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# Neural Reactivity to Social Punishment Predicts Future Engagement in Nonsuicidal Self-injury Among Peer-Rejected Adolescents

Olivia H. Pollak, Seh-Joo Kwon, Nathan A. Jorgensen, Kristen A. Lindquist, Eva H. Telzer, and Mitchell J. Prinstein

## ABSTRACT

**BACKGROUND:** Rates of nonsuicidal self-injury (NSSI) increase dramatically in adolescence. Affective reactivity and adverse social experiences have been linked to NSSI, but less is known about whether these factors may separately or interactively predict NSSI, especially longitudinally. This study combined functional magnetic resonance imaging and a sociometric measure to test whether a combination of neural (e.g., amygdala) reactivity to social punishment and peer-nominated peer acceptance/rejection predicts NSSI longitudinally in adolescence. Amygdala reactivity was examined as a potential neural marker of affective reactivity to social punishment, which may heighten NSSI risk in contexts of social adversity.

**METHODS:** One hundred twenty-five adolescents (63 female) completed a social incentive delay task during neuroimaging and school-based peer nominations to measure peer acceptance/rejection. NSSI engagement was assessed at baseline and 1-year follow-up.

**RESULTS:** Greater amygdala reactivity to social punishment predicted greater NSSI engagement 1 year later among adolescents with high peer rejection. This effect for the amygdala was specific to social punishment (vs. reward) and held when controlling for biological sex and pubertal development. Exploratory analyses found that ventral striatum reactivity to social reward and punishment similarly interacted with peer rejection to predict NSSI but that amygdala connectivity with salience network regions did not.

**CONCLUSIONS:** Amygdala reactivity to social punishment, in combination with high peer rejection, may increase NSSI risk in adolescence, possibly via heightened affective reactivity to adverse social experiences. Objective measures of neurobiological and social risk factors may improve prediction of NSSI, while therapeutic approaches that target affective reactivity and increase prosocial skills may protect against NSSI in adolescence.

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Nonsuicidal self-injury (NSSI), or purposeful damage to body tissue without intent to die (1), is prevalent among adolescents, with rates ranging from 17% to 67% across community and clinical samples (2,3). NSSI typically begins in early to middle adolescence (i.e., ages 12–14 years) and its prevalence increases dramatically by late adolescence (4), yet few studies have tested prospective NSSI risk factors during this developmental period. Longitudinal approaches are needed that consider interactions of individual-level risk factors with environmental experiences that may be particularly salient in adolescence.

Clinically, there is robust evidence that NSSI is associated with affective reactivity (5–8) and distressing social experiences (9,10). Emotionally distressing social experiences may precede NSSI across short timescales (10–12) and serve socially relevant functions when an individual is in distress [e.g., communicate distress, avoid social situations (6,13)]. Individuals frequently endorse both affective and social motivations for engaging in NSSI episodes (14), further suggesting that both social (e.g., adverse social experiences) and affective (e.g., affective reactivity) factors may interact within individuals to predict NSSI. However, not all adolescents who experience adverse social situations engage in NSSI, and the mechanisms that may make some adolescents susceptible to NSSI in adverse social contexts warrant further investigation.

In particular, it is not well understood how affective reactivity and social experiences may separately or interactively predict NSSI in adolescence, a period when neurodevelopmental changes orient adolescents toward peers and increase sensitivity to social rewards and punishments (15–17). This study tested the hypothesis that neural markers of affective responsivity, when anticipating aversive social stimuli (i.e., social punishment), interact with adolescents' actual social context to predict longitudinal increases in NSSI. Specifically, we tested whether amygdala reactivity to social punishment would interact with adolescents' peer-nominated acceptance/rejection to predict NSSI 1 year later.

## Amygdala Reactivity and Adolescent NSSI

Neurobiological vulnerabilities are associated with NSSI in youth, including those that may signal heightened reactivity to

 

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adverse experiences in the social environment (18,19). For example, adolescents with NSSI histories exhibit differential peripheral nervous system (e.g., hypothalamic-pituitary-adrenal axis, cortisol) responses to acute social stress (20–23). These physiological responses may underlie affective responses to social stress (22,24) and be heightened in adolescence due to pubertal changes in neurobiological stress responsiveness and emotional reactivity (25). While understudied, neural responses to social punishment may similarly suggest underlying processes, such as affective reactivity to social incentives, that may link adverse social experiences and NSSI in adolescence. In tasks involving aversive social feedback [e.g., negative evaluative peer feedback (26), peer rejection (27,28), angry faces (20,29)], adolescents with NSSI histories have shown heightened neural activation (i.e., during anticipation and receipt) in multiple regions, including those known to represent affective salience and responsivity to the social environment, such as the amygdala (20,29). However, neuroimaging studies of NSSI in youth are few and cross-sectional. It is unknown whether particular neural, including amygdalar, responses to social punishment are prospective risk factors for future NSSI in youth, possibly by amplifying affective reactivity.

