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Research paper

Aberrant connectivity in the right amygdala and right middle temporal gyrus before and after a suicide attempt: Examining markers of suicide risk

Audreyana Jagger-Rickels [a,b,c,*], Anna Stumps [d], David Rothlein [a,c], Travis Evans [b,c], Daniel Lee [a,b], Regina McGlinchey [e,f,g], Joseph DeGutis [c,e,f], Michael Esterman [a,b,c,h]

[a] National Center for PTSD, VA Boston Healthcare System, United States of America
[b] Boston University Chobanian and Avedisian School of Medicine, Department of Psychiatry, United States of America
[c] Boston Attention and Learning Lab, VA Boston Healthcare System, United States of America
[d] Department of Psychological and Brain Sciences, University of Delaware, United States of America
[e] Translational Research Center for TBI and Stress Disorders (TRACTS), VA Boston Healthcare System, United States of America
[f] Department of Psychiatry, Harvard Medical School, United States of America
[g] Geriatric Research, Education and Clinical Center (GRECC), VA Boston Healthcare System, United States of America
[h] Neuroimaging Research for Veterans (NeRVe) Center, VA Boston Healthcare System, United States of America

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ABSTRACT

Functional neuroimaging has the potential to help identify those at risk for self-injurious thoughts and behaviors, as well as inform neurobiological mechanisms that contribute to suicide. Based on whole-brain patterns of functional connectivity, our previous work identified right amygdala and right middle temporal gyrus (MTG) connectivity patterns that differentiated Veterans with a history of a suicide attempt (SA) from a Veteran control group. In this study, we aimed to replicate and extend our previous findings by examining whether this aberrant connectivity was present prior to *and* after a SA. In a trauma-exposed Veteran sample (92 % male, mean age = 34), we characterized if the right amygdala and right MTG connectivity differed between a psychiatric control sample ($n = 56$) and an independent sample of Veterans with a *history* of SA ($n = 17$), using fMRI data before and after the SA. Right MTG and amygdala connectivity differed between Veterans with and without a history of SA (replication), while MTG connectivity also distinguished Veterans prior to engaging in a SA (extension). In a second study, neither MTG or amygdala connectivity differed between those with current suicidal ideation ($n = 27$) relative to matched psychiatric controls ($n = 27$). These results indicate a potential stable marker of suicide risk (right MTG connectivity) as well as a potential marker of acute risk of or recent SA (right amygdala connectivity) that are independent of current ideation.

1. Introduction

Assessing risk for suicide, while critical for prevention and treatment, has only modestly improved in the past 50 years (Nock et al., 2008; Franklin et al., 2017), indicating the need to identify new predictors of self-injurious thoughts and behaviors (SITBs). In response to this need, recent work has focused on identifying the neurobiological mechanisms underlying SITBs, which could serve as novel and complementary predictors of suicide risk. This growing neuroimaging literature has revealed associations between SITBs and brain regions involved in emotion regulation, inhibitory control, cognitive flexibility, and reward networks (Schmaal et al., 2020; Bryan and Rozek, 2018; Auerbach et al., 2017). One brain region that has drawn recent attention is the lateral temporal cortex, specifically the superior and middle temporal gyri, which have been structurally and functionally associated with suicide attempts (Pan et al., 2015; Chen et al., 2022; Stumps et al., 2021), suicidal ideation (Chen et al., 2022; Vidal-Ribas et al., 2021; Wiglesworth et al., 2021), lethality of attempts (Soloff et al., 2014), and have been implicated in inhibitory control and emotion processing deficits related to SITBs (Soloff et al., 2014; Crawford et al., 2020; Feng et al., 2015; Ballard et al., 2019). Despite these advances, the current literature has primarily been limited to observing brain connectivity or activation related to current or past SITBs, leaving open the question of whether these markers are present prior to SITBs, thus representing a potential risk factor (Schmaal et al., 2020; Huang et al., 2020). Further, while some consistent brain correlates of SITBs have emerged (Schmaal

* Corresponding author at: National Center for PTSD, VA Boston Healthcare System, United States of America.
E-mail address: acrickel@bu.edu (A. Jagger-Rickels).

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et al., 2020; Auerbach et al., 2021), results have varied considerably, including a prominent null finding in a large sample (Campos et al., 2021). Therefore, independent replication is critical to assessing the reliability and utility of these neurobiological markers of SITBs.

In our recent work, Stumps and colleagues (Stumps et al., 2021) examined resting-state functional connectivity in individuals with a history of suicide attempt relative to a control group with matched PTSD and depression symptoms, using a graph-analytic approach that identified "hubs of dysfunction" that differentiated these two groups. This study identified two brain regions, the right amygdala and the right middle temporal gyrus (MTG), as hubs with a greater number of connections across the brain that differed between those with versus without a history of a suicide attempt. The right amygdala's aberrant connectivity pattern in those with a suicide attempt was distributed across multiple brain networks including the frontoparietal control network (Stumps et al., 2021). Connectivity between the amygdala and the frontoparietal control network supports emotion regulation and cognitive control (Banks et al., 2007; Morawetz et al., 2017), and dysfunction of this pathway could contribute to reduced control of suicide cognitions (Schmaal et al., 2020; Jollant et al., 2011). The amygdala is also involved in stress, threat, and negative affect, such that broader changes in amygdala functional connectivity could be related to suicidal ideation (Ballard et al., 2020), as well as posttraumatic stress disorder (PTSD; Jagger-Rickels et al., 2021; Liberzon and Abelson, 2016). In contrast to the amygdala, the right MTG's aberrant connectivity pattern was primarily with regions in the default mode network (DMN) (Stumps et al., 2021). Less is known about the MTG's role in SITBs (Just et al., 2017); however, since the DMN is often implicated in rumination (Zhou et al., 2020) and mind wandering (Godwin et al., 2017), alterations in this region's connectivity could increase rumination or negative self-related thoughts. Despite these initial positive findings, given the small sample, inconsistencies in the suicide/fMRI literature, and more broad replication concerns in neuroimaging of psychopathology (Marek et al., 2022; Esterman et al., 2020; Ben-Zion et al., 2023), attempts to replicate these brain markers are critical. Even if replicable, it remained an open question if these brain markers were present prior to an attempt, reflecting a potential risk factor for SITBs, or were rather a consequence of acute stressors surrounding suicidal behavior.

