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A multi-modal assessment of self-knowledge in adolescents with non-suicidal self-injury: a research domains criteria (RDoC) study

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Abstract

Background. Adolescence is a critical period for brain development, consolidation of self-understanding, and onset of non-suicidal self-injury (NSSI). This study evaluated the RDoC (Research Domain Criteria) sub-construct of Self-Knowledge in relation to adolescent NSSI using multiple units of analysis.

Methods. One hundred and sixty-four adolescents assigned female at birth (AFAB), ages 12–16 years with and without a history of NSSI entered a study involving clinical assessment and magnetic resonance imaging (MRI), including structural, resting-state functional MRI (fMRI), and fMRI during a self-evaluation task. For imaging analyses, we used an *a priori* defined Self Network (anterior cingulate, orbitofrontal, and posterior cingulate cortices; precuneus). We first examined interrelationships among multi-level Self variables. We then evaluated the individual relationships between NSSI severity and multi-level Self variables (self-report, behavior, multi-modal brain Self Network measures), then conducted model testing and multiple regression to test how Self variables (together) predicted NSSI severity.

Results. Cross-correlations revealed key links between self-reported global self-worth and self-evaluation task behavior. Individually, greater NSSI severity correlated with lower global self-worth, more frequent and faster negative self-evaluations, lower anterior Self Network activation during self-evaluation, and lower anterior and posterior Self Network resting-state connectivity. Multiple regression analysis revealed the model including multi-level Self variables explained NSSI better than a covariate-only model; the strongest predictive variables included self-worth, self-evaluation task behavior, and resting-state connectivity.

Conclusions. Disruptions in Self-Knowledge across multiple levels of analysis relate to NSSI in adolescents. Findings suggest potential neurobiological treatment targets, potentially enhancing neuroplasticity in Self systems to facilitate greater flexibility (more frequently positive) of self-views in AFAB adolescents.

Non-suicidal self-injury (NSSI), the deliberate harming of one's own bodily tissue without suicidal intent (Winchel & Stanley, 1991), frequently emerges during adolescence (Brown & Plener, 2017) with a prevalence of approximately 17% in adolescence (Mars et al., 2019; Swannell, Martin, Page, Hasking, & St John, 2014). NSSI is associated with risk for suicide attempts (Mars et al., 2019; Swannell et al., 2014). Few evidence-based interventions address NSSI in adolescents (Glenn, Esposito, Porter, & Robinson, 2019; Turner, Austin, & Chapman, 2014; Westlund Schreiner, Klimes-Dougan, Parenteau, Hill, & Cullen, 2019). Development of new treatments for NSSI is hindered by limited understanding of the mechanisms underlying its onset and maintenance, which likely involves multiple systems (Kaess et al., 2021). An approach consistent with the research domain criteria (RDoC) initiative (Insel et al., 2010), systematically studying domains of functioning relevant to NSSI using multiple different levels of analysis, holds promise for discovering neurodevelopmental mechanisms implicated in NSSI that may guide intervention development (Schreiner, Klimes-Dougan, Begnel, & Cullen, 2015).

Multiple theories have been developed to attempt to explain NSSI. While initial conceptualizations outlined both intrapersonal (e.g. affect regulation) and interpersonal (e.g. help-seeking) functions (Nock, 2009), subsequent work has noted the relatively smaller prevalence of interpersonal functions (Taylor et al., 2018) and more recent theories have tended to highlight the central roles of negative affect and emotion dysregulation in NSSI (Hasking, Whitlock, Voon, & Rose, 2017; Hooley & Franklin, 2018). Two recent theories have highlighted the importance of the self in NSSI. The benefits and barriers model of NSSI (Hooley & Franklin, 2018) proposes that positive self-views act as a barrier that an individual must surpass to engage in NSSI. In a similar vein, the cognitive-emotional model of NSSI (Hasking et al., 2017) theorizes that negative self-schemas (e.g. low self-efficacy) contributes to the likelihood of engaging in NSSI. Drawing from these more recent theories pertaining to the self and taking an RDoC approach, here we choose to focus on the RdoC domain of Self-Knowledge as a domain that needs more investigation in the context of NSSI.

The RDoC sub-construct of Self-Knowledge, which falls under the construct of perception and understanding self (within the larger domain of social processes) and represents the ability to judge one's current cognitive or emotional internal states, traits, and/or abilities, has special relevance to NSSI, a behavior literally representing an assault on the self. The temporal coinciding of the typical onset of NSSI in adolescence (Plener, Schumacher, Munz, & Groschwitz, 2015) with identity development (Marcia, 1966; Meeus, Schoot, Keijsers, Schwartz, & Branje, 2010), a growing sense of uniqueness and connection with others (Harter & Leahy, 2001), and important developmental changes in brain regions underlying self-processing, underscores the importance of a comprehensive examination of the self in relation to NSSI in adolescence.

Converging evidence suggests vulnerability for and maintenance of NSSI in adolescence could involve abnormal development of systems underlying how adolescents perceive and understand themselves. NSSI urges often accompany thoughts of self-criticism and self-punishment (Burke et al., 2021). Negative self-views is a well-documented risk factor for the onset (Andrews, Martin, Hasking, & Page, 2014; Cawood & Huprich, 2011; Claes, Houben, Vandereycken, Bijttebier, & Muehlenkamp, 2010; Hawton, Kingsbury, Steinhardt, James, & Fagg, 1999) and maintenance (Cohen et al., 2015; You, Lin, & Leung, 2015) of NSSI in adolescents. Self-criticism can also impact perception of pain such that greater self-criticism is associated with a greater pain tolerance (Hooley, Ho, Slater, & Lockshin, 2010). According to the benefits and barriers model, negative self-views increase the likelihood of engaging in NSSI by fostering an urge to end negative affect, a desire for self-punishment, and greater awareness of and identification with self-harm (Hooley & Franklin, 2018). Negative self-perceptions can alter adolescents' response styles (Urbán, Szigeti, Kökönyei, & Demetrovics, 2014) and likely arise from disruptions in self-referential brain processing.