Given the amygdala's role in detecting cues in the social environment and modulating affective responses to these cues (30,31), amygdala reactivity to social punishment may be a promising neural marker of NSSI risk. The amygdala is central to representing affective salience and is part of a network of regions implicated in responsivity to salient social stimuli and generation of affective states (32–34). Importantly, the amygdala has been shown to respond to both social punishment and reward (35,36) and may be particularly engaged during anticipation of these outcomes (37). Anticipation of social punishment has been shown to elicit negative affective responses (38,39), and amygdala reactivity during anticipation of social punishment (e.g., peer rejection feedback, angry faces) is thought to underlie heightened emotional reactivity in other forms of psychopathology (e.g., social anxiety) (40,41). These neural responses may be particularly heightened in adolescence and may be linked to behavioral increases in emotional reactivity in this period (42–45). Anticipation of social punishment is also a key motivational driver of behaviors such as avoidance, which may be pertinent given that some individuals report engaging in NSSI to avoid distressing social situations (6,12).

Therefore, amygdala reactivity during anticipation of social punishment may reflect heightened affective reactivity to adverse social experiences and predict behaviors such as NSSI, which has been frequently linked to affective reactivity in contexts of social distress (5,10,46). Among adolescents, NSSI urges often occur in social contexts (e.g., with peers or friends) (47), and affective distress related to adverse social experiences may predict NSSI across short timescales (10,11). Indeed, adverse social experiences (e.g., peer rejection) are robust correlates of adolescent NSSI (48,49).

## Experiences in the Peer Environment

While amygdala reactivity to adverse social experiences may be heightened for many adolescents in this developmental period (50,51), NSSI risk is likely increased in combination with environmental stressors, particularly stressors in the social environment (9). Neural reactivity to aversive peer feedback (e.g., peer exclusion) correlates with real-world social vulnerabilities [e.g., less peer connectedness (52)] and may predict elevated risk for psychopathology (e.g., internalizing symptoms) only among adolescents with histories of social adversity [e.g., peer victimization (53)]. Thus, it is critical that research considers adolescents' actual social context when testing neural-based risk for NSSI.

Adverse experiences in the peer environment may be particularly relevant. Peer-related stressors (e.g., peer rejection) are among the most frequently cited precipitants of self-injurious behaviors in adolescence (54,55), a period marked by increases in the frequency and emotional intensity of peer interactions and neurobiological changes that may underlie heightened sensitivity to peer experiences (50,51,56). Negative peer experiences are both correlates of and risk factors for adolescent NSSI (48,49,57) and may be stronger predictors of future NSSI than stress in other interpersonal domains (e.g., family) (58). Indeed, multiple aspects of adolescents' peer relationships (e.g., negative beliefs about peers) may contribute to risk (58,59). However, prior work has largely relied on self-report measures of adverse social experiences, which may capture a narrow range of peer experiences and present confounds when assessing adverse peer-related experiences in adolescents with psychopathology (60).

More rigorous measures are needed to provide ecologically valid indices of adverse peer experiences, including peer rejection, given its association with NSSI (55). A different, underused approach in this literature involves the use of sociometric measures, which rely on peers' views of an adolescent and capture cumulative, peer-related experiences across peer informants. More specifically, sociometric measures using peer nominations of how well one is liked among peers offer a global, ecologically valid marker of peer status (61,62). For decades, developmental psychologists have used peer-nominated peer rejection scores to identify adolescents who experience higher levels of peer victimization, social exclusion, ostracism, poor friendship quality, and numerous other adverse peer experiences (63). A sociometric measure of peer rejection may moderate the influence of neural reactivity on NSSI risk such that adolescents who exhibit neural (i.e., amygdala) sensitivity to social punishment and who also experience greater peer rejection may be at elevated risk.

