Title

A preliminary investigation into cortical structural alterations in adolescents with nonsuicidal self-injury.

Authors

Patel, Kinjal

Sheridan, Margaret

Bonar, Adrienne

et al.

Publication Date

2023-12-01

DOI

10.1016/j.pscychresns.2023.111725

Peer reviewed

HHS Public Access

Author manuscript

Psychiatry Res Neuroimaging. Author manuscript; available in PMC 2024 December 01.

Published in final edited form as:

Psychiatry Res Neuroimaging. 2023 December ; 336: . doi:10.1016/j.pscychresns.2023.111725.

A preliminary investigation into cortical structural alterations in adolescents with nonsuicidal self-injury

Kinjal K. Patel[a], **Margaret A. Sheridan**[a], **Adrienne S. Bonar**[a], **Matteo Giletta**[b,c], **Paul D. Hastings**[d], **Matthew K. Nock**[e], **Karen D. Rudolph**[f], **George M. Slavich**[g], **Mitchell J. Prinstein**[a], **Adam Bryant Miller**[a,h]

[a]Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

[b]Department of Developmental, Personality, and Social Psychology, Ghent University, Ghent, Belgium

[c]Department of Developmental Psychology, Tilburg University, Tilburg, Netherlands

[d]Department of Psychology, University of California, Davis, Davis, CA, USA

[e]Department of Psychology, Harvard University, Cambridge, MA, USA

[f]Department of Psychology, University of Illinois at Urbana-Champaign, Champaign, IL, USA

[g]Cousins Center for Psychoneuroimmunology and Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, Los Angeles, CA, USA

[h]RTI International, Research Triangle Park, NC, USA

Abstract

The structural neural correlates underlying youth nonsuicidal self-injury (NSSI) warrant further exploration. Few studies have explored the association between NSSI and brain structure in adolescence, and no studies have investigated differences in the relation between age and brain structure in youth with NSSI. This preliminary investigation examined associations between NSSI history, age, and cortical structure using magnetic resonance imaging in adolescent girls (N=100, M_{age}=13.4 years) at increased risk for psychopathology. We conducted whole-brain analyses to investigate the associations between age and cortical structure, NSSI history and cortical structure, and NSSI history as a moderator of the association between age and cortical structure. Results suggested that age was associated with less cortical thickness and surface area in the left and right prefrontal, temporal, and parietal cortex. NSSI history was associated with less left insula and left inferior parietal cortex cortical surface area. Among adolescents with NSSI history, older age predicted greater left inferior parietal cortex surface area and was not associated with left

Declaration of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

precentral cortex surface area. Among adolescents without NSSI history, older age predicted smaller surface areas as expected with the typical trajectory of neurodevelopment. Overall, our results suggest differences in cortical surface area development in adolescents with NSSI history.

Keywords

nonsuicidal self-injury; adolescence; magnetic resonance imaging; brain structure

1. Introduction

Adolescence is a developmental period characterized by substantial neurobiological changes (Casey et al., 2008; Giedd et al., 1999; Somerville et al., 2010; Spear, 2000) and is associated with increases in engagement in risky behaviors (Dahl, 2004; Steinberg, 2008), including nonsuicidal self-injury (NSSI). NSSI is defined as direct and deliberate self-harm without intent to die (Nock, 2009). NSSI typically begins in early adolescence around ages 12–14 years old (Ammerman et al., 2018; Whitlock et al., 2011; Zetterqvist et al., 2013), and rates of NSSI are higher in girls as compared to boys (Swannell et al., 2014). Prevalence of NSSI peaks during adolescence, with high rates in both community (18%; Muehlenkamp et al., 2012) and clinical (50%; Asarnow et al., 2011; Nock, 2010) samples. NSSI is associated with significant distress and injury (Glenn & Klonsky, 2013; Klonsky et al., 2014) and is a prospective predictor of suicide attempts (e.g., Asarnow et al., 2011; Guan et al., 2012; Klonsky et al., 2013). Research has examined psychological correlates of NSSI, but few studies have investigated the neural underpinnings of NSSI, which may uncover novel mechanisms contributing to NSSI.

1.1. Theories of NSSI

Prevailing theoretical models of NSSI focus on the reinforcing properties of NSSI. For example, the Four Function Model (FFM) specifically posits NSSI as a behavior that regulates internal/intrapersonal (automatic function) or interpersonal (social function) experiences (Nock & Prinstein, 2004). Within this model, automatic and social functions are reinforced by either generating desired cognitive-affective or social states (positive reinforcement) or by decreasing aversive cognitive-affective or social states (negative reinforcement). Research supports this model (Nock, 2009; Nock & Mendes, 2008; Nock & Prinstein, 2005), and implicates automatic negative reinforcement as the most prevalent function of NSSI (Bentley et al., 2014; Liu, 2017). Similarly, other theories highlighting the reinforcing properties of NSSI suggest that this behavior provides an affect-regulation function (Hooley & Franklin, 2018; Klonsky, 2007), or avoidance or escape from unwanted emotional experiences (Chapman et al., 2006). In sum, these theories suggest that NSSI may aid in reduction of negative affect and often serves a regulatory function among adolescents.

1.2. Neural structural correlates and NSSI

Neural structure in the prefrontal cortex and parietal cortex may be associated with NSSI given their substantial role in emotion regulation (Etkin et al., 2015; Goldin et al., 2008; Ochsner et al., 2004), self-regulation (Heatherton & Wagner, 2010; Langner et al., 2018; Palacios-Barrios & Hanson, 2019), and cognitive control (Luna et al., 2015; Vijayakumar et

al., 2014). Initial research reveals structural neurobiological alterations in adolescents with a history of NSSI. A recent study found that self-injuring adolescent girls (ages 13–19) show regional reductions in gray matter volume in the insular and right inferior frontal cortex when compared to age-matched peers (N=40; Beauchaine et al., 2019). Another study comparing adolescent girls with NSSI history (ages 14–18, N=50) to an age- and gender-matched healthy control group found that NSSI history was associated with lower regional grey matter volume in the insular cortex and anterior cingulate cortex (ACC; Ando et al., 2018). Of note, only Beauchaine et al. (2019) reported covarying for age in their statistical models, and neither study explored whether NSSI altered age-related changes in the brain. Examining the role of age is paramount to further understanding of how the developmental pattern of cortical structure may differ based on NSSI history.

1.3. Typical changes in cortical structure during adolescent development

Prior research has quantified brain maturation during childhood and adolescence by measuring cortical thickness and surface area either across time or for participants of different ages (Mills & Tamnes, 2014). Cortical surface area and thickness are distinct structural components with unique cellular and genetic origins (Geschwind & Rakic, 2013; Kremen et al., 2013; Panizzon et al., 2009), that represent independent measures of cortical structure. Longitudinal magnetic resonance imaging (MRI) studies show that cortical thickness decreases approximately linearly across childhood and adolescence for most of the cortex (Giedd et al., 1999; LeWinn et al., 2017; Mills et al., 2014a; Tamnes et al., 2017; Wierenga et al., 2014). In contrast, cortical surface area increases during childhood but then decreases across adolescence (LeWinn et al., 2017; Raznahan et al., 2011; Tamnes et al., 2017; Wierenga et al., 2014), following a non-linear trajectory. Thus, typical neurodevelopment during adolescence is characterized by cortical thinning and decreases in cortical surface area. Additional evidence suggests that expansion of cortical thickness is complete by age 2, while the expansion of cortical surface area continues into childhood and early adolescence (Gilmore et al., 2018; Lyall et al., 2015), demonstrating that these measures of cortical structure are independent of one another, follow different trajectories, and develop at different rates.

Refinement of neural structure during adolescence, characterized by decreases in cortical surface area and thickness, may reflect improvement in behaviors including emotion regulation and cognitive control (Vijayakumar et al., 2014). However, excessive reductions in cortical structure during this sensitive developmental period may be detrimental. Although research has not directly examined whether NSSI is associated with age related changes in neural structure, related psychological conditions alter the association between age and cortical development. For example, in longitudinal analyses, depressive symptoms are associated with accelerated cortical thinning of the frontal lobe in adolescents (Bos et al., 2018; Luby et al., 2016). Given existing work suggesting that neurodevelopmental trajectories vary with behavior and symptoms, it is possible that similar associations may emerge with NSSI.

1.4. The current study

Developmental cognitive neuroscience research demonstrates that widespread decreases in cortical thickness and cortical surface area occur during adolescence. These changes may be particularly relevant to understanding adolescents' engagement in health risk behaviors, including NSSI. Few studies have explored the association between NSSI and brain structure in adolescence, and no studies have investigated whether there are differences in the relation between age and brain structure in NSSI populations.

In this preliminary study, we first examined associations between age and cortical thickness and surface area in a sample of adolescent girls. Consistent with prior research, we hypothesized that increased age would be associated with reductions in cortical thickness and surface area. Next, we investigated group differences in cortical thickness and surface area in adolescents with versus without NSSI history. We hypothesized that lifetime history of NSSI would be associated with less cortical thickness and surface area in the prefrontal cortex and parietal cortex. Finally, we examined the association between age and neural structure in adolescents with NSSI history versus without NSSI history. We hypothesized that NSSI history would moderate the association between age and cortical surface area and cortical thickness. Because cortical thickness and surface area tends to decline in the age range of our sample (LeWinn et al., 2017; Mills et al., 2014a; Tamnes et al., 2017; Wierenga et al., 2014), we expected that the relation between age and decreased cortical structure would be stronger among adolescents with a history of NSSI compared to those without a history of NSSI. We also expected these differences would remain significant while controlling for well-known correlates of NSSI, including depressive symptoms (Schreiner et al., 2017) and medication use (Quevedo et al., 2016).