Self-referential processing is mediated by a network of medial cortical regions including the anterior cingulate cortex (ACC), medial prefrontal cortex (MPFC), orbitofrontal cortex (OFC), posterior cingulate cortex (PCC), and precuneus (Gusnard, Akbudak, Shulman, & Raichle, 2001; Murray, Debbané, Fox, Bzdok, & Eickhoff, 2015; Northoff & Bermpohl, 2004; Northoff, Qin, & Feinberg, 2011), hereafter referred to as the 'Self Network.' Functional magnetic resonance imaging (fMRI) research has frequently utilized self-evaluation tasks (asking participants to make judgments about themselves) to probe the Self Network. During self-evaluation, adolescents engage the Self Network to a greater extent than adults (Pfeifer, Lieberman, & Dapretto, 2007). Longitudinal data suggests rostral Self Network activation during self-evaluations may increase during early adolescence (Pfeifer et al., 2013), although the literature is mixed (Barendse et al., 2020a; Cosme et al., 2022; van Buuren et al., 2022; van der Cruijsen, Peters, van der Aar, & Crone, 2018). One prior study showed that during self-evaluations, self-injurious youth showed reduced deactivation in the posterior Self Network yet heightened bilateral limbic engagement when taking their parent's perspective while evaluating themselves (Quevedo, Martin, Scott, Smyda, & Pfeifer, 2016). Beyond task fMRI, resting-state fMRI can also characterize brain networks (Biswal, Kylen, & Hyde, 1997). While developmental change of Self Network resting-state functional connectivity (RSFC) has been relatively less studied, RSFC within the default mode network (DMN), which overlaps with Self Network (Gusnard et al., 2001; Raichle et al., 2001), is stronger in adolescents than children (Fair et al., 2008; Supekar et al., 2010). Structural imaging provides yet another window into understanding brain networks. The entire cortex undergoes a normative pattern of thinning during adolescence (Gogtay et al., 2004). While relationships between cortical thinning trajectories and NSSI has not yet been directly studied, some relevant patterns with cortical thinning include associations between socioemotional functioning and Self Network thinning in adolescence (Vijayakumar et al., 2014); between shame-proneness and thinner PCC, but attenuated age-related thinning of OFC, in adolescents and young adults (Whittle, Liu, Bastin, Harrison, & Davey, 2016); and between preschool early onset depression and cortical thinning during adolescence (Ducharme et al., 2014; Luby et al., 2016) particularly in Self Network regions (Truong et al., 2013).

While research to date has begun to shed light on how different levels of Self-Knowledge may individually relate to NSSI, questions remain about how multiple levels and within-level multimodal approaches (e.g. brain function *v.* structure) may operate in the context of development and emerging psychopathology. The current study examined associations between NSSI severity and Self-Knowledge across multiple levels of analysis (self-report, behavior, brain activation, RSFC, cortical thickness [CT]) in adolescents with and without NSSI. We hypothesized NSSI severity would be associated with negative self-views (measured by self-report and task behavior) and aberrant neural patterns within the Self Network, specifically: greater activation during self-evaluation, lower RSFC, and lower CT in key Self Network nodes. To advance the RDoC initiative, we also examined convergence and divergence of cross-method measures of Self-Knowledge.

Methods

This current work presents cross-sectional results on Self-Knowledge from a longitudinal study called the Brain Imaging Development of Girls' Emotion and Self (BRIDGES) Study. The overarching goals of the BRIDGES study are to examine the constructs of Sustained Threat (Başgöze et al., 2021a), Cognitive Control (Başgöze et al., 2023), and the sub-construct of Self-Knowledge longitudinally in a sample enriched for NSSI (IRB #1605M 881020). The study was approved by the Institutional Review Board at University of Minnesota. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Participants

We recruited adolescents with inclusion criteria of age between 12–16 years, assigned female at birth (AFAB), and post-menarcheal, aiming for a sample with NSSI severity ranging from none to severe. In the context of known sex differences in brain development (Lenroot & Giedd, 2010), to limit sex-related heterogeneity and given limited power in our expected sample size to disentangle sex effects, we focused on AFAB alone in this sample, selecting AFAB over assigned male at birth because NSSI is more common in AFAB adolescents (Andrews et al., 2014; Zetterqvist, Lundh, Dahlström, & Svedin, 2013). Exclusion criteria included bipolar disorder, psychotic disorder, intellectual or developmental disability, current substance use disorder, significant medical illness, or MRI contraindications at intake. There were no treatment-related exclusion criteria. Participants were recruited through community postings, digital marketing, and local clinics and hospitals. Following a telephone screen, participants and legal guardians were invited to complete informed assent (adolescent), consent (legal guardian), and a diagnostic clinical interview. Enrollment took place in December 2016 through June 2020. The current work is based on Time 1 assessment data.

Clinical assessment

Semi-structured interviews using the Kiddie Schedule of Affective Disorders and Schizophrenia Present and Lifetime Version (KSADS-PL) (Kaufman et al., 1997) were conducted separately with adolescents and guardians. The paper version (KSADS-PL) was administered to the initial 23% of the sample ($n = 37$) and the computerized version (KSADS-COMP) (Townsend et al., 2020) was administered to the rest. To characterize NSSI, the Self-Injurious Thoughts and Behaviors Interview (SITBI) (Nock, Holmberg, Photos, & Michel, 2007) was administered to adolescents. Adolescents completed the Beck Depression Inventory – Revised (BDI-II) (Beck, Steer, & Brown, 1996) and the Child Trauma Questionnaire (CTQ) (Fink & Bernstein, 1998). BDI-II total score was calculated without self-relevant items (items 3, 7, and 8). Parents reported on key demographic variables. Final diagnoses and eligibility were determined in a consensus meeting between evaluators.