To address these questions, the current study aimed to both replicate these prior correlates of past suicide attempt and extend these results to determine if these markers were present prior to a suicide attempt or related to current suicidal ideation. Using data from a longitudinal study of post-9/11 Veterans, we identified individuals reporting a suicide at a follow-up assessment but who had not reported any suicide attempts at a previous assessment (1–2 years earlier). Then, using the neuroimaging available either after a reported suicide attempt or prior to a reported suicide attempt, we investigated the following using a cross-sectional design. First, using the neuroimaging after a suicide attempt, we determined if the right amygdala and right MTG connectivity differentiated those who had attempted suicide from a psychiatrically matched control group that were identified using identical matching procedures to the previous study (Stumps et al., 2021). Then, using the neuroimaging from before a reported suicide attempt, we determined if the right amygdala and right MTG connectivity differentiated those who go on to suicide attempt in the next 1–2 years. Additionally, we identified participants who reported current SI (and no history of suicide attempt) at the corresponding neuroimaging sessions to determine if the right amygdala and right MTG connectivity differentiated those with current SI from a matched control group. Thus, we aimed to both replicate the prior results and determine if these resting-state connectivity patterns could be indicators of future risk or current ideation.

2. Methods

2.1. Participants

Participants were recruited from the longitudinal cohort study at the Translational Research Center for Traumatic Brain Injury and Stress Disorders (TRACTS) of the Veteran Affairs Boston Healthcare System (for a detailed description of recruitment, exclusion criterion, and the characteristics of the TRACTS dataset see (McGlinchey et al., 2017)). At the time of this study, the initial sample size was 598 post-9/11 deployed Veterans. After removing participants that were a part of our previous study ($n = 82$), 287 participants remained that had at least one suicide assessment (see Clinical Assessments: Suicide Attempt) and one resting-state fMRI measurement. All research procedures were approved by the Institutional Review Board of Human Studies Research at the VA Boston Healthcare System. Participants provided informed consent and were compensated for their participation.

2.2. Clinical assessments

Suicide Attempt: Suicide attempt was assessed with the Beck Scale for Suicide Ideation (BSSI; Beck and Steer, 1991), a self-report measure with high internal reliability (Cronbach's alpha = 0.95) in a Veteran sample (Gutierrez et al., 2019). Specifically, a suicide attempt was determined by question 20 on the scale from zero to two which directly inquires if the participant has attempted suicide (zero attempts, one attempt, two or more attempts). This question was then converted to a dichotomized variable used to indicate those with a SA (BSSI question $20 > 0$) or without an SA (BSSI question $20 = 0$).

Suicidal Ideation: Suicidal ideation was assessed using the BSSI. Specifically, we used the total score on the BSSI (the sum of questions 1–19) as the primary measure of suicidal ideation.

Psychiatric Assessment: Other psychiatric assessments were used to match the SA/SI and Psychiatric Control (PC) groups based on psychopathology. Major depressive disorder (MDD; current and history) as well as current anxiety and substance use disorders, were diagnosed using the Structured Clinical Interview for DSM-IV Axis I Disorders Non-patient Edition (SCID-I/NP; First et al., 2002). Self-reported depression and anxiety symptom severity were assessed using the Depression, Anxiety, and Stress Scale (DASS-21; Henry and Crawford, 2005; Lovibond and Lovibond, 1995), posttraumatic stress disorder (PTSD) diagnosis and severity were assessed using the Clinician-Administered PTSD Scale (CAPS-IV; David Blake et al., 1995). To further characterize theses samples, we also obtained demographics (age, gender identity, race and ethnicity, verbal IQ, combat exposure) and clinical comorbidities (lifetime TBIs, pain, and sleep; see Supplemental Methods).