## Current Study

This aim of this longitudinal study was to understand the real-world social contexts in which neural reactivity to the social environment may increase future NSSI risk in adolescence by combining functional magnetic resonance imaging (fMRI) with a sociometric index of peer acceptance/rejection. First, we tested whether greater amygdala reactivity during anticipation of social punishment would predict increases in NSSI engagement 1 year later. Specifically, adolescents completed a social incentive delay (SID) task in which they anticipated and sought to avoid social punishment (i.e., a scowling peer face) and anticipated and sought to gain social reward (i.e., a smiling peer face). Past work suggests that neural activity during

anticipation of social reward and punishment in the SID may reflect individual differences in adolescents' sensitivity to the social environment (16,64). Second, and most importantly, we tested the interaction of amygdala reactivity to anticipation of social punishment with school-based peer acceptance/rejection to examine whether longitudinal associations between amygdala reactivity and NSSI were strongest among adolescents experiencing greater levels of real-world peer rejection.

Supplemental analyses tested amygdala connectivity with 3 salience network regions (i.e., ventral striatum [VS], insula, subgenual anterior cingulate cortex) to further examine patterns of amygdala responsivity to social punishment that may heighten or attenuate NSSI risk (see the Supplement). Exploratory analyses tested activation in these salience network regions during anticipation of social reward and punishment, and amygdala reactivity during anticipation of social reward, to examine region (i.e., amygdala) and feedback condition (i.e., social punishment) specificity. By jointly considering individual-level neural responses and environment-level stressors in a longitudinal design, this study tested vulnerability-stress models of NSSI risk using objective measures. The large, demographically diverse sample stands in contrast to prior neuroimaging studies of adolescent self-injurious thoughts and behaviors, which have largely relied on smaller samples examined cross-sectionally (18).

## METHODS AND MATERIALS

### Participants

Participants were recruited from a larger longitudinal study conducted in a diverse, rural community in the southeastern United States. Eligibility required that participants be at least 11 years, 10 months of age. Exclusion criteria included diagnosis of a learning disability, history of seizures or head trauma, or dental work involving metal. Adolescent participants and parent/guardian(s) provided written assent/consent according to the university's Institutional Review Board. Of the original 143 participants who completed the fMRI scan, 2 were excluded from analyses due to not completing the scan, 2 for excessive motion (>2 mm across more than 10% of volumes), 1 for technical errors, 1 for an MRI artifact, and 12 for missing NSSI data at follow-up, leading to a total sample of 125 adolescents ($mean_{age}$ = 12.82, SD = 0.53; 50.4% female). The sample was diverse with regard to race/ethnicity (23.2% Black, 8.8% mixed race, 4.0% other, 31.2% White, 32.8% Hispanic/Latinx) and socioeconomic background[1] [area deprivation index (ADI) (65,66): mean = 67.30, SD = 17.66].

Adolescent participants completed self-report measures of NSSI at baseline and 1-year follow-up and a sociometric nomination procedure at baseline in school. Adolescent participants and primary caregiver(s) attended an fMRI scan session in the same academic year (days between school assessment and scan: mean = 165, SD = 78). Adolescents were trained in the SID task and acclimated to a mock scanner before the scan.

[1]ADI scores in this sample indicated that participants came primarily from relatively deprived areas.

### Measures

**SID Task.** Participants completed the SID task (67) during fMRI to measure neural responses when anticipating (i.e., attempting to gain and avoid) social rewards and punishments (Figure 1). Primary analyses focused on social punishment anticipation. See the Supplement for further task description.

**Nonsuicidal Self-injury.** NSSI was assessed with a questionnaire adapted from prior research (68–70). Items assessed past-year engagement (i.e., number of times) in 5 NSSI behaviors (i.e., cutting or carving skin, inserting objects under nails or skin, burning skin, scraping or picking skin to the point of drawing blood, hitting self on purpose) using a 5-point scale commonly used to assess health risk behaviors in community samples (1 = *never*, 2 = *1-2 times*, 3 = *4-5 times*, 4 = *6-9 times*, 5 = *10 or more times*). NSSI engagement was calculated as the mean of past-year NSSI engagement across the 5 behaviors (with higher scores indicating more engagement) and yielded acceptable internal consistency (Cronbach's $\alpha$ = 0.70–0.74).

**Peer Acceptance/Rejection.** Peer acceptance/rejection was measured using a standard sociometric peer nomination procedure in school classrooms. Adolescents were provided an alphabetized roster of all grade-mates, counterbalanced A–Z or Z–A, and asked to identify an unlimited number of peers they liked most and liked least. As in past research (61), a standardized difference score between standardized (i.e., within-grade) liked-most and liked-least nominations was calculated to yield a social preference score (i.e., peer acceptance/rejection), with higher scores indicating greater peer acceptance and lower scores indicating greater peer rejection (61). Sociometric procedures have been shown to be reliable and valid and are considered among the most ecologically valid, robust approaches for assessing peer rejection (61,71).