Self-report assessment of self

Adolescents completed the Self Perception Profile for Adolescents (SPP-A) (Harter, 2012). Our self-report variable of interest was the Global Self Worth score (a general evaluation of how much one likes and is happy with oneself and the way one is as a human being).

MRI data acquisition and preprocessing

Structural and functional (resting-state and task) data were collected using a Siemens 3 Tesla Prisma scanner (Erlangen, Germany) and a 32-channel receive only head coil, using the Human Connectome Project (HCP) (UpAndRunning, 2023) multi-band sequences to collect high spatial and temporal resolution fMRI data. See Supplementary Materials for further details of acquisition parameters, HCP pipelines used to process the neuroimaging data (Glasser et al., 2013), and strategies used to address head motion.

Self v. Change (SvC) task

Adolescents were prompted to evaluate negatively and positively valenced attributional words relevant to interpersonal relationships (e.g. friendly, popular, awkward, selfish) (Barendse et al., 2020a, 2020b; Pfeifer et al., 2007, 2013) in two fMRI runs (5–6 min each). During Self blocks, participants judged whether the attribute described themselves. During Change blocks, participants judged whether the attribute could change.

SvC behavioral data

We calculated normalized values for positive (saying 'yes' to a positive or 'no' to a negative word while describing oneself) and negative (saying 'yes' to a negative or 'no' to a positive word while describing oneself) self-evaluation reaction times (RT) and for negative self-evaluation frequency (not for positive self-evaluation frequency because it provides redundant information with negative self-evaluation frequency). For frequencies, we divided the number of negative evaluations by the total number of successful responses (thus accounting for the missing trials). For RT, we divided the mean RT during positive and negative evaluations each by the mean RT for all self-evaluations (regardless of word valence or the outcome of the self-evaluation).

Defining the Self Network (across imaging modalities)

All imaging analyses focused on the Self Network *a priori* defined to include midline cortical brain regions implicated in self-processing: ACC, mPFC, OFC, PCC, and precuneus (Gusnard et al., 2001; Murray et al., 2015; Northoff et al., 2006; Northoff & Bermpohl, 2004) using the Glasser parcellation (Glasser et al., 2016) (see Fig. 1 and Supplementary Materials.) To balance precision and need to limit the number of tests, and in consideration of research indicating the anterior Self Network node (ACC,

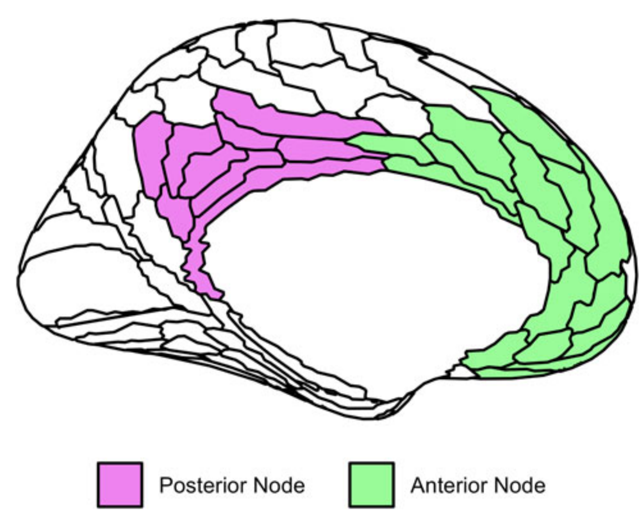

Figure 1. Glasser parcellations defining the Self Network.
Note: Locations of Glasser regions of interest included in the Self Network. The anterior Self Network node was composed of the following Glasser regions from the right and left hemisphere: ACC/mPFC (Glasser Cluster 19) 33pr, p24pr, a24pr, p24, a24, p32pr, a32pr, d32, p32, s32, 8BM, 9 m, 10v, 10r, 25 and OFC. The posterior Self Network node was composed of the following Glasser regions from the right and left hemisphere: RSC, v23ab, d23ab, 31pv, 31pd, 31a, 23d, 23c, PCV, and 7 m. See Supplemental Materials for more information.

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mPFC, OFC) is more centrally involved in self-conceptualization while the posterior Self Network regions (PCC, precuneus) integrates perspectives of others into the self-concept (Murray et al., 2015) as well as autobiographical memory and immersion in self-relevant experiences (Cavanna & Trimble, 2006), we employed averaging techniques to create anterior and posterior Self Network nodes for all brain imaging modalities.

Self Network function

We conducted a whole-brain linear regression analysis of the SvC task model against the Glasser parcellated task fMRI data using FSL FEAT as implemented in the HCP pipeline. Contrasts of interest were Negative greater than Positive Valence (N > P) of the adjective (regardless of the context of self-evaluation *v.* change), and Self greater than Change (S > C) (regardless of valence of the adjectives). Sub-contrasts (e.g. negative adjectives during self-evaluation only) were not the main contrasts of interest due to limited power (See supplementary materials for results on the Negative Self-Evaluation > Positive Self-Evaluation contrast and the Negative > Positive contrast during self-trials only). While the fMRI task analysis was conducted in volumetric space, the resulting z-score statistical maps were projected back to CIFTI space for further analyses. Values for the Glasser parcels categorized as part of the anterior and posterior Self Network nodes were extracted and averaged to compute mean anterior and posterior Self Network z-scores.

Self Network RSFC

Mean time series from the Self Network regions were derived from the dense, grayordinate-wise time series using a combination of the Glasser (cortical) parcellation and Harvard-Oxford (subcortical) atlas. Within the anterior and posterior Self Network nodes, between-region correlations were computed followed by Fisher's z-transformation. Connectivity values within each node were averaged to yield mean values for anterior and posterior Self Network RSFC.