2.3. Clinical group assignment

2.3.1. Study 1

Suicide Attempt Groups (SA+): First we identified TRACTS participants that reported a SA on the BSSI at a follow-up assessment. Since these participants had a prior study visit (i.e., 1–2 year prior), the prior suicide assessment was examined to determine if the suicide attempt was between baseline and follow-up, as indicated by no SA reported at baseline. However, the BSSI was not initially included in TRACTS' study design, but was added later due to the steep increase in the suicide rate among trauma-exposed Veterans (Black et al., 2011; United States Department of the Army, 2010; United States Department of Defense, 2018). For those with a BSSI at follow-up that reported a SA but who did not have a BSSI at a previous assessment, we used the SCID-I/NP, which was administered to all participants, to determine a potential history of SA prior to the follow-up assessment. We identified 17 participants who met the criterion of reporting a SA at follow-up without a prior history of SA 1–2 years earlier at the baseline assessment (see Fig. 1A). Next, the Pre-SA+ and Post-SA+ groups were defined based on the available

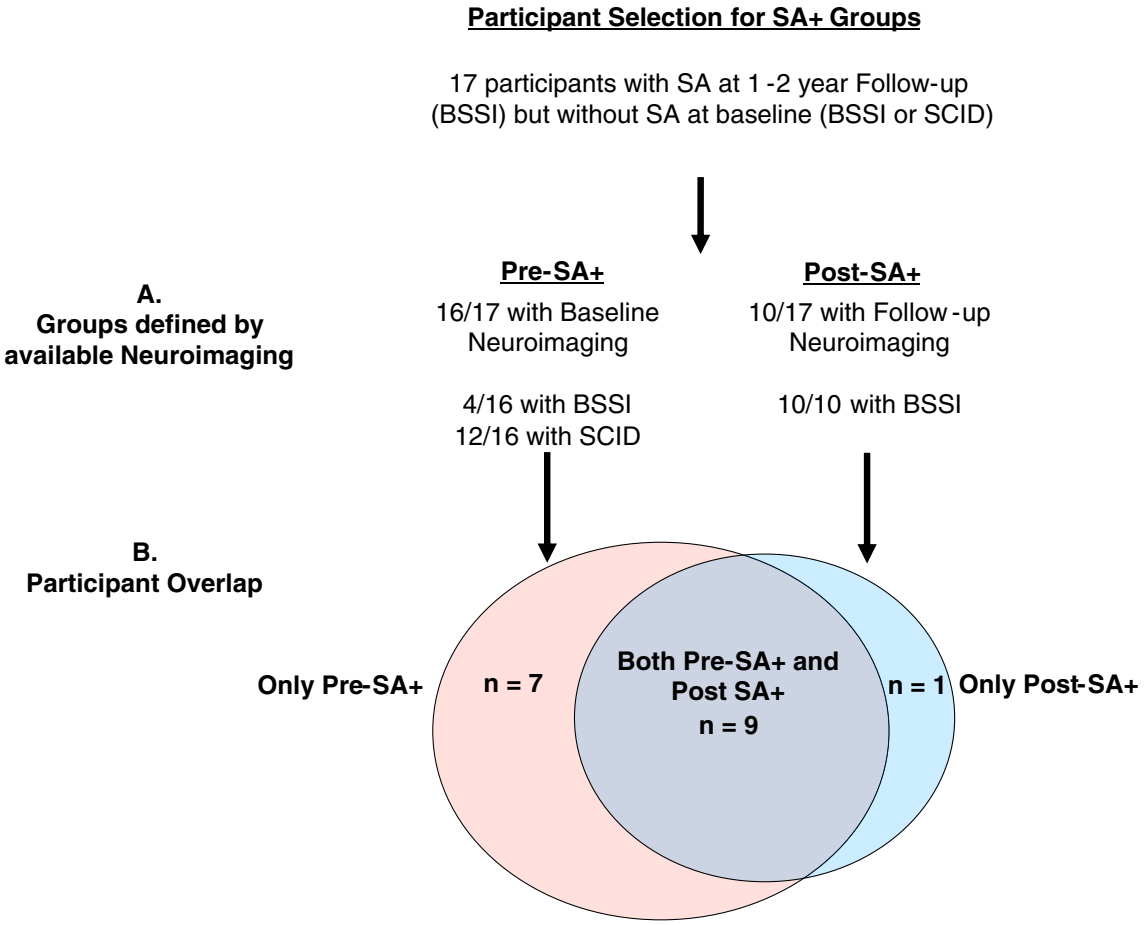


Fig. 1. Description of SA+ groups: This flow chart describes the selection of the participants in the Pre-SA+ and Post-SA+ groups. **Pre-SA+** = group with a history of suicide attempt, neuroimaging before a reported suicide attempt, **Post-SA+** = group with a history of suicide attempt, neuroimaging after a reported suicide attempt, **BSSI** = Beck Scale for Suicide Ideation, **SCID** = Structured Clinical Interview for DSM-IV.

neuroimaging before (Pre) and/or after (Post) reporting a SA (see Fig. 1A). Those with neuroimaging data available after this reported SA (at follow-up) were included in the Post-SA+ group ($n = 10$), and those with neuroimaging before a reported SA (at baseline) were included in the Pre-SA+ group ($n = 16$). Nine of the 17 participants had neuroimaging both before and after the reported SA (Fig. 1B).

Matched Control Group (SA−): We restricted the Matched Control (SA−) group selection to only those with baseline neuroimaging and no reported history of a SA on either their SCID or BSSI ($n = 270$). We used an a priori matching algorithm in R Studio ('MatchIt'; Allaire, 2012; Ho et al., 2007) identical to the algorithm used in our previous study (Stumps et al., 2021) to match the SA+ and SA− groups based on their baseline PTSD, depressive, and anxiety symptom severity (CAPS-IV and DASS-21), age, and education. To this end, we identified 56 Veterans with baseline neuroimaging and matched symptoms and demographics to our SA+ group. Of these 56 without SA, 26 participants' SA history was identified with the BSSI and 30 participants' SA history was identified using the SCID. A matched control group ensured that group differences in functional connectivity were not due to differences in observable clinical symptom severity.

