolescents with NSSI. In social media, which is nearly ubiquitous in adolescents [6], young people frequently judge themselves and others. Therefore, the electronic, interactive format represents an accessible platform for assessing perceived interpersonal judgments that is similar to adolescents' real-life experiences. Additionally, the authors' transdiagnostic approach (using NSSI as an inclusion criterion as opposed to a diagnosis) is promising for advancing knowledge about the biology of NSSI which occurs across diagnoses [7]. Finally, authors applied robust neuroimaging analysis methodology including protection against false positives, an issue that has become increasingly important in the field [8].

In addition to these noteworthy contributions, several limitations of this study and unanswered questions are notable. First, self-reported rejection sensitivity (e.g. queries about adolescents' experiences in their daily lives) would have provided an opportunity to further validate the behavioral paradigm. Second, while intriguing, the machine learning classification results leave us wondering whether these brain and behavioral metrics relate to clinical domains (i.e. depression, anxiety, history of trauma, etc.). Third, while limiting the small sample to females to limit heterogeneity is justified, this approach further widens the gap on knowledge about sex differences in the neurobiology underlying NSSI. To date, virtually nothing is known about brain mechanisms of NSSI in males. Finally, although the sample size is large in comparison to the nascent NSSI neurobiology literature, it is small enough to preclude firm conclusions on the neural mechanisms of social rejection in this population. Confirmation of these results with larger samples is needed.

The findings reported by Perini and colleagues add to a growing body of research documenting the role of key risk factors for NSSI. A supportive family is vital for fostering skills to allow healthy adolescent peer relationships. Disrupted parental attachment and peer victimization are both capable of rendering youth more vulnerable to peer evaluations and to developing NSSI [3,9]. Anxiety can heighten this vulnerability, priming the system to respond to social evaluation with stronger amygdala response [10,11]. Adolescence itself adds additional risk, as a time frame when social evaluative fears increase [12], physiological stress reactivity hormones increase [13,14], and key frontolimbic connectivity changes occur [15]. Finally, the high rate of social media use by adolescents in contemporary society provides ready access to NSSI modeling and frequent opportunities to engage in evaluative interactions [16]. Given that girls are the highest users of social media platforms [13] and interpersonal relationships are particularly relevant to functioning for females (e.g., "tend and befriend" theory) [17], this NSSI risk mechanism may be particularly applicable to adolescent girls.

The findings reported by Perini et al. suggest potential new research avenues for treatment development. Neural and behavioral metrics of rejection sensitivity could represent targets for intervention research, testing how current established treatments (e.g. dialectic behavioral

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therapy) or novel experimental approaches may be capable of altering these metrics as a mechanism of addressing NSSI. Further, since rejection sensitivity is a risk factor for NSSI and is likely present before the first onset of NSSI episodes, this target engagement approach may also be relevant for pursuing the development of neurobiologically-based prevention strategies.

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