Self Network CT

CT values from Glasser parcels in the anterior and posterior Self Network nodes were extracted from the HCP-derived vertex-wise thickness maps, by calculating the weighted average of thickness weighted by the ROIs' surface area:

$$\frac{(\mathrm{ROI1}_{\mathrm{thickness}} * \mathrm{ROI1}_{\mathrm{surfarea}}) + (\mathrm{ROI2}_{\mathrm{thickness}} * \mathrm{ROI2}_{\mathrm{surfarea}}) + (\mathrm{ROI3}_{\mathrm{thickness}} * \mathrm{ROI3}_{\mathrm{surfarea}})}{\mathrm{ROI1}_{\mathrm{surfarea}} + \mathrm{ROI2}_{\mathrm{surfarea}} + \mathrm{ROI3}_{\mathrm{surfarea}}}$$

Statistical analysis

NSSI severity was indexed by self-reported number of lifetime NSSI episodes (per the SITBI). We log-transformed the data to correct for skewness (we used the formula $\log(x+1)$ to account for 0′s). Our overarching goal was to examine relationships between NSSI severity and the multi-modal Self-Knowledge measures (see Table S1 in supplementary materials). First, to test the coherence of the selected Self-Knowledge measures (how they map onto each other as multimodal measures of the Self-Knowledge subconstruct), we examined correlation patterns and report uncorrected and Hochberg corrected p values. Second, we conducted a series of 13 simple regression analyses, using NSSI severity as the outcome variable and each of the Self-Knowledge measures as the predictor variables to investigate the individual relationships between each Self-Knowledge measure and NSSI. We used the False Discovery Rate (FDR) to adjust for multiple comparisons within each modality: (1) self-report (SPP-A – global self-worth); (2) SvC task behavior (RT for positive and negative evaluations and negative evaluation frequency); (3) SvC task anterior and posterior Self Network node brain activation (N > P and S > C contrasts), (4) anterior and posterior Self Network node RSFC; and (5) anterior and posterior Self Network node CT. We report uncorrected and FDR-adjusted p values. Since NSSI commonly co-occurs with depression symptoms (Başgöze, Wiglesworth, Carosella, Klimes-Dougan, & Cullen, 2021b), past adverse experiences can shape self-views, and medication treatment can impact brain-behavior relationships, follow-up analyses used BDI-II total scores, CTQ total scores, and medication status (taking antidepressants *v.* not), and age as covariates to identify when/how the relationships between Self variables and NSSI exist above and beyond links with depression, past trauma, medications, and age.

Next, using all Self-Knowledge variables, we conducted stepwise model selection to identify the best explanatory variables. Models were evaluated in reference to the Akaike information criterion (AIC). A multiple linear regression was then conducted on the variables from this 'best' model to examine unique contributions from each retained variable. Follow-up analyses included covariates of age, BDI-II, CTQ scores, and medication status to test if relationships between Self-Knowledge variables and NSSI were independent of these factors.

Because NSSI and suicidal thoughts and behavior are highly comorbid and both are associated with negative self-views (Hamza, Stewart, & Willoughby, 2012), we conducted exploratory analyses with Beck Scale for Suicidal Ideation (BSSI) as our outcome variable instead of NSSI to determine whether our findings are unique to NSSI. See supplementary materials for results with BSSI.

Power and sample size calculation

Our recruitment target of 152 participants were initially designed for analyses based on NSSI severity groups (no NSSI, mild, moderate, and severe NSSI) with a goal of 30 participants per group with usable data. With $N = 152$, we determined we would have 85% power to detect correlations as small as 0.25 of NSSI severity with the RDoC measures we had proposed to examine. This was based on our initial pilot data demonstrating correlations ($r = 0.45$ to 0.56) between the multiple measures (self-report, brain activation, RSFC and CT) relevant to Self-Knowledge that had been collected in our prior study of adolescents with NSSI (Westlund Schreiner, Cullen, & Klimes-Dougan, 2017) and which were further refined to better capture the Self-Knowledge construct (adding the Self *v.* Change task instead of a threat response task, replacing the Personality Assessment Inventory [PAI]-Borderline-Identity Problems subscale as our measure of Self-Knowledge with the SPP-A to better capture this construct).