2.3.2. Study 2

Of the participants that had not already been included in the SA+ or SA− groups, 143 participants had a BSSI measurement and neuroimaging at the same assessment. This allowed the identification of groups with and without suicidal ideation, all of whom did not have a reported SA.

Current Suicidal Ideation Group (SI+): Participants that scored greater than zero on their total BSSI score (without reporting SA) were included in the SI+ group ($n = 27$).

Matched Control Group (SI−): Those participants that scored a zero on their BSSI total score, were included in the Matched Control (SI−) selection process. Using the same matching algorithm described in the previous section, we identified 27 Veterans with matched clinical symptoms and demographics to the SI+ group.

2.4. Resting-state fMRI acquisition and processing

2.4.1. MRI acquisition and processing

Two T1-weighted anatomical MPRAGE scans (TR = 2530 ms, TE = 3.32 ms, flip angle: 7°, 1-mm isotropic) were acquired for inter-participant registration and normalization. Two six-minute T2* weighted fMRI scans (gradient echo-planar imaging – TR: 3000 ms, TE: 30 ms, flip angle: 90°, 3 × 3 × 3.7 mm slices for 38 slices, total of 240 volumes) were acquired during resting-state. During resting state scanning, Veterans were instructed to keep their eyes open and stay awake. Resting state data was acquired on either a 3 T Siemens MAGNETOM Trio, using a 12-channel head coil, or PrismaFit, using a 20-channel head coil (scanner upgrade; Trio: 76 % participants, Prisma: 24 % participants).

Image Processing: Resting-state fMRI images were preprocessed using AFNI (Cox, 1996) was identical to the previous suicide-fMRI study (Stumps et al., 2021). This processing pipeline included motion correction, registration to standard space, slice time correction, scan

concatenation, censoring of timepoints with a framewise displacement (>0.5 mm), 6 mm FWHM Gaussian smoothing, followed by regression of motion parameters, white matter time series, ventricle time series, global signal, and high-pass filtering via linear, quadratic and cubic detrending. We chose to include global signal regression since it removes motion and respiratory artifacts and previous work suggests that regressing out global signal improves resting-state connectivity/behavior relationships (Li et al., 2019). Control for head motion confounds in resting-state involved removing individuals with >20 % of their functional MRI scan censored during preprocessing ($n = 12$). Those with mean edge-wise functional connectivity greater than three standard deviation from the mean were removed as functional connectivity outliers, but no participants met this criteria in this sample. The timeseries from each voxel went through additional cleaning steps. First, if the mode of the timeseries value at a given voxel composed >20 % of the values within that voxel, that voxel was removed due to signal loss. Next, for each timeseries, timepoints censored in preprocessing were imputed via linear interpolation. Finally, in order to reduce the influence of extreme values when computing functional connectivity, outliers in each timeseries that were greater than or less than four standard deviations from the mean were reassigned the threshold value at four standard deviations (i.e. clipping; McNorgan and Joanisse, 2014).

Brain Parcellation: The brain was parcellated using a 7-network atlas from Schaefer and colleagues (Schaefer et al., 2018) that parses the cortex into 200 nodes (regions) embedded within 7 large-scale cortical networks identified by Yeo et al (Thomas Yeo et al., 2011). In addition, we extracted the timeseries of the bilateral amygdala and hippocampus from a subcortical atlas developed by Tullo and colleagues (Tullo et al., 2018), as these regions are commonly implicated in neuropsychiatric disorders, including STBs (Jollant et al., 2011; Lippard et al., 2014; Schmaal et al., 2020). The final parcellation included 204 parcels/ROIs. The average timeseries were extracted from each node (averaged across the set of voxels within the node) and correlated (Pearson) across nodes for a total of 20,706 pairwise correlations or connectivity features.

2.5. Analysis plan

Overview. The goal of the current study was to examine if functional connectivity hubs (the right amygdala and right MTG) previously associated with a history of suicide attempt 1) replicated in an independent sample 2) were present 1–2 years before a suicide attempt 3) were associated with current suicidal ideation. This required several steps to test each of these three aims. The first step was to select all of the connections found to be associated with SA in the previous study (34 with right amygdala and 25 with the right MTG). We reasoned that some, but not all of these connections would replicate in these new samples and analyses. Thus, we examined if all, or a subset of these connections differentiated our clinical groups (i.e., Post-SA+, Pre-SA+, SI+) from matched control groups (SA−, SI−). This was done by considering a range of hub thresholds, from all the connections in the hub to only the most significant connection for the hub, based on our previous study (independent data). For the second step, we computed hub scores across this range of thresholds (from all connections to the single most significantly reliable connection) in our current sample (thresholds based on independent data). Lastly, after comparing these hub scores between groups (e.g., Pre-SA+ vs SA−) at all thresholds, a rigorous multiple comparisons correction was conducted to account for considering whether 1:n (differentially thresholded) hub scores differentiated the groups. Details of each step follow.

2.5.1. Step 1: a priori definition of hub scores

Step 1a. Selection of functional connections: The connectivity examined in this study were defined from the results of our previous study, which used the same imaging acquisition, pre-preprocessing, and parcellation in an independent sample (Stumps et al., 2021). Stumps and colleagues (Stumps et al., 2021) identified two "hub" regions, the right amygdala and right medial temporal gyrus (MTG), that exhibited significantly more connections across the parcellation that differed between Veterans with a prior SA compared to trauma-exposed control Veterans. In this previous study, the right amygdala exhibited 34 significant connections that differentiated between groups (Fig. 2A), while the right MTG exhibited 25 significant connections that differentiated between groups (Fig. 2B).