2. Method

2.1. Participants

Participants (N=138) were drawn from a larger parent study of 229 girls examining risk for depression and self-injurious thoughts and behaviors. For the parent study, participants were recruited from a variety of sources, including Internet ads, flyers, university listserv e-mails, and medical chart reviews. A mixture of typically developing youth and youth with increased risk for self-injurious thoughts and behaviors (e.g., depression history, childhood adversity, prior suicidal thoughts), who were between the ages of 9 and 14, and assigned female sex at birth as reported by caregivers during screening were enrolled and followed for 12 months in the parent study. Exclusion criteria for the parent study included endorsement of intellectual disability, autism, pervasive developmental disorders, active and/or history of psychotic disorder, chronic physical illness that would impact blood draws or inflammatory markers (of interest to the larger parent study), and lack of ability to speak/read English. Study eligibility was determined using a brief screening procedure. Caregivers responded to a series of yes/no single-item questions for each of the exclusion criteria listed above. For the present study, the same exclusion and inclusion criteria described above applied to those with and without NSSI histories. MRI scan exclusion criteria included history of head trauma, left-handedness, metal braces, pregnancy, and any other MRI contraindications (e.g., metal in body).

Of the 229 parent study participants, 138 (60%; ages 9–17 years, M=12.55, SD=2.00) girls completed the MRI scan visit. There were no significant differences in age, $t(227)=-1.80$, p=.07, depressive symptoms, $t(224)=-.61$, p=.54, and NSSI, $\chi^2(1)=3.23$, p=.07, between participants who enrolled in the subsequent MRI visit and those who did not. Participants' assent and caregiver consent was obtained prior to study participation. All procedures were approved by the local university institutional review board.

For the present study, initial analyses included MRI data from 135 (ages 9–17 years, M=12.57, SD=2.00) participants: two participants were excluded due to unusable data (excessive head motion) and one participant was excluded due to a structural brain abnormality. Initial models were run with all 135 participants, however results appeared to be strongly driven by age (see Supplement). To reduce the strong influence of age, we implemented an age-matching procedure like approaches by others (Asarnow et al., 2014; Chen et al., 2010; Gotlib et al., 2010), resulting in a sample of 100 participants (ages 9–17 years, M=13.40, SD=1.61): 50 participants with NSSI and 50 age-matched participants with no NSSI. The age-matching procedure reduced but did not eliminate the confound of age. Thus, in whole brain analyses, we controlled for the effects of age. Additionally, we examined age as a moderator of the association between NSSI and cortical structure. Hereafter, statistics reported will be from these 100 participants unless otherwise noted. These 100 participants self-identified as Black or African-American (n=30, 30%), Asian (n=3, 3%), White (n=49, 49%), American Indian or Alaska Native (n=2, 2%), Hispanic/Latine (n=5, 5%), and mixed race (n=11, 11%). Table 1 presents demographic and other study variables by group.

2.2. Procedures

The parent study included a baseline study visit and three follow-up time points (4, 8, and 12-months, 75.7%−85.7% retention). At baseline, adolescents and parents completed clinical interviews and self-report questionnaires described below. On a diagnostic structured clinical interview at baseline, 70.3% of participants from the whole MRI study sample met criteria for at least one disorder and 34.8% of participants met criteria for an internalizing disorder diagnosis. The MRI scan visit involved a high resolution T1 weighted scan and other functional MRI scans that are not the focus of the present manuscript. On average, the MRI scan visit was completed 5.5 months after the baseline study visit (M=168.35 days, SD=230.67 days).

2.3. Image acquisition and processing

Scanning was performed on a 3.0-T Siemens Prisma Scanner, using a 32-channel head coil[1]. We followed standard pediatric scanning acquisition parameters. T1-weighted multiecho MPRAGE volumes (anatomical scans) were acquired (repetition time=2530 msec, echo time=1.670–7.25 msec, flip angle=7°, field of view=192×192 mm, 176 slices, in-plane voxel size=1 mm). T1-weighted images were analyzed with the FreeSurfer image analysis suite (version 6.0) which performs automated cortical reconstruction and segmentation of the brain to estimate cortical thickness and surface area (Fischl et al., 2002, 2004).

[1]Two participants used a 20-channel head coil due to head size (see supplement).

The automated segmentation and reconstruction results were inspected for all participants. Where necessary, manual adjustments were made to optimize accurate placement of gray/white and gray/cerebrospinal fluid borders (overseen by KP). Each brain was rerun through recon-all following edits, inspected, and edited again if indicated. After reconstruction, the cortex was parcellated based on the structure of gyri and sulci using the Desikan-Killiany atlas (Desikan et al., 2006). FreeSurfer has demonstrated good test-retest reliability across scanner manufacturers and field strengths (Han et al., 2006) and has been used in prior samples of children (e.g. Luby et al., 2016; Mahone et al., 2011).

2.4. Measures

2.4.1. Self-injurious thoughts and behaviors.—

Trained research assistants administered the Self-Injurious Thoughts and Behaviors Interview (SITBI; Nock et al., 2007), a structured clinical interview assessing history of self-injurious thoughts and behaviors, at baseline and follow-ups. The present analyses focused on NSSI presence (1) or absence (0) with the question "Have you ever purposefully hurt yourself without wanting to die?". History of NSSI prior to baseline was assessed at the baseline visit. At each follow-up assessment, participants reported any NSSI occurring since the last assessment time point. Participants were considered to have a lifetime history of NSSI if they reported engaging in NSSI either prior to baseline or within any follow-up assessment time point. The SITBI demonstrates strong interrater and test-retest reliability (Nock et al., 2007).

2.4.2. Depressive symptoms.—

Depressive symptoms at baseline were measured using the Mood and Feelings Questionnaire (MFQ; Costello & Angold, 1988), a 33-item self-report inventory that measures depressive moods and behaviors over the past two weeks. Missing items on the MFQ were mean imputed, if 80% or more of items had valid responses. We excluded four items referring to suicidal ideation to eliminate conflations between suicidal and non-suicidal self-injurious thoughts and the remaining 29 items were summed with higher scores indicating higher levels of depressive symptoms. The MFQ is a reliable and valid measure of depressive symptoms among children and adolescents (Wood et al., 1995; Burleson Daviss et al., 2006) and demonstrated high internal consistency in the parent study sample (Cronbach's α=0.93).

2.4.3. Medication usage.—

At the MRI scan visit, information about medication usage was obtained from the accompanying guardian. Fifty-five youth (55%) in the study sample endorsed medication usage (e.g., psychiatric, allergy) which is included as a covariate in the final model. Specifically, 44% of the study sample endorsed psychiatric medication usage and 24% of the sample endorsed allergy medication usage.

2.5. Data analysis plan

Descriptive statistics were computed in SPSS Version 27. We examined group differences on main study variables using independent-samples *t*-tests and chi-square differences tests using an alpha threshold value of .05. In the subsample used in these analyses, 24 participants (24%) missed one or more follow-up assessments. If participants did not complete a follow-up assessment, we conservatively estimated no NSSI engagement occurred in the months prior to that particular follow-up assessment.

To test study hypotheses, we conducted general linear models (GLM) using the whole-brain vertex-wise analysis tool in FreeSurfer to examine associations between NSSI, age, cortical surface area, and thickness. The data were smoothed using a 10-mm full-width half-maximum Gaussian kernel prior to statistical analysis. The Different-Offset, Different-Slope (DODS) model option in FreeSurfer was used for the GLM analyses (Fischl & Dale, 2000). To reduce type 1 error, results from each GLM were cluster-threshold corrected at $p<0.05$ and then an additional cluster-level correction based on two-tailed Monte Carlo simulation at $p<0.05$ (Hagler et al., 2006). Results were visualized by overlaying significant clusters on an inflated cortical surface using FreeSurfer.

First, we examined the effect of exact age on cortical thickness or cortical surface area controlling for lifetime history of NSSI. Second, we investigated whether a lifetime history of NSSI (vs. no lifetime history of NSSI) was associated with differences in cortical thickness or cortical surface area controlling for exact age at the MRI scan visit. Finally, we examined interactions between NSSI history and age predicting cortical thickness or cortical surface area. Whole-brain models covaried for depressive symptoms and medication use[2].

To probe significant interactions between age and NSSI history, we conducted simple slopes analyses (see Supplement for more details).

3. Results

3.1. Descriptive analyses

Forty girls (40%) reported a history of NSSI at baseline. Additionally, 10 girls reported NSSI at some point in the follow-up (and did not report NSSI at the baseline assessment). In total, 50 girls (50%) reported lifetime NSSI at some point during the study observation period. Table 1 presents results from univariate analyses. Youth in the NSSI group were older (M_{age} = 13.83 years, SD = 1.66) as compared to those in the non-NSSI group, (M_{age} = 12.96 years, SD = 1.44; $t(98) = 2.78$, $p < .01$, $d = .56$); additionally, depressive symptoms were higher in the NSSI group (M = 19.23, SD = 12.72) as compared to non-NSSI group (M = 9.39, SD = 6.96; $t(98) = 4.80$, $p < .001$, $d = .96$). We also found a significant association between medication usage and NSSI history ($\chi^2(1) = 6.83$, $p < .01$).