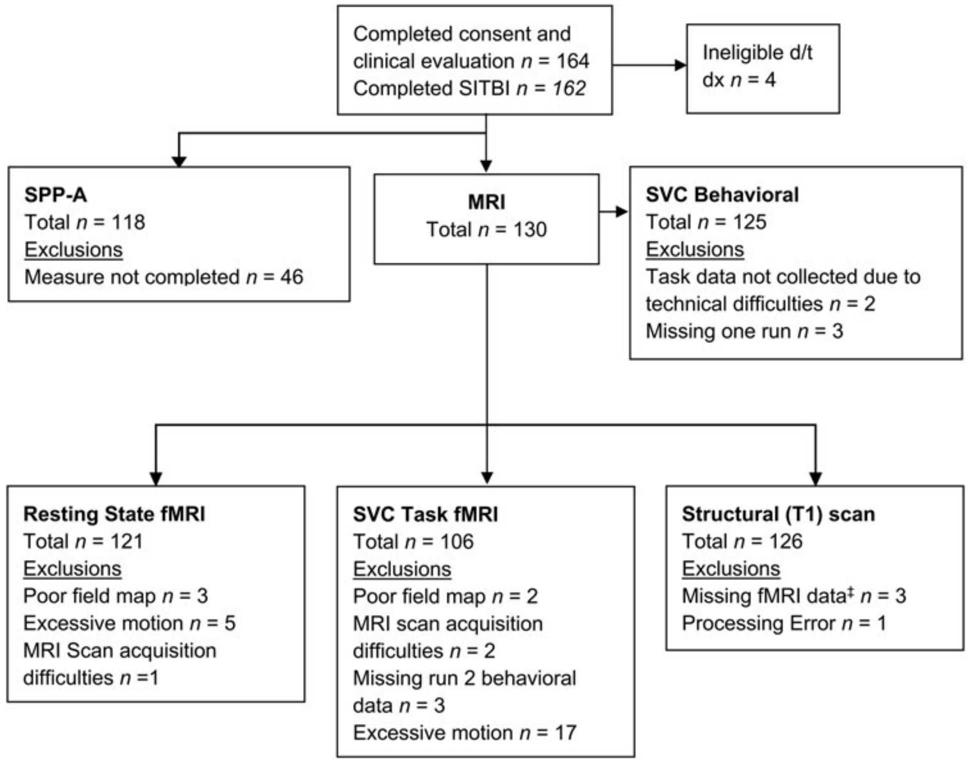

Figure 2. Self Predictors Consort diagram for the BRIDGES study.
Note: This figure illustrates the number of participants who completed the study visits where self-data was collected that was analyzed in this paper, and how many of those participants had usable data. ‡cortical thickness values maps were parcellated after multimodal surface matching (MSMAll) in order to get better functional alignment across subjects. As such, subjects require both structural and functional data to have cortical thickness values. dx, diagnosis; SITBI, Self-Injurious Thoughts and Behaviors Interview; SPP-A, self perception profile for adolescents, global self worth; SVC, self versus change.

Missing data imputation

Due to the COVID-19 pandemic, we had higher rates of missing data and retention difficulties and although we surpassed our initial recruitment goal of $N = 152$ (we enrolled $N = 168$), we did not have complete data from all participants. To address missingness, we imputed missing data using a random forest based algorithm (missForest); (Stekhoven, 2013; Stekhoven & Bühlmann, 2012). Missingness (including data that was not collected or was not usable) ranged from 0% (age) to 35.37% (fMRI data for the SVC task). See supplementary materials for complete-case analyses results without data imputation; notably, missing data diminishes power in these analyses without data imputation.

Results

Participants

Figure 2 displays a flow diagram summarizing the activities completed by all participants, capturing missing data and dropout. Table 1 summarizes demographic and clinical data for participants with usable data for at least one of the study variables.

Integrative analyses: correlations across levels

We examined relationships between all study measures, with a particular interest in assessing patterns of convergence and divergence among multiple levels of Self-Knowledge. Results are shown in Fig. 3. As expected, NSSI severity correlated positively with depressive symptoms (BDI-II) and childhood trauma (CTQ), and negatively with self-worth (SPP-A). Key integrative findings included lower self-worth (SPP-A) correlated with more frequent and faster RT during negative self-evaluations, and with slower RT during positive self-evaluations during the SvC task. No other correlations remained significant after the Hochberg correction. See supplementary table S2 for results without data imputation; the same pattern of correlations was largely found with the non-imputed data.

Multi-level Self Variables predicting NSSI severity: individual and multiple regression results

Individual regressions

Table 2 (3rd and 4th columns from right) presents a summary of the individual regression results in which variables within each level of analysis were used to predict NSSI severity. Key findings revealed inverse relationships between NSSI severity and SPP-A global self-worth, negative evaluation RT, S > C anterior Self Network activation, anterior and posterior Self Network RSFC as well as a positive relationship with negative evaluation frequency. Of these, only the SPP-A and S > C anterior Self Network findings remained after co-varying for age, medication status, BDI-II, CTQ scores.

Stepwise model selection with imputed data

Stepwise model selection, which considered all Self variables, revealed the best model explaining NSSI severity included: (1) SPP-A global self-worth, (2) SvC task behavior for negative self-

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Table 1. Clinical and demographic information

N	140
Age – mean (std)	14.99 (1.22)
Grade	
6	1 (0.71%)
7	13 (9.29%)
8	32 (22.86%)
9	37 (26.43%)
10	30 (21.43%)
11	17 (12.14%)
12	1 (0.71%)
Homeschooled	1 (0.71%)
Race – *N* (%)	
Asian	3 (2.14%)
Black/African American	3 (2.14%)
More than one race	19 (13.57%)
Native American	1 (0.71%)
Other race	1 (0.71%)
White	113 (80.71%)
Lifetime NSSI episodes – mean (s.d.) (range)	48.41 (138.70) (0–1000)
Beck Depression Inventory – mean (s.d.)[a]	13.02 (11.78)
Beck Scale for Suicidal Ideation – mean (s.d.)	4.86 (7.46)
History of suicide attempts – *N* (%) (range)	43 (30.71%)
Currently receiving medication (*N*, %)	73 (52.14%)
Child Trauma Questionnaire – mean (s.d.)	37.47 (12.71)

NSSI, non-suicidal self-injury.
Note: Participants included in this table had data for at least one self-measure.
[a]The Beck Depression Inventory total score was calculated without self-relevant items (items 3, 7, and 8).

evaluation frequency, (3) SvC task behavior for positive self-evaluation RT, (4) SvC task S > C posterior Self Network activation, (5) SvC task N > P anterior Self Network activation, and (6) SvC task N > P posterior Self Network activation, and (7) posterior Self Network RSFC.

Multiple regression

A multiple regression model with the Self-Knowledge variables identified by the stepwise model selection significantly predicted NSSI severity (adjusted $R^2 = 0.32$, $F(7,\ 156) = 11.99$, $p < 0.001$). Table 2 (columns 5 and 6) shows the relationship between each of the included Self-Knowledge variables and NSSI severity within this model. In this set of results, NSSI severity was significantly associated with SPP-A global self-worth, negative self-evaluation frequency, positive self-evaluation RT, and posterior Self Network RSFC while S > C and N > P posterior node Self Network activation trended toward significance (all relationships were negative except N > P posterior Self Network activation and negative self-evaluation frequency).

Multiple regression with covariates

A follow-up analysis model with BDI-II, age, psychotropic medications, and CTQ as covariates still significantly predicted NSSI severity (adjusted $R^2 = 0.43$, $F(11,\ 152) = 12.12$, $p < 0.001$), and the remaining significant predictors were positive self-evaluation RT. The model including both the Self variables and covariates (AIC = 320.45) was significantly superior to the model including only the covariates (AIC = 326.87), $F(7,\ 152) = 2.88$, $p = 0.007$.