Step 1b. Reversing Negative Associations: Next, we had to consider whether the connection was positively or negatively associated with a suicide attempt in the original independent data. To compute an average hub score, any connection that demonstrated a negative association (e.g., lower connectivity associated with a prior SA) was reversed by simply multiplying by −1. This ensured that the mean of all connections reflected a positive "suicide-related" score that could be evaluated in the current study's independent data. Critically, the connections were reversed based solely on the original, independent dataset, and then applied to the current dataset in Step 2.

Step 1c. Hub score computation: It is plausible that some of those observed hub connections from our previous study were spurious. Therefore, we considered a range of possible hub score thresholds, ranging from the original total hub score (the mean of all 34 or 25 connections, depending on the hub) to only the most statistically reliable connection (strongest connection of each hub). This led to 34 hub scores for the right amygdala, and 25 hubs scores for the right MTG. A visualization of this procedure is provided in Fig. 2C.

2.5.2. Step 2. Comparing hub scores across clinical groups

Once hub scores were calculated for both the right amygdala and right MTG, we conducted non-parametric tests (Wilcoxon Rank Sum) comparing each hub scores across all three analyses (Post-SA+ vs. SA−, Pre-SA+ vs. SA−, and SI+ vs SI−). This resulted in 34 statistical tests for the amygdala hub and 25 for the MTG hub for each group comparison.

2.5.3. Step 3. Multiple comparison correction

To correct for multiple comparisons inherent to calculating 34 or 25 statistical tests for each hub respectively, we used the following procedure. First, we randomized group membership (e.g., of the Pre-SA+ group and SA− group), then calculated the statistical difference (p-value) between these randomized groups for all hub score thresholds. This was repeated 10,000 times, generating a distribution of p-values that we used to calculate an empirical alpha that corrects for multiple comparisons. Specifically, we identified the minimum p-value across all hub scores (i.e., either the minimum of 25 or 34 scores) across each of the 10,000 random iterations. Of these 10,000 minimum p-values, we identified the minimum p-value cutoff that encompassed the lowest 5 % of random iterations. This 5 % alpha-value served as the alpha corrected for multiple comparisons (i.e., corrected p-value of 0.05) for the p-values observed across all thresholds of hub scores. This randomization and calculation of a corrected p-value procedure were repeated for each of the six analyses: amygdala hub for Post-SA+ versus SA−, amygdala hub for Pre-SA+ versus SA−, amygdala hub for SI+ versus SI−, MTG hub for Post-SA+ versus SA−, and MTG hub for Pre-SA+ versus SA−, and MTG hub for SI+ versus SI−.

3. Results

3.1. Demographics

SA+ groups did not significantly differ from SA−, nor did SI+ from SI−, on psychiatric and demographic variables. See Table 1 for more details. This demonstrates the success of the matching process.