3.2. Whole brain models

3.2.1. Cortical thickness.—Consistent with hypotheses, whole-brain vertex-wise analyses revealed that age was associated with less cortical thickness in the left and right prefrontal and temporal cortex, controlling for the effect of NSSI history, depressive symptoms, and medication usage (Table 2, Figure 1). Whole-brain vertex-wise analyses controlling for age, depressive symptoms, and medication usage did not reveal any associations between NSSI group membership and cortical thickness. In addition, whole-brain vertex-wise analyses indicated that there was no significant interaction between age and NSSI history predicting cortical thickness.

[2]Additional sensitivity analyses (e.g., time between baseline and MRI scan) are presented in the supplement, but results were largely consistent across all models (See Supplement).

3.2.2. Cortical surface area.—Results of whole-brain vertex-wise analyses indicate that age was associated with less cortical surface area in the left and right prefrontal and parietal cortex, controlling for the effect of NSSI history, depressive symptoms, and medication usage (Table 3, Figure 2).

3.2.3. Cortical surface area and NSSI history.—Consistent with hypotheses, whole-brain vertex-wise analyses revealed that NSSI history was associated with less cortical surface area in left inferior parietal cortex and the left insula, controlling for the effect of age, depressive symptoms, and medication usage (Table 4, Figure 3).

In addition, there was a significant interaction between age and NSSI history predicting cortical surface area in the left inferior parietal cortex and left precentral cortex (Table 5, Figure 4). Simple slopes analyses revealed that among adolescents without NSSI history, older age predicted less cortical surface area in the left inferior parietal cortex (b=−.03, p<.001) and left precentral cortex (b=−.02, p<.001) as expected with the trajectory of typical adolescent neurodevelopment. Contrary to hypotheses, among adolescents with NSSI history, older age predicted more surface area in the left inferior parietal cortex (b=.01, p=.04) and was not associated with surface area in the left precentral cortex (b=.004, p=.37; Table 6, Figures 5 and 6).

4. Discussion

The overarching aim of this study was to examine whether NSSI history in adolescents was associated with differences in cortical surface area and thickness and to explore how NSSI history may be associated with age-related changes in the brain. We replicated previous results in representative samples (LeWinn et al., 2017; Raznahan et al., 2011; Tamnes et al., 2017; Wierenga et al., 2014), showing that increased age was associated with decreased cortical surface area and thickness broadly in prefrontal and parietal cortex. Furthermore, consistent with previous work showing reductions in cortical volume in adolescents with NSSI history (Ando et al., 2018; Beauchaine et al., 2019), we found less surface area in the left insula and left inferior parietal cortex in adolescents with NSSI history compared to adolescents with no NSSI history.

The insular cortex is involved in the integration of emotional and cognitive information during decision making (Menon & Uddin, 2010). Decreased activation of the insula is associated with risky decision-making during adolescence (Eshel et al., 2007) and it is theorized that the ongoing development of this neural structure may bias adolescents towards affectively driven actions and decisions (Smith et al., 2014). Engagement in health-risk behaviors, such as NSSI, could be influenced by insular dysfunction during adolescence. Moreover, the left insular cortex is involved in socio-emotional processing including emotion recognition, empathy, and social cognition (Fan et al., 2011; Uddin et al., 2017), and the insula is substantially implicated in emotion regulation (Goldin et al., 2008; Grecucci et al., 2013). Specifically, Goldin et al. (2008) found greater insula activation was associated with expressive suppression, which can be defined as attempts to hide, or reduce, emotional expression (Gross & Levenson, 1993). Expressive suppression is an inefficient form of emotion regulation, and prior research has shown that expressive

suppression may play a role in the onset and maintenance of NSSI in adolescents (Hasking et al., 2010; Andrews et al., 2013). It may be that attempts to suppress or hide away emotions (expressive suppression) represent a form of avoidance, or escape from, unwanted emotional experiences. Indeed, avoidance or escape from aversive emotional experiences has been posited as a reinforcing function of NSSI (Chapman et al., 2006; Haywood et al, 2023). Our results suggest atypical development of neural regions involved in emotional processing and regulation in adolescents with a history of NSSI.

The main effect of NSSI history predicting cortical surface area in the left inferior parietal cortex was qualified by a significant interaction with age. Contrary to hypotheses, age was associated with more cortical surface area in the left inferior parietal cortex and was not associated with surface area in the left precentral cortex among adolescents with NSSI history. Among adolescents without NSSI history, a more typical pattern was observed whereby age was associated with reduced cortical surface area in the left inferior parietal cortex and left precentral cortex. Although preliminary, these results suggest NSSI history is associated with a deviation from typical neurodevelopment during adolescence that has not been observed previously.

The left precentral cortex contains the primary and supplementary motor areas that are responsible for execution of voluntary motion (Porro et al., 1996). In addition to involvement in motor function, the left precentral cortex may aid other cognitive abilities such as response inhibition (Bush et al., 1998; Carter et al., 1997). Throughout adolescence, cognitive and executive function typically becomes refined, both behaviorally and neurally (Casey et al., 2005; Constantinidis & Luna, 2019; Vijayakumar et al., 2014). However, it may be the case that the development of these processes is altered in adolescents with NSSI history. In fact, prior research reveals that individuals with a history of NSSI show impaired response inhibition in the context of negative emotional stimuli (Allen & Hooley, 2015, 2019). Our results are consistent with these findings and may suggest that NSSI history is associated with deviations in typical neurodevelopment in regions responsible for motor and cognitive function. Given the cross-sectional nature of our findings, we are unable to determine whether altered neurodevelopment in the precentral cortex preceded or followed the development of NSSI. This represents an important area for future research.

We also observed a significant interaction between NSSI and age predicting more cortical surface area in the left inferior parietal cortex. The left inferior parietal cortex is typically associated with integrating input from sensory, emotion, and motor systems and acts as a convergence zone for conceptual functions including social cognition and language (Binder & Desai, 2011; Saalasti et al., 2019). Additionally, the left inferior parietal cortex is implicated in semantic processing (Saalasti et al., 2019), defined as an ability to access knowledge in reasoning and problem solving (Binder et al., 2009). Semantic processing is a component of cognitive reappraisal, which is a commonly employed emotion regulation strategy (Ochsner & Gross, 2005; Ochsner et al., 2012), and emotion regulation difficulties are viewed as a core component of engagement in and maintenance of NSSI behavior (Adrian et al., 2011; Gratz & Roemer, 2008). The present data add to the body of research suggesting that there may be alterations in neural regions subserving emotion regulation, thereby conferring risk for NSSI. This will need to be confirmed using larger,

longitudinal research designs in conjunction with behavioral measures or tasks assessing emotion regulation.

Interestingly, our findings also indicated that cortical thickness did not differ in adolescents with NSSI history compared to adolescents without NSSI history and NSSI did not moderate the association between age and cortical thickness. Prior research has suggested that cortical surface area and thickness are distinct structural components and have unique cellular and genetic origins (Geschwind & Rakic, 2013; Kremen et al., 2013; Panizzon et al., 2009). Furthermore, cortical surface area and thickness develop and mature independent of one another (Raznahan et al., 2011; Wierenga et al., 2014). Results from our study suggests that alterations in surface area, rather than cortical thickness, may account for the volumetric differences that have been previously associated with NSSI history in adolescence (Ando et al., 2018; Beauchaine et al., 2019). The specificity of these results with regards to cortical measurement warrant replication and further longitudinal research should examine the neuroanatomical mechanisms that may account for this difference.

Furthermore, imaging studies of infants and adolescents demonstrate that cortical thickness expansion and growth is complete by age 2, while surface area expansion continues into childhood and early adolescence (Gilmore et al., 2018; Lyall et al., 2015). It is possible that variability in environmental experiences in childhood and adolescence could impact cortical surface area development, due to the ongoing refinement and plasticity of this brain measure (Mackes et al., 2020). Additionally, alterations in overall cortical surface area and the trajectory of development in cortical surface area associated with NSSI in adolescence may reflect underlying vulnerabilities with which individuals enter adolescence. Variation in cortical surface area and trajectory of development of cortical surface area have been associated with stressful early life experiences (Gehred et al., 2021; Hodel et al., 2015; Machlin et al., 2023; Opel et al., 2019) which have been linked with NSSI (Cassels et al., 2018; Zetterqvist et al., 2014), and could be one potential source of these vulnerabilities. It will be important for future research to further examine these potential transactional relations between cortical structure, NSSI, and early life stress exposure.

Our results are preliminary and should be interpreted within the context of several limitations. First, because the study was conducted in the context of a larger parent study, our results may not generalize to larger samples of adolescents and these results need to be reproduced and elaborated on in samples including boys. Second, the present analyses are cross-sectional, which limits inferences that can be made about the timing of NSSI relative to the development of structural deviations in the brain. Because our hypotheses are developmental in nature, future research that can parse timing of cortical development and emergence of NSSI would greatly strengthen our understanding of these relations. Third, our measurement of observed lifetime history of NSSI possibly was overly conservative due to censoring the minimal amount of missing data during the observation period. Fourth, although consistent with past approaches, our choice to age-match participants further limits our ability to draw strong conclusions about the developmental trajectory of brain development and NSSI in our sample. A larger age range that is followed longitudinally may allow for better detection of age-related structural alterations spanning adolescence. Finally, it should be noted that the cluster-forming threshold (p<.05) used in analyses may

be susceptible to false-positive rates (Greve & Fischl, 2018) and future research with larger samples should ensure adequate power to conduct analyses with more stringent thresholds.