Discussion

This study examined the RDoC Self-Knowledge sub-construct using multiple levels of analysis in adolescents with a continuum of NSSI severity. Key strengths of the current work include the transdiagnostic and multi-level (e.g. self-report, behavior, multimodal neuroimaging) approach to systematically study how a relevant RDoC sub-construct relates to a common and concerning behavior in adolescents. It can be challenging to isolate mechanisms underlying NSSI because NSSI is usually comorbid with other psychiatric symptoms (Başgöze et al., 2021b). Because our inclusion criteria did not require any specific psychiatric diagnoses and participants without a history of NSSI could have past or current psychiatric diagnoses, our results may be more generalizable to the construct of NSSI as a whole and can help isolate features unique to NSSI compared to other psychiatric symptoms. We found evidence that NSSI severity in adolescents is associated with disruptions in Self-Knowledge across multiple levels. Together these levels provide critical information for predicting/accounting for NSSI severity in adolescents. Toward the goal of advancing the RDoC initiative, our examination of relationships across levels of analysis revealed convergence across self-report and behavioral Self-Knowledge measures and shed new light on patterns of integration across self-report, behavior, and brain function, connectivity, and structure.

Results of the correlation analyses and individual-level simple regression analyses revealed, as expected, those with higher NSSI severity viewed themselves more negatively, as assessed via both self-report and a behavioral task. This fits with prior research repeatedly showing that youth who engage in NSSI have lower self-esteem (Andrews et al., 2014; Cawood & Huprich, 2011; Hawton et al., 1999; Iannaccone et al., 2013; Leong, Wu, & Poon, 2014; Nelson & Muehlenkamp, 2012) and high self-criticism (Claes et al., 2010; Cohen et al., 2015; You et al., 2015). In comparison to self-reports, behavioral assessment of Self-Knowledge has been much less common in the literature. The findings reported here are consistent with a prior study using a similar self-evaluation task in which adolescents with depression (both with and without NSSI, and with and without a history of abuse) showed less frequent positive and more frequent negative self-evaluations than healthy controls (Quevedo et al., 2016, 2017).

Number of lifetime NSSI episodes was further related to both task-elicited activation and RSFC: those with higher NSSI severity show lower anterior and posterior Self Network connectivity during rest and low anterior Self Network S > C task activation. Impaired synchrony within the Self Network at rest may disrupt efficiency of the system, leading to lower recruitment of Self Network regions during self-processing. Lower engagement of the Self Network during self-evaluation may result in superficial and quick judgments about oneself. Individuals with a history of NSSI may draw on habitual negative self-judgments rather than make comprehensive self-evaluations. This multimodal dysfunction could underlie the tendency to persistently and inflexibly view oneself in a negative light.