3.2. SA-related hubs of dysfunction (HoD)

Post-SA+ HoD: We found evidence for both the right amygdala and

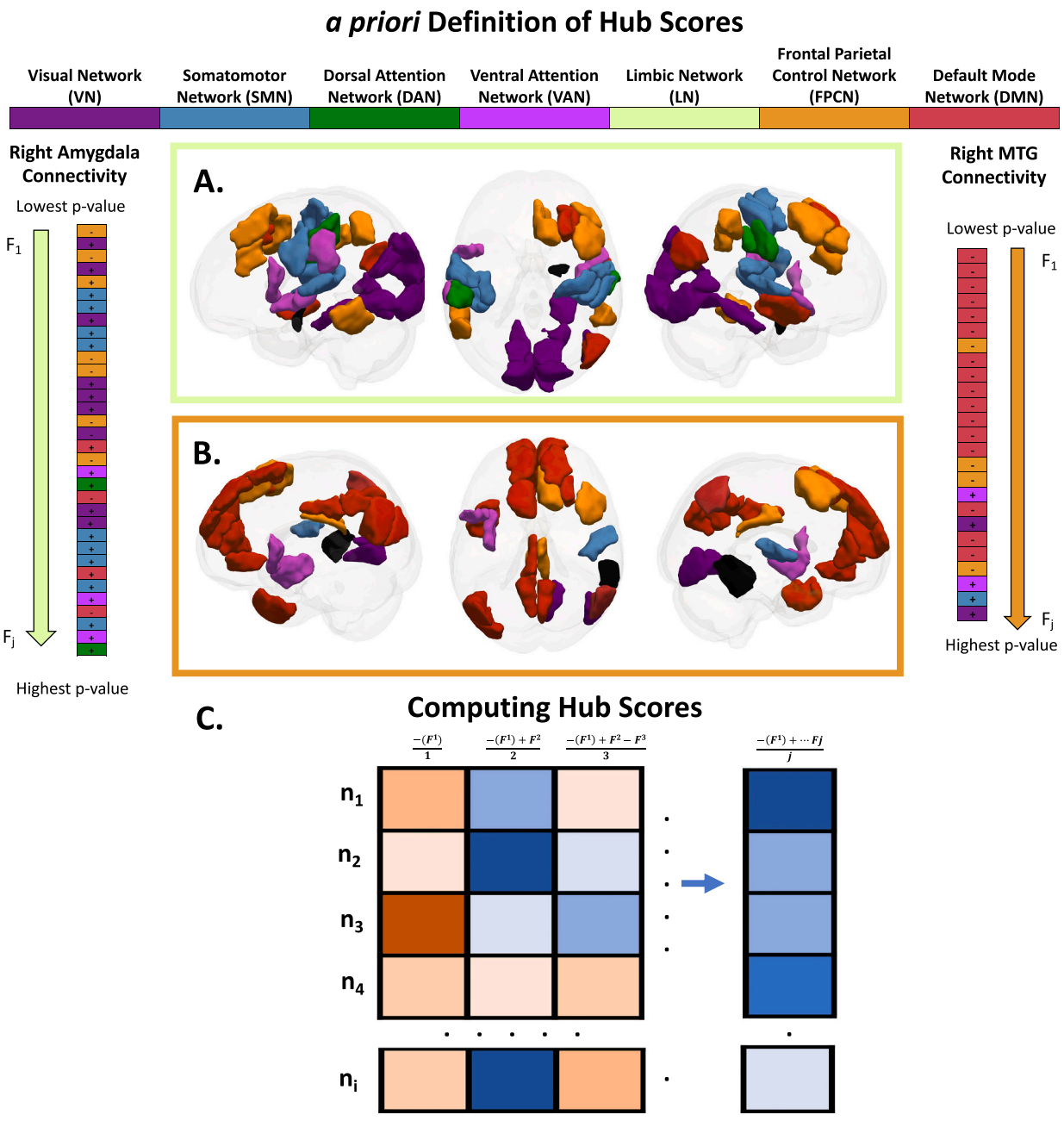


Fig. 2. Description of a priori definition of hub scores based on independent data: *Step 1a.* The functional connections were selected from an *independent dataset* (Stumps et al., 2021) based on the connectivity with the **A.** right amygdala or **B.** right middle temporal gyrus (MTG) that significantly differentiated participants with a history of suicide attempt from controls. Both the right amygdala and right MTG seeds are displayed in black. These functional connections (denoted as *F*) are derived from a 200-region parcellation across 7 large-scale networks, color-coded (Schaefer et al., 2018). *Step 1b.* The connections of each hub (34 for the amygdala or 25 for the MTG) were sorted from lowest *p* value (i.e., largest t-value) to highest *p*-value (i.e., smallest t-value). We ensured that the hub values reflected a positive "suicide-related" score that could be evaluated in the current study's data by multiplying negative associations by −1. **C.** *Step 1c.* Hub scores, or the mean of the selected hub connections, were computed with the current *independent* dataset. Hub scores were computed at various thresholds, ranging from the average connectivity of all regions (34 for the amygdala or 25 for the MTG) to only the most statistically robust single connection in each hub (based on the previous independent dataset). The colors (orange to blue) are for descriptive purposes to indicate the theoretical value (sign and strength) of the association between each functional connection and SA. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

right MTG hub scores as differing between the Post-SA+ group and SA− group, consistent with our previous study (Fig. 3). For the right amygdala hub, 31 out of the 34 hub scores passed the uncorrected threshold ($p < 0.05$), with nine surviving correction for multiple comparisons (corrected threshold $p < 0.0098$). The functional connections within these hub scores were spread across visual, somatomotor, and frontoparietal control networks (Figs. 2 and 4). These nine hub scores surviving correction for multiple comparisons include a range of hub score from as many as 23/34 functional connections to as few as 5/34 connections. For the right MTG hub, six out of the 25 of the hub scores passed the uncorrected threshold ($p < 0.05$), with two surviving corrections for multiple comparisons (corrected threshold $p < 0.0178$). MTG connections within these hub score thresholds were exclusively within the DMN (Figs. 2 and 5). Note that in Figs. 4 and 5, we display both the full hub scores and brain regions, as well as the hub scores/regions with the maximum number of connections that survived

Table 1
Demographic and clinical group differences.

	SA− ($n = 56$)	Post-SA+ ($n = 10$)	p-value[f]	Pre-SA+ ($n = 16$)	p-value[f]	SI− ($n = 27$)	SI+ ($n = 27$)	p-value[f]
	Mean (SD); %	Mean (SD); %		Mean (SD); %		Mean (SD); %	Mean (SD); %	
Age	30.39 (7.19)	32.00 (4.78)	0.08	30.44 (6.07)	0.80	33.07 (8.62)	35.22 (8.44)	0.40
Gender (% male)	91.07 %	80.00 %	0.30	81.25 %	0.40	100.00 %	88.89 %	0.20
Education[a]	13.57 (1.58)	13.90 (1.73)	0.50	13.81 (1.38)	0.40	13.48 (1.50)	13.74 (1.81)	0.50
Race/Ethnicity[b]								
American Indian	0.00 %	0.00 %	–	6.25 %	0.22	3.70 %	0.00 %	>0.90
Asian	0.00 %	0.00 %	–	12.50 %	0.05	3.70 %	3.70 %	1.00
Black	5.36 %	0.00 %	>0.90	6.25 %	>0.90	3.70 %	11.11 %	0.61
Pacific Island	0.00 %	0.00 %	–	0.00 %	–	0.00 %	0.00 %	–
White	75.00 %	90.00 %	0.43	62.50 %	0.35	70.37 %	74.07 %	>0.90
Other	0.00 %	0.00 %	–	0.00 %	–	3.70 %	0.00 %	>0.90
Hispanic	17.86 %	10.00 %	>0.90	12.50 %	>0.90	14.81 %	14.81 %	1.00
PTSD[c]	63.82 (20.83)	61.30 (28.25)	>0.90	66.62 (30.43)	0.30	62.81 (24.84)	71.74 (31.82)	0.20
Anxiety[d]	9.93 (9.16)	11.40 (9.80)	0.60	12.00 (10.11)	0.50	12.00 (7.17)	12.74 (8.58)	0.70
Depression[d]	12.52 (10.10)	14.00 (9.98)	0.60	14.29 (12.96)	0.80	12.44 (9.02)	16.44 (12.07)	0.30
Suicidal Ideation[e]	1.81 (3.25)	2.30 (4.81)	0.70	6.75 (9.07)	0.13	0.00 (0.00)	6.04 (6.58)	0.001