**Demographic Measures.** Participants self-reported their biological sex and race/ethnicity. Socioeconomic status and pubertal development were assessed using the ADI (65,66) and the Pubertal Development Scale (72), respectively (see the Supplement).

### fMRI Data Acquisition and Analysis

Imaging data were collected using a 3T Siemens Prisma MRI scanner (Siemens Corp.). MRI data acquisition and preprocessing are described in the Supplement. Individual-level, fixed-effects analyses were estimated using the general linear model convolved with a canonical hemodynamic response function in SPM8. Six motion parameters were modeled as regressors of no interest. Using the parameter estimates from the general linear model, linear contrast images comparing each of the conditions of interest were calculated for each individual. The primary contrast of interest was social punishment anticipation (i.e., angry face) versus neutral anticipation (i.e., blurred face) to examine neural activation during social punishment anticipation (i.e., controlling for neutral), given evidence linking sensitivity to anticipated social punishment in socioaffective salience regions and psychopathology

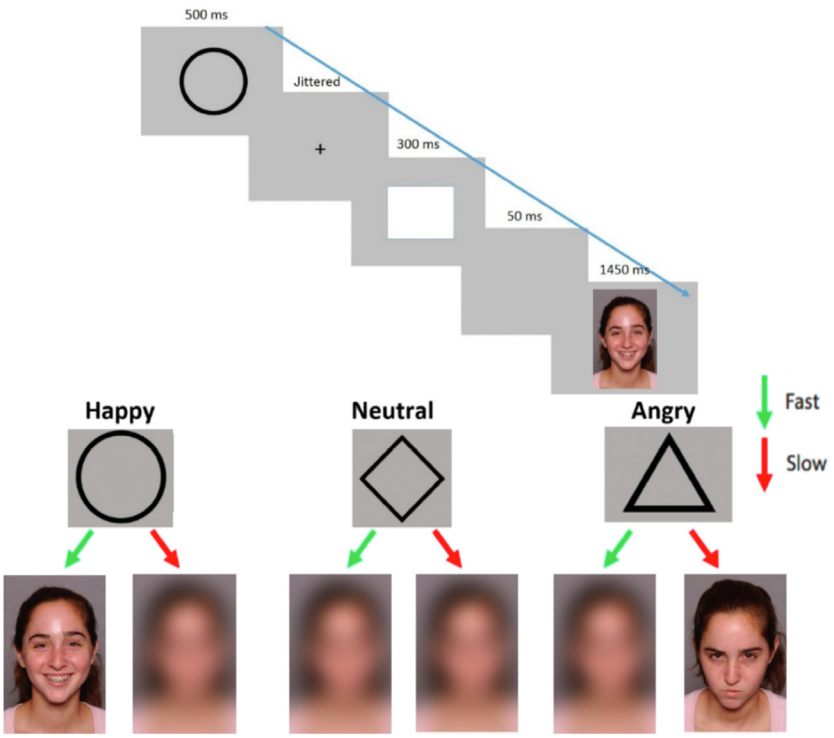


**Figure 1.** Social incentive delay task. Trials consist of a circle, diamond, or triangle cue; a jittered crosshair delay; a white square target prompting participants to press a button; and feedback (e.g., angry face). Cues and corresponding feedback are depicted in the lower panel of the figure.

in adolescents (15,35,64). Individual-level subject contrasts were submitted to random effects, group-level analyses in GLMFlex (73). To examine amygdala reactivity, we used the bilateral amygdala as our region of interest, defined using the Harvard-Oxford Atlas (74). Parameter estimates of amygdala activation were extracted from the condition of interest (i.e., social punishment anticipation vs. neutral). Connectivity analyses are reported in the Supplement.

## Statistical Analysis

NSSI variables were log-transformed to reduce positive skew. Little's missing completely at random test examined randomness of missing data (i.e., 1.6% missing baseline NSSI) and was not significant, $\chi^2_8 = 4.16$, $p = .84$, indicating that assumptions for missing completely at random were met. Missing data were handled using listwise deletion. There was no evidence of multicollinearity (variance inflation factor values = 1.05–1.28; tolerance values = 0.78–0.95). Linear regressions examined associations between amygdala reactivity and NSSI engagement at 1-year follow-up, controlling for baseline NSSI engagement. In moderation analyses, predictor and moderator variables were mean centered prior to calculating interaction terms. Simple slopes were tested at low (−1 SD; i.e., high peer rejection), average (mean), and high (+1 SD; i.e., high peer acceptance) levels of peer acceptance/rejection. The Johnson-Neyman technique was used to determine significance regions (75). Connectivity analyses are described in the Supplement. Sensitivity analyses also examined the positive (i.e., liked-most) and negative (i.e., liked-least) dimensions of social preference as separate moderators (see the Supplement).