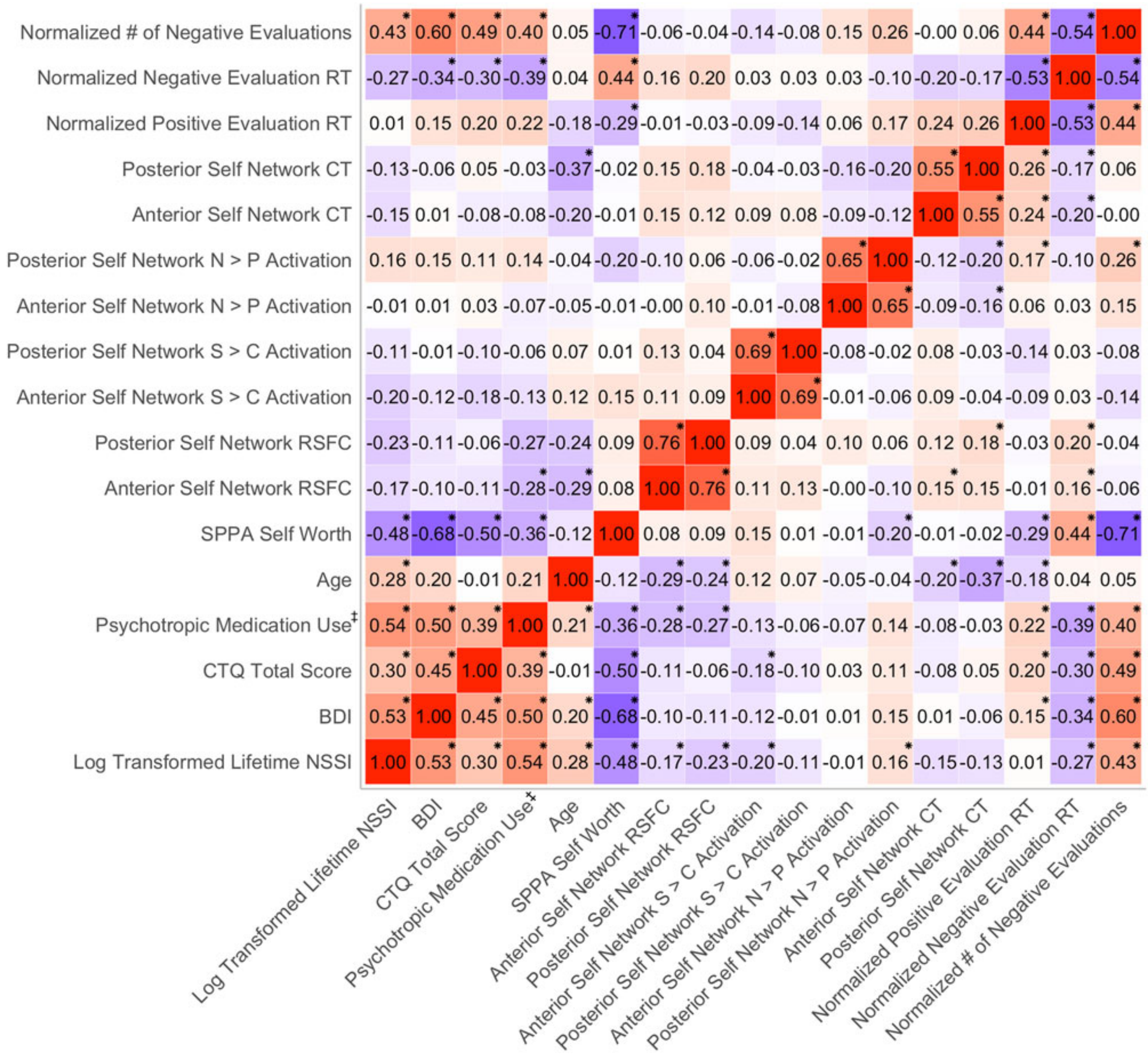

Figure 3. Correlations across all study measures.
RT, reaction time; N, negative; P, positive; S, self; C, change; RSFC, resting-state functional connectivity; SPP-A, self perception profile for adolescents, global self worth; CT, cortical thickness; CTQ, Child Trauma Questionnaire; BDI, Beck Depression Inventory; NSSI, non-suicidal self-injury. ‡Spearman's Rho was used for psychotropic medication use* $p < 0.05$ (Hochberg corrected p values in the upper matrix and uncorrected p values in the lower matrix).

Our combined approach for examining the relationships between multi-modal Self-Knowledge variables with NSSI both *separately* and *together* underscore how each approach can provide important and supplementary information. For one example, although positive self-evaluation RT did not emerge as related to NSSI severity in the correlations or individual regressions, when all variables were considered together, positive self-evaluation RT was significantly negatively related to NSSI. This might suggest that while independently, positive self-evaluation RT may not explain NSSI severity, it can play an important role when combined with other key variables. In a second example, when considered individually, lower anterior and posterior Self Network RSFC related to NSSI, but when considered together with the rest of the Self Knowledge variables, only posterior Self Network RSFC remained significant, which may highlight the prominence of the posterior node of the Self Network in NSSI. Prior research has suggested that while both nodes are highly involved in Self and Other processing, the posterior node is relatively more involved in other processing (Murray et al., 2015). Although the task used here focused only on self-evaluations and did not involve any other-evaluation, the process of self-evaluation is informed by a lifetime of experiencing, perceiving and interpreting judgments from others (Cooley, 1902). Indeed, the posterior Self Network node is centrally involved in episodic memory (Cavanna & Trimble, 2006). When evaluating themselves, adolescents with more severe NSSI may tend to judge themselves in the context of their ingrained beliefs about how others judge them, a process that may involve aberrant functioning of the posterior Self Network. While speculative, further investigation of this idea could shed light on the neural basis of

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Table 2. Relationships between multi-level self-measures and lifetime NSSI episodes

Level of analysis *N* Individual regression | *N* Individual regression with covariates Statistical approach		Measure	Parameter estimate, *p* value* (95% CI) Individual regression without covarying age, BDI, CTQ, medication status	Parameter estimate, *p* value* (95% CI) Individual regression covarying age, BDI, CTQ, medication status	Parameter estimate, *p* value (95% CI) Multiple regression without covarying for age, BDI, CTQ, medication status	Parameter estimate, *p* value (95% CI) Multiple regression covarying for age, BDI, CTQ, medication status
Self-report	SPP-A	Global Self Worth	−0.51, <0.001* (−0.65 to −0.36)	−0.21, 0.019* (−0.39 to −0.04)	−0.31, 0.002 (−0.51 to −0.12)	−0.17, 0.1 (−0.37 to 0.034)
Behavior	Self-evaluations – Frequency	Negative	2.57, <0.001* (1.74–3.39)	0.89, 0.063 (−0.05 to 1.83)	1.72, 0.0041 (0.55–2.89)	0.94, 0.1 (−0.19 to 2.1)
	Self-evaluations – Reaction time	Negative	−1.25, <0.001* (−1.95 to −0.56)	−0.29, 0.37 (−0.91 to 0.34)	NI	
		Positive	0.19, 0.87 (−2.05 to 2.43)	−0.99, 0.29 (−2.83 to 0.85)	−3.47, 0.0012 (−5.54 to −1.4)	−2.57, 0.011 (−4.5 to −0.61)
Brain – self network	SVC task – Negative > Positive valence	Anterior	−0.01, 0.93 (−0.24 to 0.22)	−0.0017, 0.99 (−0.19 to 0.18)	−0.21, 0.12 (−0.46 to 0.05)	−0.15, 0.22 (−0.39 to 0.09)
		Posterior	0.17, 0.044 (0–0.34)	0.081, 0.24 (−0.05 to 0.21)	0.17, 0.072 (−0.02 to 0.36)	0.14, 0.12 (−0.035 to 0.31)
	SVC task – Self > Change	Anterior	−0.23, 0.011* (−0.4 to −0.05)	−0.17, 0.016 (−0.31 to −0.03)	NI	
		Posterior	−0.11, 0.17 (−0.26 to 0.05)	−0.098, 0.12 (−0.22 to 0.02)	−0.12, 0.077 (−0.25 to 0.01)	−0.12, 0.057 (−0.24 to 0.0033)
	RSFC	Anterior	−1.68, 0.031* (−3.21 to −0.16)	−0.19, 0.77 (−1.49 to 1.11)	NI	
		Posterior	−2.1, 0.0028* (−3.47 to −0.73)	−0.86, 0.14 (−2.02 to 0.29)	−1.74, 0.0038 (−2.91 to −0.57)	−0.93, 0.10 (−2.1 to 0.19)
	Cortical thickness	Anterior	−0.92, 0.057 (−1.87 to 0.03)	−0.69, 0.08 (−1.46 to 0.08)	NI	
		Posterior	−0.96, 0.096 (−2.09 to 0.17)	−0.39, 0.43 (−1.36 to 0.58)	NI	

CI, confidence interval; NS, not significant; NI, not included in final model for multiple regression; SPP-A, self perception profile for adolescents, global self worth; SVC, self versus change; RSFC, resting-state functional connectivity; BDI, Beck Depression Inventory; CTQ, Child Trauma Questionnaire; NSSI, non-suicidal self-injury.