Despite these limitations, this preliminary study represents an important first step to better understand the relation between neural development and NSSI in adolescence. Our results suggest differences in the development of cortical surface area in adolescents with NSSI history versus those without NSSI history, specifically in regions that may be involved in higher-order cognition, integration of sensory and affective information, and regulatory behaviors. This study thus lays the foundation for future research into neural risk factors associated with NSSI history in adolescence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

Data and preparation of this manuscript was supported by grants from the National Institutes of Mental Health (K01MH116325; R01MH107479, R01MH107479-S1; R01MH115004).

REFERENCES

Adrian M, Zeman J, Erdley C, Lisa L, & Sim L (2011). Emotional dysregulation and interpersonal difficulties as risk factors for nonsuicidal self-injury in adolescent girls. Journal of Abnormal Child Psychology, 39(3), 389–400. 10.1007/s10802-010-9465-3 [PubMed: 20953828]

Allen KJD, & Hooley JM (2015). Inhibitory control in people who self-injure: Evidence for impairment and enhancement. Psychiatry Research, 225(3), 631–637. 10.1016/j.psychres.2014.11.033 [PubMed: 25510907]

Allen KJD, & Hooley JM (2019). Negative Emotional Action Termination (NEAT): Support for a cognitive mechanism underlying negative urgency in nonsuicidal self-injury. Behavior Therapy, 50(5), 924–937. 10.1016/j.beth.2019.02.001 [PubMed: 31422848]

Ammerman BA, Jacobucci R, Kleiman EM, Uyeji LL, & McCloskey MS (2018). The relationship between nonsuicidal self-injury age of onset and severity of self-harm. Suicide & Life-Threatening Behavior, 48(1), 31–37. 10.1111/sltb.12330 [PubMed: 28160318]

Ando A, Reichl C, Scheu F, Bykova A, Parzer P, Resch F, Brunner R, & Kaess M (2018). Regional grey matter volume reduction in adolescents engaging in non-suicidal self-injury. Psychiatry Research: Neuroimaging, 280, 48–55. 10.1016/j.pscychresns.2018.08.005 [PubMed: 30149362]

Andrews T, Martin G, Hasking P, & Page A (2013). Predictors of continuation and cessation of nonsuicidal self-injury. Journal of Adolescent Health, 53(1), 40–46. 10.1016/j.jadohealth.2013.01.009

Asarnow JR, Porta G, Spirito A, Emslie G, Clarke G, Wagner KD, Vitiello B, Keller M, Birmaher B, McCracken J, Mayes T, Berk M, & Brent DA (2011). Suicide attempts and nonsuicidal self-injury in the treatment of resistant depression in adolescents: Findings from the TORDIA Trial. Journal of the American Academy of Child and Adolescent Psychiatry, 50(8), 772–781. 10.1016/j.jaac.2011.04.003 [PubMed: 21784297]

Asarnow LD, Thompson RJ, Joormann J, & Gotlib IH (2014). Children at risk for depression: Memory biases, self-schemas, and genotypic variation. Journal of Affective Disorders, 159, 66–72. 10.1016/j.jad.2014.02.020 [PubMed: 24679392]

Beauchaine TP, Sauder CL, Derbidge CM, & Uyeji LL (2019). Self-injuring adolescent girls exhibit insular cortex volumetric abnormalities that are similar to those seen in adults with borderline personality disorder. Development and Psychopathology, 31(04), 1203–1212. 10.1017/S0954579418000822 [PubMed: 30394252]

Bentley KH, Nock MK, & Barlow DH (2014). The four-function model of nonsuicidal self-injury: Key directions for future research. Clinical Psychological Science, 2(5), 638–656. 10.1177/2167702613514563

Binder JR, & Desai RH (2011). The neurobiology of semantic memory. Trends in Cognitive Sciences, 15(11), 527–536. 10.1016/j.tics.2011.10.001 [PubMed: 22001867]

Binder JR, Desai RH, Graves WW, & Conant LL (2009). Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. Cerebral Cortex, 19(12), 2767–2796. 10.1093/cercor/bhp055 [PubMed: 19329570]

Bos MGN, Peters S, Kamp FC van de, Crone, E. A., & Tamnes, C. K. (2018). Emerging depression in adolescence coincides with accelerated frontal cortical thinning. Journal of Child Psychology and Psychiatry, 59(9), 994–1002. 10.1111/jcpp.12895 [PubMed: 29577280]

Bush G, Whalen PJ, Rosen BR, Jenike MA, McInerney SC, & Rauch SL (1998). The counting stroop: An interference task specialized for functional neuroimaging—validation study with functional MRI. Human Brain Mapping, 6(4), 270–282. 10.1002/(SICI)1097-0193(1998)6:4<270::AID-HBM6>3.0.CO;2-0 [PubMed: 9704265]

Carter CS, Mintun M, Nichols T, & Cohen JD (1997). Anterior cingulate gyrus dysfunction and selective attention deficits in schizophrenia: [15O]H2O PET study during single-trial stroop task performance. American Journal of Psychiatry, 154(12), 1670–1675. 10.1176/ajp.154.12.1670 [PubMed: 9396944]

Casey B, Galvan A, & Hare TA (2005). Changes in cerebral functional organization during cognitive development. Current Opinion in Neurobiology, 15(2), 239–244. 10.1016/j.conb.2005.03.012 [PubMed: 15831409]

Casey BJ, Getz S, & Galvan A (2008). The adolescent brain. Developmental Review, 28(1), 62–77. 10.1016/j.dr.2007.08.003 [PubMed: 18688292]

Cassels M, van Harmelen A, Neufeld S, Goodyer I, Jones PB, & Wilkinson P (2018). Poor family functioning mediates the link between childhood adversity and adolescent nonsuicidal self-injury. Journal of Child Psychology and Psychiatry, and Allied Disciplines, 59(8), 881–887. 10.1111/jcpp.12866 [PubMed: 29363128]

Chapman AL, Gratz KL, & Brown MZ (2006). Solving the puzzle of deliberate self-harm: The experiential avoidance model. Behaviour Research and Therapy, 44(3), 371–394. 10.1016/j.brat.2005.03.005 [PubMed: 16446150]

Chen MC, Hamilton JP, & Gotlib IH (2010). Decreased hippocampus volume in healthy girls at risk for depression. Archives of General Psychiatry, 67(3), 270–276. 10.1001/archgenpsychiatry.2009.202 [PubMed: 20194827]

Cohen J, Cohen P, West SG, & Aiken LS (2003). Applied multiple regression/correlation analysis for the behavioral sciences, 3rd ed (pp. xxviii, 703). Lawrence Erlbaum Associates Publishers.

Constantinidis C, & Luna B (2019). Neural substrates of inhibitory control maturation in adolescence. Trends in Neurosciences, 42(9), 604–616. 10.1016/j.tins.2019.07.004 [PubMed: 31443912]

Costello EJ, & Angold A (1988). Scales to assess child and adolescent depression: Checklists, screens, and nets. Journal of the American Academy of Child & Adolescent Psychiatry, 27(6), 726–737. 10.1097/00004583-198811000-00011 [PubMed: 3058677]

Dahl RE (2004). Adolescent brain development: A period of vulnerabilities and opportunities. Keynote address. Annals of the New York Academy of Sciences, 1021(1), 1–22. 10.1196/annals.1308.001 [PubMed: 15251869]

Daviss WB, Birmaher B, Melhem NA, Axelson DA, Michaels SM, & Brent DA (2006). Criterion validity of the Mood and Feelings Questionnaire for depressive episodes in clinic and non-clinic subjects. Journal of Child Psychology and Psychiatry, 47(9), 927–934. 10.1111/j.1469-7610.2006.01646.x [PubMed: 16930387]

Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, Buckner RL, Dale AM, Maguire RP, Hyman BT, Albert MS, & Killiany RJ (2006). An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. NeuroImage, 31(3), 968–980. 10.1016/j.neuroimage.2006.01.021 [PubMed: 16530430]

Eshel N, Nelson EE, Blair J, Pine DS, & Ernst M (2007). Neural substrates of choice selection in adults and adolescents: Development of the ventrolateral prefrontal and anterior

cingulate cortices. Neuropsychologia, 45(6), 1270–1279. 10.1016/j.neuropsychologia.2006.10.004 [PubMed: 17118409]

Etkin A, Büchel C, & Gross JJ (2015). The neural bases of emotion regulation. Nature Reviews Neuroscience, 16(11), 693–700. 10.1038/nrn4044 [PubMed: 26481098]

Fan Y, Duncan NW, de Greck M, & Northoff G (2011). Is there a core neural network in empathy? An fMRI based quantitative meta-analysis. Neuroscience & Biobehavioral Reviews, 35(3), 903–911. 10.1016/j.neubiorev.2010.10.009 [PubMed: 20974173]

Fischl B, & Dale AM (2000). Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proceedings of the National Academy of Sciences, 97(20), 11050–11055. 10.1073/pnas.200033797

Fischl B, Salat DH, Busa E, Albert M, Dieterich M, Haselgrove C, van der Kouwe A, Killiany R, Kennedy D, Klaveness S, Montillo A, Makris N, Rosen B, & Dale AM (2002). Whole brain segmentation: Automated labeling of neuroanatomical structures in the human brain. Neuron, 33(3), 341–355. 10.1016/S0896-6273(02)00569-X [PubMed: 11832223]