Demographic and clinical sample characteristics. The statistical tests performed to detect significant group differences were Wilcoxon rank-sum tests. [a]Education was measured as the number of years of education, [b]Participants could identify with multiple or none of the Race and Ethnicity categories, [c]PTSD was measured as the total score on the Clinician-Administered PTSD Scale (CAPS IV), [d]Anxiety and Depression were total scores from the Depression, Anxiety, and Stress Scale (DASS-21). [e]Suicidal ideation was measured as the total score on the Beck Scale for Suicide Ideation (BSSI). The BSSI was available only in 26 of the SA− group, in 10 of the Post-SA+ group, and in four of the Pre-SA+ group. All participants in the SI− and SI+ groups had a BSSI. [f] these p-values report the group differences between either the Pre-SA+ and the SA− group or Post-SA+ and the SA− group. **SA−** = group without a history of suicide attempt but matched demographics to the Pre-SA+ and Post-SA+ groups, **Post-SA+** = group with a history of suicide attempt, neuroimaging after a reported suicide attempt, **Pre-SA+** = group with a history of suicide attempt, neuroimaging before a reported suicide attempt, **SI−** = group without current suicidal ideation or history suicide attempt, but matched demographics and psychiatric severity to the SI+ group, **SI+** = group with current ideation, and no history of suicide attempt.

multiple comparison correction. Thus, the amygdala results were broadly consistent with the prior hub connections differentiating a suicide attempt history across a range of connections. In contrast, the most statistically reliable MTG connections with the DMN from the original study continued to differentiate those with a history of suicide attempt (Fig. 5B), but this was not broadly consistent across all hub score thresholds (Fig. 5A).

Pre-SA+ HoD: We repeated these analyses to examine if the Pre-SA+ group, for which neuroimaging took place prior to the suicide attempt, exhibited differences in these hub connections compared to those who did not go on to attempt suicide (Figs. 3 and 5). None of the right amygdala hub scores differentiated between Pre-SA+ from SA− groups (all $ps > 0.05$). For the right MTG hub, seven out of the 25 hub scores differentiated between Pre-SA+ and SA− groups ($p < 0.05$), with five scores surviving correction for multiple comparisons (corrected threshold $p < 0.0153$). Similar to the Post-SA+ analyses, the most statistically reliable MTG connections with the DMN from the original study continued to differentiate those with a history of suicide attempt (Fig. 5C), but this was not broadly consistent across all hub score thresholds (Fig. 5A).