Results from individual (left) and multiple (right) regression analyses with multi-level Self variables as predictors and NSSI Lifetime Episodes (log transformed) as the outcome using imputed data ($N = 164$). Results are organized by level of analysis (self-report, behavior, each type of brain imaging modality).

*Corrected *p* value still <0.05 after FDR correction for individual regressions.

aberrant self-concept in adolescents as a biological mechanism of NSSI. These findings highlight both the promise and challenge of integrative analyses to understand the complex and highly interconnected systems implicated in psychopathology.

An important consideration acknowledged in the work here is the overlap between NSSI, depression and past trauma. Negative self-judgment is a core feature of depression, which commonly co-occurs in adolescents struggling with NSSI (Başgöze et al., 2021b), including in this sample. Indeed, we found depression scores also correlated with SvC negative evaluation frequencies and RT, and when depression scores were covaried, the relationships between the speed and frequency of negative self-judgments and NSSI severity was no longer significant. Based on the knowledge that a history of maltreatment increases risk for both depression and NSSI, we also explored relationships with past trauma experiences, and indeed found that those reporting greater childhood adversity evaluated themselves negatively more frequently and quickly. A developmental explanation for the shared variance here could be that for some adolescents, early adverse experiences set the stage for negative self-perceptions, a core feature of both depression and NSSI. This idea could contribute to expanding existing developmental theories which have largely focused on how early adverse experiences set the stage for the development of emotion dysregulation (Beauchaine & McNulty, 2013; Crowell, Beauchaine, & Linehan, 2009). The issue of shared variance among emotion-related constructs and NSSI is increasingly clear in the literature (Haywood, Hasking, & Boyes, 2022). Longitudinal research is needed to disentangle the developmental sequence of events and identify more precisely opportunities for intervention.

Relatedly, although NSSI and suicidal behavior are distinct behaviors, they are also comorbid behaviors and are both related to negative self-views, with 33–37% of adolescents who engage in NSSI also engaging in suicidal behaviors (Hamza et al., 2012). In our sample, 43 participants have a history of suicide attempts (40 of these participants also have engaged in NSSI). However, NSSI and suicidal ideation showed a different pattern of results and only had a moderate correlation in this sample ($r = 0.47$, $p < 0.001$). Positive self-evaluation RT was significantly positively associated with suicidal ideation but not with NSSI. In contrast, anterior and posterior Self Network RSFC was significantly associated with NSSI but not suicidal ideation (see supplementary materials for more information). These different patterns of findings suggest that the results of this paper are specific to NSSI and not suicidality.

Several limitations should be considered. First, by focusing on the Self Network, this approach did not utilize the full dataset of whole-brain data. A challenge inherent to *a priori* region-of-interest-driven approaches is that much depends on the selection and definition of the regions selected. While the selections here were based on prior meta-analyses of self-processing, other approaches (e.g. different atlas, coarser or finer nodes, narrower *v.* broader definition of the Self Network) could have led to different results. Additionally, it is possible that other networks (beyond the Self Network) could have been identified as correlates of NSSI severity using other analytical approaches. Second, there are challenges inherent to examining NSSI severity. While the Lifetime number of NSSI episodes as our main index of NSSI severity provides good information about the lifetime engagement with substantial variability, especially given our study design, it (a) does not always reflect severity at the time of assessment; (b) does not take into account the severity of tissue damage, which varies across subjects, and (c) risks error related to participants' estimation and retrospective reporting, which is especially difficult when there have been many episodes. Third, there are limitations regarding the generalizability of the findings. Since our study recruited AFAB individuals, and the sample was predominantly White, future work is needed that includes participants identified as male at birth, as well as greater racial, ethnic and gender diversity. Stronger associations are found between self-criticism and depression in adolescent girls compared to boys, so these patterns of results may not generalize to individuals who identify as male (Shahar, Blatt, Zuroff, Kuperminc, & Leadbeater, 2004). Marginalized populations may also exhibit unique risk factors like discrimination experiences (Smith, Wang, Carter, Fox, & Hooley, 2020). We further did not collect information about recruitment sources for each participant (e.g. community postings *v.* clinical services), which may also limit the generalizability of our sample. Fourth, the cross-sectional nature of the data reported on here prohibits examination of within-person changes to understand how developmental trajectories in the Self Network may relate to NSSI severity, which may be more revealing compared to results gleaned from a single time point. Likewise, participants in this study were recruited based on a history of NSSI, and may or may not have been actively engaging in NSSI while participating in the study, limiting interpretations about the temporal dynamics of the results reported here. Future longitudinal work, such as prospective studies using dense sampling approaches, holds promise for advancing knowledge in this area. Finally, due to missing data, differences in samples may account for the different findings in individual- and multiple-level analyses with and without covariates.

In conclusion, we report that across multiple levels of analysis, adolescents with NSSI demonstrate disruptions in Self-Knowledge. While individual-level analyses showed that most Self variables were related to NSSI severity, integrative analyses shed light on how these systems operate together in predicting NSSI. The findings suggest different neural patterns which could underlie the tendency to persistently and inflexibly view oneself in a negative light. Considering these results, intervention strategies might be conceived to focus on enhancing neuroplasticity to boost efficiency of the Self Network in tandem with greater flexibility of the neural circuits underlying self-evaluations, helping adolescents with NSSI build self-esteem, view themselves more positively and begin to appreciate their true potential.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291724001399.

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Competing interests. The author(s) declare none.

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