Fischl B, Salat DH, van der Kouwe AJW, Makris N, Ségonne F, Quinn BT, & Dale AM (2004). Sequence-independent segmentation of magnetic resonance images. NeuroImage, 23, S69–S84. 10.1016/j.neuroimage.2004.07.016 [PubMed: 15501102]

Gehred MZ, Knodt AR, Ambler A, Bourassa KJ, Danese A, Elliott ML, Hogan S, Ireland D, Poulton R, Ramrakha S, Reuben A, Sison ML, Moffitt TE, Hariri AR, & Caspi A (2021). Long-term neural embedding of childhood adversity in a population-representative birth cohort followed for 5 decades. Biological Psychiatry, 90(3), 182–193. 10.1016/j.biopsych.2021.02.971 [PubMed: 33952400]

Geschwind DH, & Rakic P (2013). Cortical evolution: Judge the brain by its cover. Neuron, 80(3), 633–647. 10.1016/j.neuron.2013.10.045 [PubMed: 24183016]

Giedd JN, Blumenthal J, Jeffries NO, Castellanos FX, Liu H, Zijdenbos A, Paus T, Evans AC, & Rapoport JL (1999). Brain development during childhood and adolescence: A longitudinal MRI study. Nature Neuroscience, 2(10), 861–863. 10.1038/13158 [PubMed: 10491603]

Gilmore JH, Santelli RK, & Gao W (2018). Imaging structural and functional brain development in early childhood. Nature Reviews. Neuroscience, 19(3), 123–137. 10.1038/nrn.2018.1 [PubMed: 29449712]

Glenn CR, & Klonsky ED (2013). Nonsuicidal self-injury disorder: An empirical investigation in adolescent psychiatric patients. Journal of Clinical Child & Adolescent Psychology, 42(4), 496–507. 10.1080/15374416.2013.794699 [PubMed: 23682597]

Goldin PR, McRae K, Ramel W, & Gross JJ (2008). The neural bases of emotion regulation: Reappraisal and suppression of negative emotion. Biological Psychiatry, 63(6), 577–586. 10.1016/j.biopsych.2007.05.031 [PubMed: 17888411]

Gotlib IH, Hamilton JP, Cooney RE, Singh MK, Henry ML, & Joormann J (2010). Neural processing of reward and loss in girls at risk for major depression. Archives of General Psychiatry, 67(4), 380–387. 10.1001/archgenpsychiatry.2010.13 [PubMed: 20368513]

Gratz KL, & Roemer L (2008). The relationship between emotion dysregulation and deliberate self-harm among female undergraduate students at an urban commuter university. Cognitive Behaviour Therapy, 37(1), 14–25. 10.1080/16506070701819524 [PubMed: 18365795]

Grecucci A, Giorgetta C, Bonini N, & Sanfey A (2013). Reappraising social emotions: The role of inferior frontal gyrus, temporo-parietal junction and insula in interpersonal emotion regulation. Frontiers in Human Neuroscience, 7, 523. 10.3389/fnhum.2013.00523 [PubMed: 24027512]

Greve DN, & Fischl B (2018). False Positive Rates in Surface-based Anatomical Analysis. NeuroImage, 171, 6–14. 10.1016/j.neuroimage.2017.12.072 [PubMed: 29288131]

Gross JJ, & Levenson RW (1993). Emotional suppression: Physiology, self-report, and expressive behavior. Journal of Personality and Social Psychology, 64(6), 970. 10.1037/0022-3514.64.6.970 [PubMed: 8326473]

Guan K, Fox KR, & Prinstein MJ (2012). Nonsuicidal self-injury as a time-invariant predictor of adolescent suicide ideation and attempts in a diverse community sample. Journal of Consulting and Clinical Psychology, 80(5), 842–849. 10.1037/a0029429 [PubMed: 22845782]

Hagler DJ, Saygin AP, & Sereno MI (2006). Smoothing and cluster thresholding for cortical surface-based group analysis of fMRI data. NeuroImage, 33(4), 1093–1103. 10.1016/j.neuroimage.2006.07.036 [PubMed: 17011792]

Han X, Jovicich J, Salat D, van der Kouwe A, Quinn B, Czanner S, Busa E, Pacheco J, Albert M, Killiany R, Maguire P, Rosas D, Makris N, Dale A, Dickerson B, & Fischl B (2006). Reliability of MRI-derived measurements of human cerebral cortical thickness: The effects of field strength, scanner upgrade and manufacturer. NeuroImage, 32(1), 180–194. 10.1016/j.neuroimage.2006.02.051 [PubMed: 16651008]

Hasking PA, Coric SJ, Swannell S, Martin G, Thompson HK, & Frost ADJ (2010). Brief report: Emotion regulation and coping as moderators in the relationship between personality and self-injury. Journal of Adolescence, 33(5), 767–773. 10.1016/j.adolescence.2009.12.006 [PubMed: 20056516]

Haywood SB, Hasking P, & Boyes ME (2023). Associations between non-suicidal self-injury and experiential avoidance: A systematic review and Robust Bayesian Meta-analysis. Journal of Affective Disorders, 325, 470–479. 10.1016/j.jad.2023.01.027 [PubMed: 36638968]

Heatherton TF, & Wagner DD (2011). Cognitive neuroscience of self-regulation failure. Trends in Cognitive Sciences, 15(3), 132–139. 10.1016/j.tics.2010.12.005 [PubMed: 21273114]

Hodel AS, Hunt RH, Cowell RA, Van Den Heuvel SE, Gunnar MR, & Thomas KM (2015). Duration of early adversity and structural brain development in post-institutionalized adolescents. NeuroImage, 105, 112–119. 10.1016/j.neuroimage.2014.10.020 [PubMed: 25451478]

Hooley JM, & Franklin JC (2018). Why do people hurt themselves? A new conceptual model of nonsuicidal self-injury. Clinical Psychological Science, 6(3), 428–451. 10.1177/2167702617745641

Klonsky ED, Victor SE, & Saffer BY (2014). Nonsuicidal self-injury: What we know, and what we need to know. Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie, 59(11), 565–568. [PubMed: 25565471]

Klonsky ED (2007). The functions of deliberate self-injury: A review of the evidence. Clinical Psychology Review, 27(2), 226–239. 10.1016/j.cpr.2006.08.002 [PubMed: 17014942]

Klonsky ED, May AM, & Glenn CR (2012). The relationship between nonsuicidal self-injury and attempted suicide: Converging evidence from four samples. Journal of Abnormal Psychology, 122(1), 231. 10.1037/a0030278 [PubMed: 23067259]

Kremen WS, Fennema-Notestine C, Eyler LT, Panizzon MS, Chen C-H, Franz CE, Lyons MJ, Thompson WK, & Dale AM (2013). Genetics of brain structure: Contributions from the Vietnam era Twin Study of Aging. American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics : The Official Publication of the International Society of Psychiatric Genetics, 0(7), 751–761. 10.1002/ajmg.b.32162

Langner R, Leiberg S, Hoffstaedter F, & Eickhoff SB (2018). Towards a human self-regulation system: Common and distinct neural signatures of emotional and behavioural control. Neuroscience & Biobehavioral Reviews, 90, 400–410. 10.1016/j.neubiorev.2018.04.022 [PubMed: 29730485]

LeWinn KZ, Sheridan MA, Keyes KM, Hamilton A, & McLaughlin KA (2017). Sample composition alters associations between age and brain structure. Nature Communications, 8(1), 874. 10.1038/s41467-017-00908-7

Liu RT (2017). Characterizing the course of non-suicidal self-injury: A cognitive neuroscience perspective. Neuroscience & Biobehavioral Reviews, 80, 159–165. 10.1016/j.neubiorev.2017.05.026 [PubMed: 28579492]

Luby JL, Belden AC, Jackson JJ, Lessov-Schlaggar CN, Harms MP, Tillman R, Botteron K, Whalen D, & Barch DM (2016). Early childhood depression and alterations in the trajectory of gray matter maturation in middle childhood and early adolescence. JAMA Psychiatry, 73(1), 31–38. 10.1001/jamapsychiatry.2015.2356 [PubMed: 26676835]

Luby JL, Belden A, Harms MP, Tillman R, & Barch DM (2016). Preschool is a sensitive period for the influence of maternal support on the trajectory of hippocampal development. Proceedings of the National Academy of Sciences of the United States of America, 113(20), 5742–5747. 10.1073/pnas.1601443113 [PubMed: 27114522]

Luna B, Marek S, Larsen B, Tervo-Clemmens B, & Chahal R (2015). An integrative model of the maturation of cognitive control. Annual Review of Neuroscience, 38, 151–170. 10.1146/annurev-neuro-071714-034054

Lyall AE, Shi F, Geng X, Woolson S, Li G, Wang L, Hamer RM, Shen D, & Gilmore JH (2015). Dynamic development of regional cortical thickness and surface area in early childhood. Cerebral Cortex, 25(8), 2204–2212. 10.1093/cercor/bhu027 [PubMed: 24591525]

Mackes NK, Golm D, Sarkar S, Kumsta R, Rutter M, Fairchild G, Mehta MA, Sonuga-Barke EJS, & Team, on behalf of the E. Y. A. F. (2020). Early childhood deprivation is associated with alterations in adult brain structure despite subsequent environmental enrichment. Proceedings of the National Academy of Sciences, 117(1), 641–649. 10.1073/pnas.1911264116