Biological sex and pubertal development were correlated with at least one predictor and/or outcome variable(s) and were examined as covariates in sensitivity analyses. Exploratory analyses examined other salience network regions of interest (i.e., VS, insula, subgenual anterior cingulate cortex) and positive feedback (i.e., social reward anticipation) to test whether results were specific to the amygdala and to social punishment. The Benjamini-Hochberg procedure (76) was applied to control the false discovery rate set at .05.

## RESULTS

NSSI was endorsed by 37.6% of participants at baseline and 25.6% of participants at 1-year follow-up; 4.8% were new-onset cases at follow-up (20.8% maintenance, 16.8% cessation). Amygdala reactivity was not correlated with peer acceptance/rejection at baseline. Amygdala reactivity and peer acceptance/rejection were significantly inversely correlated with baseline NSSI. Biological sex and pubertal development, but not socioeconomic status, were correlated with baseline and/or 1-year NSSI (Table 1). There were no differences in amygdala reactivity, peer acceptance/rejection, or NSSI (i.e., baseline, 1-year) based on race/ethnicity ($F$s = 0.64–1.86, $p$s = .12–.64).

Prospectively, amygdala reactivity did not predict 1-year NSSI engagement, controlling for baseline NSSI engagement ($b = 0.008$, $p = .789$, CI = −0.053 to 0.069). As hypothesized, a significant interaction of amygdala reactivity with peer acceptance/rejection was found for prediction of 1-year NSSI

**Table 1. Descriptive Statistics and Bivariate Correlations Among Study Variables**

| Variable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 Amygdala Reactivity | – | – | – | – | – | – | – | – | – | – |
| 2 Amygdala-VS | −0.15 | – | – | – | – | – | – | – | – | – |
| 3 Amygdala-Insula | −0.05 | 0.38[a] | – | – | – | – | – | – | – | – |
| 4 Amygdala-sgACC | −0.11 | 0.51[a] | 0.13 | – | – | – | – | – | – | – |
| 5 Peer Acceptance/Rejection | 0.02 | 0.06 | −0.14 | −0.05 | – | – | – | – | – | – |
| 6 NSSI Engagement, Baseline | −0.22[b] | −0.01 | 0.09 | 0.06 | −0.22[b] | – | – | | – | – |
| 7 NSSI Engagement, 1-Year Follow-up | −0.11 | 0.05 | 0.17 | 0.08 | −0.14 | 0.60[a] | – | – | – | – |
| 8 Biological Sex[c] | 0.05 | 0.06 | 0.05 | 0.08 | 0.10 | 0.13 | 0.20[b] | – | – | – |
| 9 Pubertal Development | −0.12 | 0.16 | −0.01 | 0.19[b] | 0.04 | 0.22[a] | 0.20[b] | 0.36[a] | – | – |
| 10 SES (ADI Score) | −0.08 | −0.08 | 0.00 | −0.03 | 0.01 | −0.03 | −0.12 | −0.10 | −0.01 | – |
| Mean | 0.08 | 0.12 | −0.00 | 0.13 | 0.15 | 0.18 | 0.12 | – | 2.42 | 67.30 |
| SD | 0.64 | 0.83 | 0.77 | 0.96 | 0.90 | 0.31 | 0.26 | – | 0.63 | 17.66 |

Descriptive statistics and correlations for NSSI use the log-transformed variables. Pearson's correlations are presented for all variables except biological sex. Point-biserial correlations are presented for correlations between biological sex and other variables.

ADI, area deprivation index; NSSI, nonsuicidal self-injury; SES, socioeconomic status; sgACC, subgenual anterior cingulate cortex; VS, ventral striatum.

[a] $p < .01$.

[b] $p < .05$.

[c] Females had greater NSSI engagement at 1-year follow-up and more advanced pubertal development compared to males.

($b = -0.110$, $p = .017$, CI = −0.199 to −0.020) (Table 2). At high levels of peer rejection, greater amygdala reactivity was associated with greater NSSI engagement at 1-year follow-up ($b = 0.142$, SE = 0.062, $p = .026$) (Figure 2). Amygdala reactivity was not associated with 1-year NSSI at average levels of peer acceptance/rejection ($b = 0.042$, SE = 0.033, $p = .210$) or at high levels of peer acceptance ($b = -0.058$, SE = 0.041, $p = .159$). The simple slope of amygdala reactivity on NSSI was significant and positive at more than 0.47 SD below, and significant and negative at more than 1.63 SD above, the mean on peer acceptance/rejection (Figure 3). In sensitivity analyses, this was shown to be specific to the positive dimension of social preference, with post hoc probing showing an identical pattern of findings (see the Supplement). In sensitivity analyses controlling for biological sex and pubertal development (see the Supplement), amygdala reactivity remained predictive of 1-year NSSI (Table S1), such that greater amygdala reactivity was associated with greater 1-year NSSI at high levels of peer rejection ($b = 0.129$, SE = 0.063, $p = .043$).

In exploratory analyses, the interaction of VS reactivity with peer acceptance/rejection was associated with 1-year NSSI for both social punishment and reward anticipation, such that greater VS reactivity during both conditions was associated

**Table 2. Adolescents' Peer Acceptance Moderates the Association Between Amygdala Reactivity and NSSI Engagement at 1-Year Follow-up**

| Variable | $\Delta R^2$ | *b* (SE) | *p* Value | 95% CI |
|---|---|---|---|---|
| Step 1. Covariate | 0.352 | – | – | – |
| NSSI engagement, baseline | – | 0.510 (0.063) | <.001 | 0.385 to 0.635 |
| Step 2. Main Effects | 0.001 | – | – | – |
| Amygdala reactivity | – | 0.008 (0.031) | .793 | −0.053 to 0.069 |
| Peer acceptance | – | −0.004 (0.022) | .846 | −0.048 to 0.039 |
| Step 3. Interaction | 0.031 | – | – | – |
| Amygdala reactivity × peer acceptance | – | −0.110 (0.045) | .017 | −0.199 to −0.020 |
| Total $R^2$ | 0.384 | – | – | – |

NSSI, nonsuicidal self-injury.

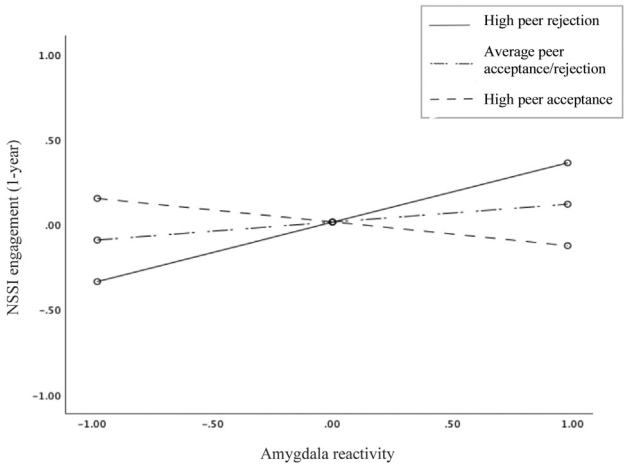


**Figure 2.** The interaction effect of amygdala reactivity and peer acceptance/rejection on nonsuicidal self-injury (NSSI) engagement at 1-year follow-up. Simple slopes were plotted at low (−1 SD, high peer rejection), average (mean), and high (+1 SD, high peer acceptance) levels of peer acceptance/rejection. The simple slope of amygdala reactivity on 1-year NSSI engagement was significant at a high level of peer rejection. For interpretability, amygdala reactivity (x-axis) and 1-year NSSI engagement (y-axis) were *z*-transformed, such that negative scores represent below-average amygdala reactivity and NSSI engagement, respectively, whereas positive scores represent above-average amygdala reactivity and NSSI engagement, respectively.

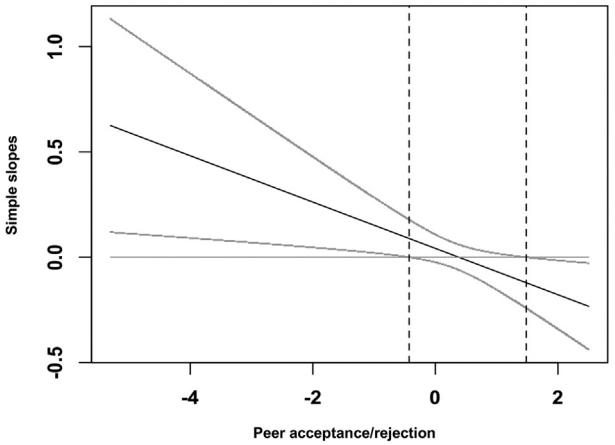


**Figure 3.** Conditional values of peer acceptance/rejection by values of the simple slope of 1-year nonsuicidal self-injury engagement regressed onto amygdala reactivity. The dotted vertical lines indicate regions of significance where simple slopes outside this region are significant. Confidence bands in gray show continuously plotted confidence intervals for simple slopes corresponding to all conditional values of peer acceptance/rejection (i.e., moderator).

with greater 1-year NSSI at high levels of peer rejection (*b*s = 0.094–0.122, SEs = 0.044–0.046, *p*s = .008–.033). Counter to findings for social punishment, the interaction of amygdala reactivity to social reward with peer acceptance/rejection was not associated with 1-year NSSI ($b = -0.072$, $p = .130$, CI = −0.166 to 0.022) (see the Supplement).