Machlin L, Egger HL, Stein CR, Navarro E, Carpenter KLH, Goel S, Patel KK, Copeland WE, & Sheridan MA (2023). Distinct Associations of Deprivation and Threat With Alterations in Brain Structure in Early Childhood. Journal of the American Academy of Child & Adolescent Psychiatry, 62(8), 885–894.e3. 10.1016/j.jaac.2023.02.006 [PubMed: 36775117]

Mahone EM, Crocetti D, Ranta ME, Gaddis A, Cataldo M, Slifer KJ, Denckla MB, & Mostofsky SH (2011). A preliminary neuroimaging study of preschool children with ADHD. Clinical Neuropsychologist, 25(6), 1009–1028. 10.1080/13854046.2011.580784 [PubMed: 21660881]

Menon V, & Uddin LQ (2010). Saliency, switching, attention and control: A network model of insula function. Brain Structure & Function, 214(5–6), 655–667. 10.1007/s00429-010-0262-0 [PubMed: 20512370]

Mills KL, Lalonde F, Clasen LS, Giedd JN, & Blakemore SJ (2014a). Developmental changes in the structure of the social brain in late childhood and adolescence. Social Cognitive and Affective Neuroscience, 9(1), 123–131. 10.1093/scan/nss113 [PubMed: 23051898]

Mills KL, & Tamnes CK (2014). Methods and considerations for longitudinal structural brain imaging analysis across development. Developmental Cognitive Neuroscience, 9, 172–190. 10.1016/j.dcn.2014.04.004 [PubMed: 24879112]

Muehlenkamp JJ, Claes L, Havertape L, & Plener PL (2012). International prevalence of adolescent non-suicidal self-injury and deliberate self-harm. Child and Adolescent Psychiatry and Mental Health, 6(1), 1–9. 10.1186/1753-2000-6-10 [PubMed: 22216948]

Nock MK (2009). Why do People hurt themselves?: New insights into the nature and functions of self-injury. Current Directions in Psychological Science, 18(2), 78–83. 10.1111/j.1467-8721.2009.01613.x [PubMed: 20161092]

Nock MK (2010). Self-injury. Annual Review of Clinical Psychology, 6(1), 339–363. 10.1146/annurev.clinpsy.121208.131258

Nock MK, Holmberg EB, Photos VI, & Michel BD (2007). Self-injurious thoughts and behaviors interview: Development, reliability, and validity in an adolescent sample. Psychological Assessment, 19(3), 309. 10.1037/1040-3590.19.3.309 [PubMed: 17845122]

Nock MK, & Mendes WB (2008). Physiological arousal, distress tolerance, and social problem-solving deficits among adolescent self-injurers. Journal of Consulting and Clinical Psychology, 76(1), 28. 10.1037/0022-006X.76.1.28 [PubMed: 18229980]

Nock MK, & Prinstein MJ (2004). A functional approach to the assessment of self-mutilative behavior. Journal of Consulting and Clinical Psychology, 72(5), 885. 10.1037/0022-006X.72.5.885 [PubMed: 15482046]

Nock MK, & Prinstein MJ (2005). Contextual features and behavioral functions of self-mutilation among adolescents. Journal of Abnormal Psychology, 114(1), 140. 10.1037/0021-843X.114.1.140 [PubMed: 15709820]

Ochsner K, & Gross J (2005). The cognitive control of emotion. Trends in Cognitive Sciences, 9(5), 242–249. 10.1016/j.tics.2005.03.010 [PubMed: 15866151]

Ochsner KN, Ray RD, Cooper JC, Robertson ER, Chopra S, Gabrieli JDE, & Gross JJ (2004). For better or for worse: Neural systems supporting the cognitive down- and up-regulation of negative emotion. NeuroImage, 23(2), 483–499. 10.1016/j.neuroimage.2004.06.030 [PubMed: 15488398]

Ochsner KN, Silvers JA, & Buhle JT (2012). Functional imaging studies of emotion regulation: A synthetic review and evolving model of the cognitive control of emotion. Annals of the New York Academy of Sciences, 1251, E1–24. 10.1111/j.1749-6632.2012.06751.x [PubMed: 23025352]

Opel N, Redlich R, Dohm K, Zaremba D, Goltermann J, Repple J, Kaehler C, Grotegerd D, Leehr EJ, Böhnlein J, Förster K, Meinert S, Enneking V, Sindermann L, Dzvonyar F, Emden D, Leenings R, Winter N, Hahn T, … Dannlowski U (2019). Mediation of the influence of childhood maltreatment on depression relapse by cortical structure: A 2-year longitudinal observational study. The Lancet Psychiatry, 6(4), 318–326. 10.1016/S2215-0366(19)30044-6 [PubMed: 30904126]

Palacios-Barrios EE, & Hanson JL (2019). Poverty and self-regulation: Connecting psychosocial processes, neurobiology, and the risk for psychopathology. Comprehensive Psychiatry, 90, 52–64. 10.1016/j.comppsych.2018.12.012 [PubMed: 30711814]

Panizzon MS, Fennema-Notestine C, Eyler LT, Jernigan TL, Prom-Wormley E, Neale M, Jacobson K, Lyons MJ, Grant MD, Franz CE, Xian H, Tsuang M, Fischl B, Seidman L, Dale A, & Kremen WS (2009). Distinct genetic influences on cortical surface area and cortical thickness. Cerebral Cortex, 19(11), 2728–2735. 10.1093/cercor/bhp026 [PubMed: 19299253]

Porro CA, Francescato MP, Cettolo V, Diamond ME, Baraldi P, Zuiani C, Bazzocchi M, & di Prampero PE (1996). Primary motor and sensory cortex activation during motor performance and motor imagery: A functional magnetic resonance imaging study. The Journal of Neuroscience, 16(23), 7688–7698. 10.1523/JNEUROSCI.16-23-07688.1996 [PubMed: 8922425]

Quevedo K, Martin J, Scott H, Smyda G, & Pfeifer JH (2016). The neurobiology of self-knowledge in depressed and self-injurious youth. Psychiatry Research, 254, 145–155. 10.1016/j.pscychresns.2016.06.015 [PubMed: 27442923]

Raznahan A, Shaw P, Lalonde F, Stockman M, Wallace GL, Greenstein D, Clasen L, Gogtay N, & Giedd JN (2011). How does your cortex grow? Journal of Neuroscience, 31(19), 7174–7177. 10.1523/JNEUROSCI.0054-11.2011 [PubMed: 21562281]

Saalasti S, Alho J, Bar M, Glerean E, Honkela T, Kauppila M, Sams M, & Jääskeläinen IP (2019). Inferior parietal lobule and early visual areas support elicitation of individualized meanings during narrative listening. Brain and Behavior, 9(5), e01288. 10.1002/brb3.1288 [PubMed: 30977309]

Schreiner MW, Klimes-Dougan B, Mueller BA, Eberly LE, Reigstad KM, Carstedt PA, Thomas KM, Hunt RH, Lim KO, & Cullen KR (2017). Multi-modal neuroimaging of adolescents with non-suicidal self-injury: Amygdala functional connectivity. Journal of Affective Disorders, 221, 47–55. 10.1016/j.jad.2017.06.004 [PubMed: 28628767]

Smith AR, Steinberg L, & Chein J (2014). The role of the anterior insula in adolescent decision making. Developmental Neuroscience, 36(3–4), 196–209. 10.1159/000358918 [PubMed: 24853135]

Somerville LH, Jones RM, & Casey BJ (2010). A time of change: Behavioral and neural correlates of adolescent sensitivity to appetitive and aversive environmental cues. Brain and Cognition, 72(1), 124–133. 10.1016/j.bandc.2009.07.003 [PubMed: 19695759]

Spear LP (2000). The adolescent brain and age-related behavioral manifestations. Neuroscience & Biobehavioral Reviews, 24(4), 417–463. 10.1016/S0149-7634(00)00014-2 [PubMed: 10817843]

Steinberg L (2008). A social neuroscience perspective on adolescent risk-taking. Developmental Review : DR, 28(1), 78–106. 10.1016/j.dr.2007.08.002 [PubMed: 18509515]

Swannell SV, Martin GE, Page A, Hasking P, & John NJS (2014). Prevalence of nonsuicidal self-injury in nonclinical samples: Systematic review, meta-analysis and meta-regression. Suicide and Life-Threatening Behavior, 44(3), 273–303. 10.1111/sltb.12070 [PubMed: 24422986]

Tamnes CK, Herting MM, Goddings A-L, Meuwese R, Blakemore S-J, Dahl RE, Güroğlu B, Raznahan A, Sowell ER, Crone EA, & Mills KL (2017). Development of the cerebral cortex across adolescence: A multisample study of inter-related longitudinal changes in cortical volume, surface area, and thickness. The Journal of Neuroscience, 37(12), 3402–3412. 10.1523/JNEUROSCI.3302-16.2017 [PubMed: 28242797]

Uddin LQ, Nomi JS, Hebert-Seropian B, Ghaziri J, & Boucher O (2017). Structure and function of the human insula. Journal of Clinical Neurophysiology : Official Publication of the American Electroencephalographic Society, 34(4), 300–306. 10.1097/WNP.0000000000000377 [PubMed: 28644199]

Vijayakumar N, Whittle S, Yücel M, Dennison M, Simmons J, & Allen NB (2014). Prefrontal structural correlates of cognitive control during adolescent development: A 4-Year longitudinal study. Journal of Cognitive Neuroscience, 26(5), 1118–1130. 10.1162/jocn_a_00549 [PubMed: 24345180]