## DISCUSSION

Research has begun to examine neural correlates of NSSI in adolescence but has not yet tested these as prospective risk factors. Furthermore, prior work has not considered functional neural markers alongside the actual social contexts in which adolescents' NSSI behaviors may onset or persist. This study provides a novel contribution by showing that amygdala reactivity during anticipation of social punishment interacts with a robust index of peer acceptance/rejection to predict future NSSI. This builds on prior work showing that neural activation to aversive peer-related stimuli (i.e., peer exclusion) may be linked to future psychopathology specifically among adolescents experiencing real-life, adverse peer experiences (53), and extends this to NSSI examined longitudinally. Findings from this study enhance clinical understanding of adolescent self-injurious behaviors by considering interactions of neurobiological and social risk factors assessed objectively (77,78).

As expected, results revealed that greater amygdala reactivity during anticipation of social punishment predicted greater NSSI engagement 1 year later among adolescents with lower peer-nominated social preference,[2] above and beyond baseline NSSI engagement. Adolescents who are both more sensitive to the prospect of social punishment and who may experience greater social adversity in their real-world peer network may be at risk for NSSI given associations between affective distress, peer victimization, and self-injurious behaviors (10–12,48,49). The amygdala is implicated in responsivity to salient social stimuli and generation of affective states and, as hypothesized, may underlie affective reactivity to social punishment (35,36,41). Affective reactivity is a robust risk factor for NSSI (7,79), whereby individuals may engage in NSSI to regulate aversive emotions via relatively immediate changes in affective and physiological arousal (80–84). Indeed, affect regulation following NSSI has been posited as a mechanism underlying reinforcement of these behaviors (6). Adolescents with greater amygdala reactivity to social punishment may therefore experience heightened affective responses during anticipated social punishment, which may increase NSSI risk for youths who are also less well-liked by peers and who may experience greater peer rejection. Rejection experiences themselves may confer further vulnerability given associations between chronic social adversity and neurobiological stress responses [e.g., heightened amygdala reactivity (85,86), maladaptive hypothalamic-pituitary-adrenal axis responses (87,88)] that may underlie affective reactivity to social stress (25). Indeed, adolescents experiencing greater peer rejection may be at risk for heightened affective reactivity across multiple neurobiological systems (22,89) that increase NSSI risk in stressful peer contexts.

While not initially hypothesized, amygdala reactivity may also be linked to NSSI among adolescents with lower social preference (i.e., lower liked-most scores specifically, as shown in sensitivity analyses) via other affect-related mechanisms, such as biased self-referential processing or self-criticism. Activation in limbic regions, including the amygdala, is heightened during exposure to personally relevant negative content (90), suggesting that these regions may subserve generation of negative affective states in response to negative self-relevant information. Heightened amygdala activation has been shown in nonclinical and self-injuring adolescent samples during processing of negative self-referential feedback from others, such as criticism (91,92). Self-criticism or self-punishment may motivate engagement in NSSI for certain individuals (93–95), and adolescents experiencing peer rejection may also be more likely to make critical self-referential attributions regarding peer experiences (96). Amygdala reactivity may possibly be linked to NSSI via involvement in self-related emotional responses or negative self-processing biases during anticipation of social punishment. Indeed, social punishment—even in the form of scowling reactions from peers, as in the SID task—may be a highly salient form of negative, self-relevant feedback in adolescence, when neurodevelopmental changes permit increased appraisals and comparisons with peers and contribute to identity development (50).