Whitlock J, Muehlenkamp J, Purington A, Eckenrode J, Barreira P, Baral Abrams G, Marchell T, Kress V, Girard K, Chin C, & Knox K (2011). Nonsuicidal self-injury in a college population: General trends and sex differences. Journal of American College Health, 59(8), 691–698. 10.1080/07448481.2010.529626 [PubMed: 21950249]

Wierenga LM, Langen M, Oranje B, & Durston S (2014). Unique developmental trajectories of cortical thickness and surface area. NeuroImage, 87, 120–126. 10.1016/j.neuroimage.2013.11.010 [PubMed: 24246495]

Wood A, Kroll L, Moore A, & Harrington R (1995). Properties of the Mood and Feelings Questionnaire in adolescent psychiatric outpatients: A research note. Journal of Child Psychology and Psychiatry, 36(2), 327–334. 10.1111/j.1469-7610.1995.tb01828.x [PubMed: 7759594]

Zetterqvist M, Lundh L-G, Dahlström Ö, & Svedin CG (2013). Prevalence and function of non-suicidal self-injury (NSSI) in a community sample of adolescents, using suggested DSM-5 criteria for a potential NSSI disorder. Journal of Abnormal Child Psychology, 41(5), 759–773. 10.1007/s10802-013-9712-5 [PubMed: 23344701]

Zetterqvist M, Lundh L-G, & Svedin CG (2014). A cross-sectional study of adolescent non-suicidal self-injury: Support for a specific distress-function relationship. Child and Adolescent Psychiatry and Mental Health, 8, 23. 10.1186/1753-2000-8-23 [PubMed: 25110519]

HIGHLIGHTS

- Adolescents with history of nonsuicidal self-injury have less cortical surface area
- Nonsuicidal self-injury may impact typical age-related changes in the brain
- Future work should use longitudinal data to uncover age-related changes over time

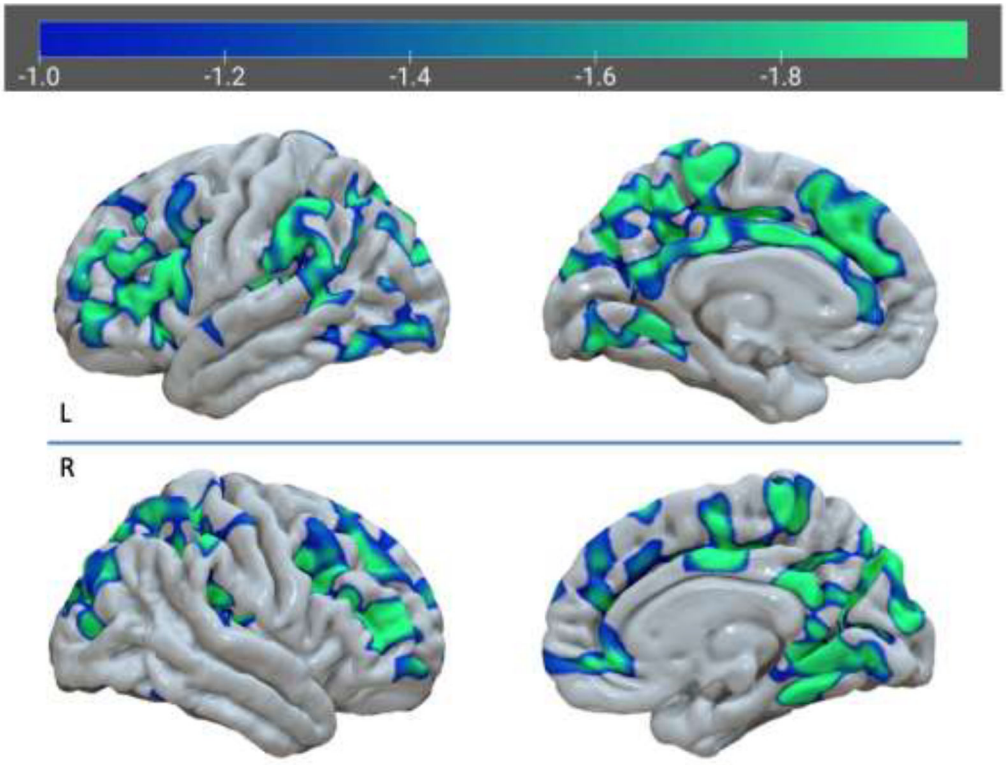

Figure 1:

Note. Age is associated with less cortical thickness in the left and right prefrontal and temporal cortex. Results are cluster-corrected with a cluster-forming threshold of $p < .05$ and a clusterwise significance of $p < .05$, adjusted for 2 hemispheres.

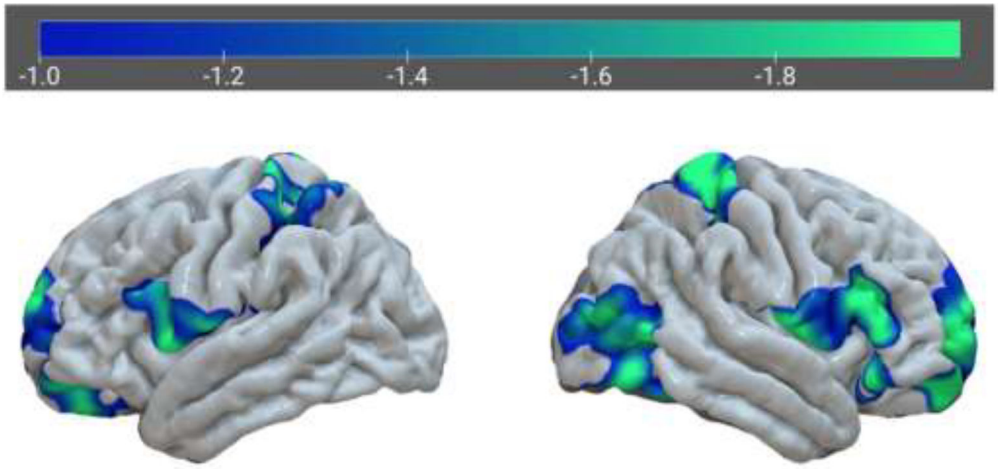

Figure 2:

Note. Age is associated with less cortical surface area in the left and right prefrontal and parietal cortex. Results are cluster-corrected with a cluster-forming threshold of $p < .05$ and a clusterwise significance of $p < .05$, adjusted for 2 hemispheres.

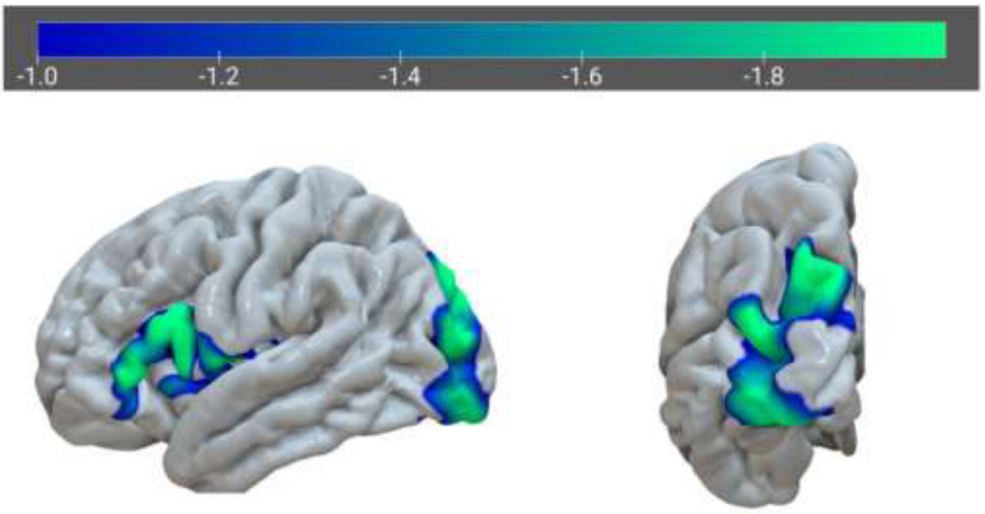

Figure 3:

Note. Nonsuicidal self-injury (NSSI) history is associated with less cortical surface area in the left insula and left inferior parietal cortex relative to adolescents without NSSI history. Results are cluster-corrected with a cluster-forming threshold of $p < .05$ and a clusterwise significance of $p < .05$, adjusted for 2 hemispheres.