Qualities of different peer contexts may also contribute to NSSI risk. NSSI, similar to other risk behaviors, may be socialized within peer groups (97,98). Future research might explore whether, for adolescents with lower social preference, amygdala reactivity to social punishment (e.g., via affective reactivity) or affiliation with self-injuring peers is most relevant to elevated NSSI risk in these peer contexts. Conversely,

[2]In sensitivity analyses, this interaction effect was shown to be specific to the liked-most dimension of social preference (i.e., a significant association at low levels of liked-most scores). Low scores on the liked-most dimension of social preference are considered indices of low peer acceptance/high peer rejection (111).

prosocial experiences or qualities of positive peer contexts may buffer against NSSI risk, particularly as greater amygdala reactivity was associated with less frequent NSSI 1 year later at very high levels of social preference. Sensitivity analyses showing effects to be specific to the positive dimension of social preference may contextualize this protective effect by demonstrating that adolescents with amygdala sensitivity who are, indeed, very well-liked (i.e., those with high liked-most scores)—compared with minimally liked or moderately disliked (those with high liked-least scores)—may be at lower risk for NSSI. This is consistent with findings that high peer acceptance may protect against externalizing symptoms and other risk behaviors (e.g., substance use) in youth (99), possibly via increased opportunity to receive prosocial feedback or other self-esteem or emotional benefits of positive peer relations (100).

The importance of adolescents' peer contexts is further emphasized by results showing that amygdala reactivity was not predictive of future NSSI in main effect analyses. This was surprising in light of cross-sectional evidence for altered amygdala reactivity (i.e., activation and connectivity) among adolescents with NSSI histories (101–104), including reactivity to social feedback [e.g., angry faces (20,29)]. Prior cross-sectional findings may be driven by contemporaneous associations between socioaffective processing and NSSI that do not emerge longitudinally. Counter to expectation, we also found an inverse cross-sectional correlation between amygdala reactivity and baseline NSSI. This nevertheless mirrors studies showing decreased amygdala activation during anticipation or simulation of pain, which may indicate a mechanism to attenuate pain-related stress responses in aversive contexts (103,105). Hypoactive or attenuated amygdala responses may be also be a consequence of NSSI itself [i.e., habituation to NSSI and aversive or pain-related stimuli (22,106)].

Our primary finding for the amygdala was specific to anticipation of social punishment and not anticipation of reward. For adolescents with lower social preference (i.e., greater peer rejection), amygdala sensitivity to threat of social punishment (vs. possibility of social reward) may be relevant to NSSI risk, consistent with evidence linking NSSI to affective reactivity in contexts of social distress (5,10,46). Exploratory analyses also revealed significant effects for the VS during anticipation of both social reward and punishment. The VS, similar to the amygdala, has been implicated in anticipation of rewards and punishments, especially in adolescents (32,37,44,107). In particular, VS activation may indicate the behavioral salience of stimuli—the likelihood that an individual needs to engage in an important behavioral response in reaction to a stimulus (108). For adolescents who are less accepted by their peers, neural sensitivity in these key social-affective salience regions may increase NSSI risk via heightened affective reactivity and behavioral potentiation to the social environment (45). Reactivity in these regions has also been posited to explain differences in social motivational sensitivity (32,37,38), which may implicate other NSSI-relevant mechanisms. Neural sensitivity when avoiding aversive stimuli (e.g., social punishment anticipation) and approaching appetitive incentives (e.g., social reward anticipation) may underlie motivational processes that map onto empirically supported, socially relevant motivations for NSSI, such as interpersonal avoidance or support seeking (6,13).

This study revealed that a combination of neural reactivity and lower social preference may increase risk for future NSSI in adolescence. Amygdala reactivity to social punishment may be a neural marker of affective reactivity to adverse social experiences and temporally precede NSSI engagement among youths experiencing less acceptance/greater rejection among peers in real life. Our results should be interpreted in light of several limitations. Neural processes that may represent NSSI risk factors are complex and implicate multiple neural networks. This investigation primarily tested regional amygdala activity and 3 additional salience network regions in exploratory analyses. Studies adopting a network neuroscience approach might further examine social, cognitive, and affective processes (e.g., self-referential processing, emotion regulation) (89,109) implicated in NSSI in adverse peer contexts. Interpretation of results would be further aided by data on the peer contexts in which NSSI may be most likely to occur (e.g., peer influence effects). A strength of this study was our use of a sociometric measure to isolate the unique effects of adverse peer experiences measured objectively, which avoided confounding social stress exposure with other stress-related processes (e.g., cognitive appraisals of stress) that may contribute to risk (110). Interventions to increase prosocial peer relationships may be helpful in reducing NSSI risk among adolescents who may be more likely to exhibit affective reactivity to social experiences.

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EHT, KAL, and MJP designed and performed research; OHP, S-JK, and NAJ analyzed data; OHP, S-JK, and NAJ wrote the manuscript; and EHT, KAL, and MJP edited and reviewed the manuscript.

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## ARTICLE INFORMATION

From the Department of Psychology and Neuroscience, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.

Address correspondence to Olivia H. Pollak, M.A., at ohpollak@ad.unc.edu.

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