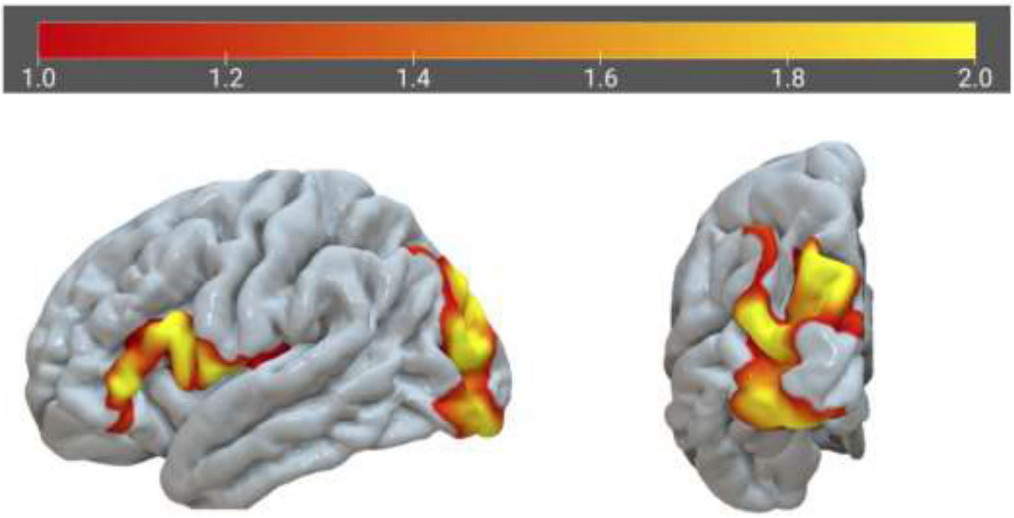

Figure 4:

Note. Nonsuicidal self-injury history and age are associated with larger cortical surface areas in the left inferior parietal cortex and left precentral cortex. Results are cluster-corrected with a cluster-forming threshold of $p < .05$ and a clusterwise significance of $p < .05$, adjusted for 2 hemispheres.

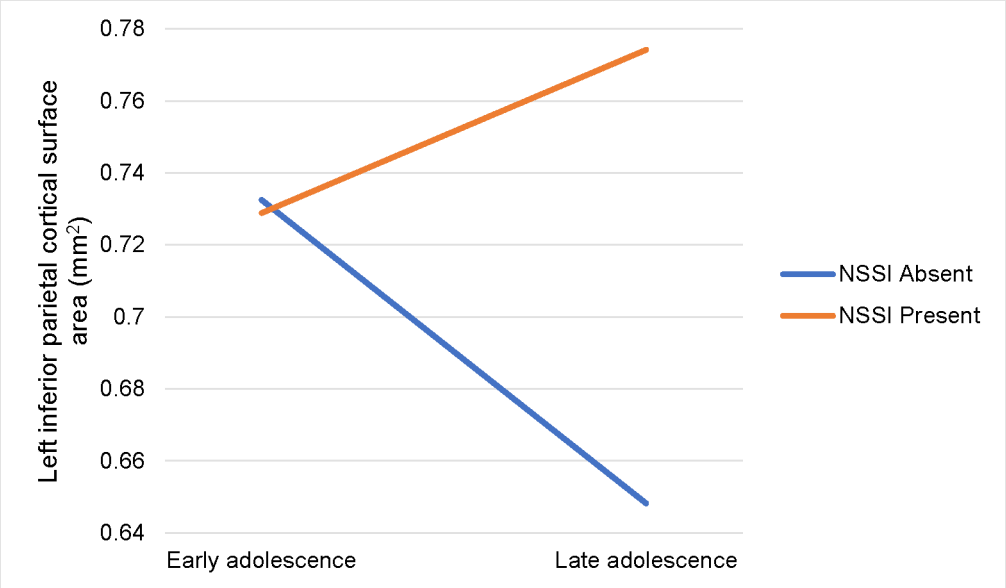

Figure 5:

Note. Nonsuicidal self-injury (NSSI) history moderates the relation between age and left inferior parietal cortical surface area. Early and late adolescence were defined as −1 SD and +1 SD, respectively (M_{age}=13.40, *SD*=1.61).

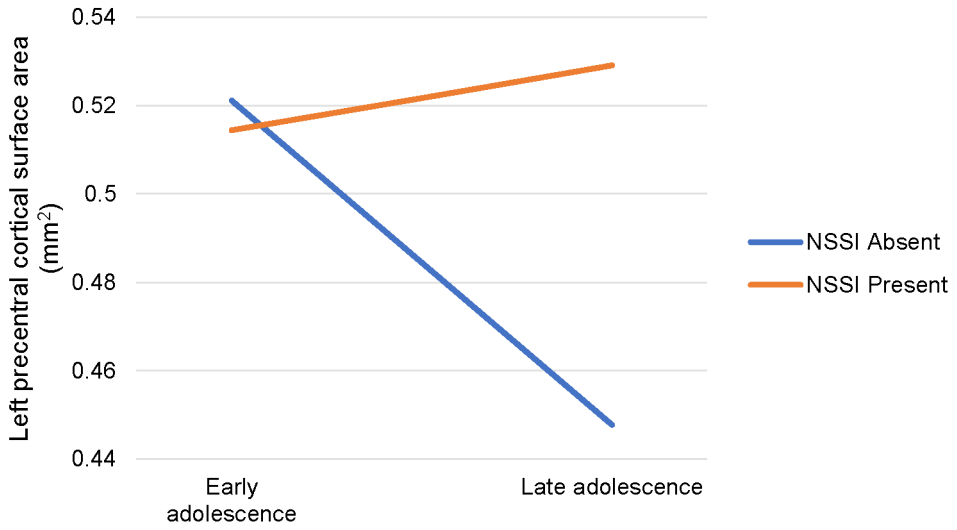

Figure 6:

Note. Nonsuicidal self-injury (NSSI) history moderates the relation between age and left precentral cortical surface area. Early and late adolescence were defined as −1 SD and +1 SD, respectively (M_{age}=13.40, *SD*=1.61).

Table 1

Sample Characteristics by Lifetime NSSI History

Variable	NSSI history present (*n* = 50) Mean ± *SD*	NSSI history absent (*n* = 50) Mean ± *SD*	Group difference *t*
Age (years)	13.83 ± 1.66	12.96 ± 1.44	2.78 **
Depressive Symptoms	19.23 ± 12.72	9.39 6.96	4.80 ***
	n (%)	*n* (%)	χ^2
Medication Usage (Yes/No)	34 (68%)	21 (42%)	6.83 **
Race/Ethnicity			
Black or African-American	12 (24%)	18 (36%)	
Asian	2 (4%)	1 (2%)	
White	24 (48%)	25 (50%)	
Hispanic/Latinx	4 (8%)	1 (2%)	
American Indian or Alaska Native	1 (2%)	1 (2%)	
Mixed Race	7 (14%)	4 (8%)	

NSSI = Nonsuicidal self-injury. *SD* = Standard Deviation.

** $p < .01$.

*** $p < .001$.

Table 2

Associations between Cortical Thickness and Age

Brain Area	Cluster size (mm^2)	Z-value of Cluster	Peak MNI Coordinate		
		z	x	y	z
Left superior frontal	23568.27	−4.92	−12.2	−9.0	46.7
Left lingual	1929.01	−3.37	−13.1	−80.2	−6.4
Left inferior temporal	1791.81	−2.46	−41.7	−55.5	−8.2
Right isthmuscingulate	12664.89	−7.08	4.6	−46.4	28.4
Right posterior cingulate	6090.83	−4.71	5.3	−8.5	39.6
Right caudal middle frontal	3720.65	−4.91	33.2	13.9	26.7
Right supramarginal	1667.08	−3.50	44.6	−33.8	26.3

mm^2 = millimeters squared. MNI = Montreal Neurological Institute. Significant clusters are shown at the $p < .05$ level.

Table 3

Associations between Cortical Surface Area and Age

Brain Area	Cluster size (mm^2)	Z-value of Cluster z	Peak MNI Coordinate x	y	z
Left superior frontal	2674.47	−2.74	−9.5	62.3	18.4
Left postcentral	2420.31	−2.66	−35.4	−35.0	57.7
Left parsopercularis	2293.53	−2.93	−51.0	7.8	0.8
Right fusiform	5563.54	−2.70	33.5	−33.1	−23.6
Right lateral orbitofrontal	3607.28	−2.72	31.5	40.2	−8.9
Right rostral middle frontal	3557.27	−4.67	41.6	25.7	22.6
Right superior parietal	3094.03	−3.37	14.6	−43.9	73.5

mm^2 = millimeters squared. MNI = Montreal Neurological Institute. Significant clusters are shown at the $p < .05$ level.

Table 4

Regions with Significant Differences in Cortical Surface Area Among Adolescents with a Lifetime History of NSSI Relative to Adolescents with no Lifetime History of NSSI

	Cluster size	Z-value of Cluster	Peak MNI Coordinate		
Brain Area	**(mm^2)**	**z**	**x**	**y**	**z**
Left inferior parietal	5403.22	−2.89	−34.9	−87.8	13.1
Left insula	4293.23	−2.85	−35.2	5.0	14.0

NSSI = Nonsuicidal self-injury. mm^2 = millimeters squared. MNI = Montreal Neurological Institute. Significant clusters are shown at the $p < .05$ level.

Table 5

Regions with Significant Differences in Cortical Surface Area from NSSI History and Age

Brain Area	Cluster size (mm^2)	Z-value of Cluster z	Peak MNI Coordinate x	y	z
Left inferior parietal	5763.63	3.31	−35.4	−87.6	13.3
Left precentral	3616.71	2.93	−53.0	−2.7	7.8

NSSI = Nonsuicidal self-injury. mm^2 = millimeters squared. MNI = Montreal Neurological Institute. Significant clusters are shown at the $p < .05$ level.

Table 6

Results of Simple Slopes Analyses Investigating the Interaction between NSSI History and Age to Predict Cortical Surface Area

Variable	b	SE	*p*
Left inferior parietal			
NSSI absence	−.03	.01	.001
NSSI presence	.01	.01	.04
Left precentral			
NSSI absence	−.02	.01	.00
NSSI presence	.004	.01	.37

NSSI = Nonsuicidal self-injury.