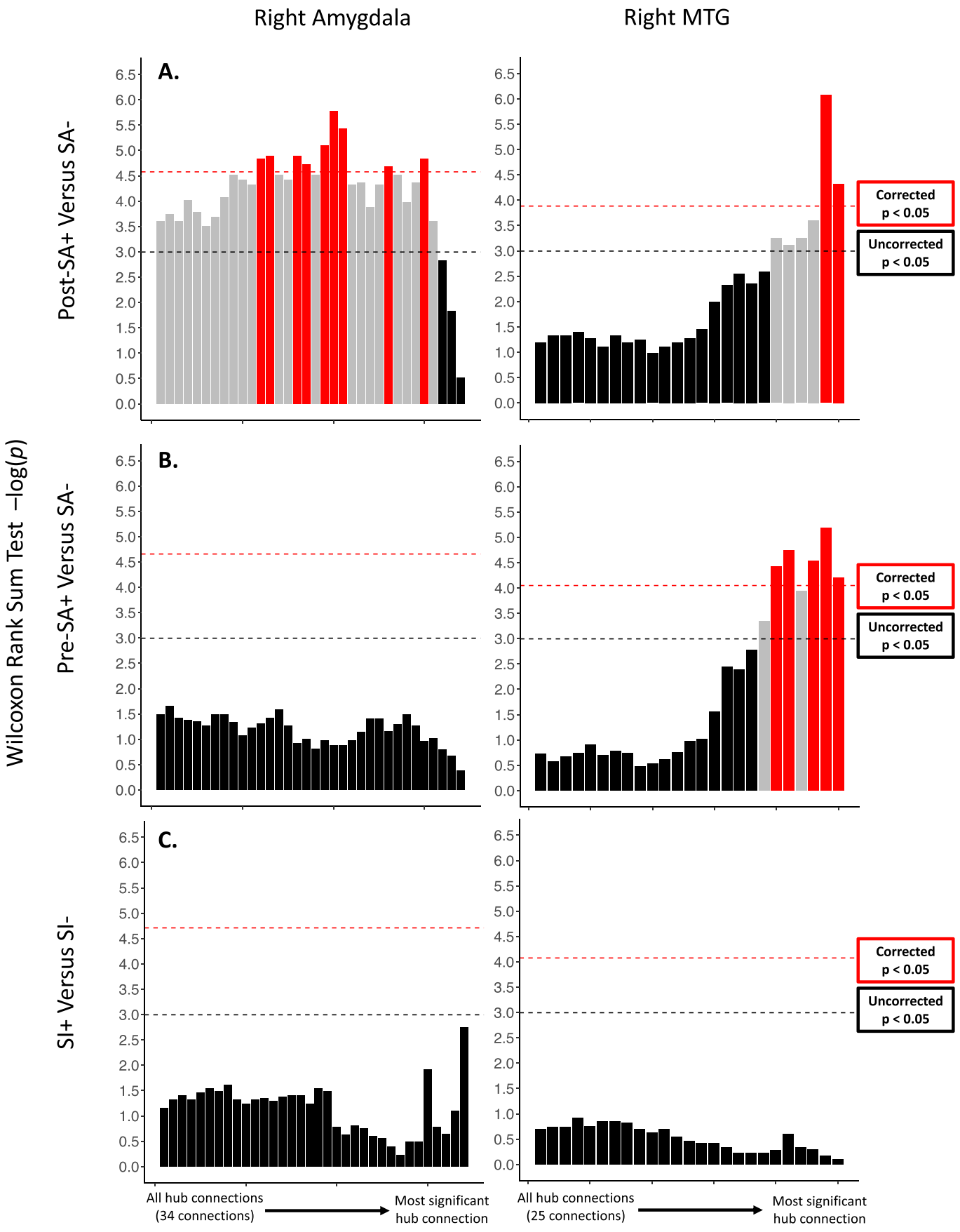
Addressing SI in the SA+ Hub Scores: One potential confound of these analyses is that the SA−related hubs results may be driven, in part, by elevated SI. We were only able to examine this possibility in the Post-SA+ analysis because a majority of the Pre-SA+ group's data were collected before the longitudinal protocol added the BSSI to assess suicidal ideation. This resulted in only four participants in the Pre-SA+ group with neuroimaging and a measurement of SI (see Fig. 1). Due to this limitation of the study protocol, we restricted our analysis of SI to the Post-SA+ sample. In the Post-SA+ vs. SA− analyses, we addressed the impact of SI in two ways. First, we determined if the groups differed in SI severity using a Welch's two sample t-test. SI severity (Total BSSI) between the Post-SA+ group (mean = 2.3, SD = 4.81, $n = 10$) and the SA− group (mean = 1.81, SD = 3.25, $n = 26$) did not statistically differ ($t(12.30) = 0.299$, $p = 0.770$). Second, we controlled for SI in our hubs analyses to determine if group differences in connectivity were independent of SI. To control for SI, we used a regression predicting each hub score (dependent measure) with SA (SA+ versus SA−) and SI (BSSI total score) as predictors. This analysis indicated an identical pattern of results, such that SA status was a significant predictor of hub scores at the same thresholds across both regions of interest (Fig. 3A). SI, on the other hand, was not a predictor of any hub scores (p values >0.05, uncorrected). This indicates that the Post-SA+ hub results are specific to SA and independent of SI.

Current SI HoD: We repeated the HoD analyses comparing the hub scores based on the presence of absence of current SI (in those without a suicide attempt). None of the right amygdala or right MTG hub score thresholds differed between the SI+ and SI− group (all $ps > 0.05$; see Fig. 3). This suggests that neither the right amygdala nor right MTG are sensitive to current SI in the absence of a SA.

Summary of Results: Overall, these results indicate that a subset of the right MTG hub connections with the DMN were present both before *and* after a suicide attempt. These connections ranged from the top two strongest MTG connections in Post-SA+ analysis to the top six connections in the Pre-SA+ analysis, and all of these connections are within the DMN (see Fig. 5B and C). In contrast, right amygdala connectivity differed between the Post-SA+ and SA− groups, but not in the Pre-SA+ analysis, and these connections ranged from the top 23 connections down to the top five connections, and contained connections to several different networks (see Fig. 4). Further, the Post-SA+ hubs were independent of SI, and the presence of current SI was unrelated to the connectivity of both amygdala and MTG hubs.

4. Discussion

Our previous study found that the right amygdala and middle temporal gyrus (MTG) were hubs of dysfunction with numerous resting-state connections associated with a history of suicide attempt (Stumps et al., 2021). In the current study, we aimed to replicate and extend this work by investigating these hubs in a new sample of Veterans with a history of suicide attempts, using neuroimaging after the SA (Post-SA+) as well as before the SA (Pre-SA+), in comparison to a matched psychiatric control group (SA−). Using the same functional connections from our previous study, we demonstrated that the right amygdala connectivity differed only between the Post-SA+ and SA− groups across a broader range of connections with the visual, somatomotor, and frontoparietal control network (Figs. 3 and 4). This suggests that right



(caption on next page)

Fig. 3. Suicide-related hubs of dysfunction. Note on y-axis, *p*-values were −log transformed for visualization purposes. Therefore, higher −log(p) values indicate lower p-values. Gray bars indicate the hub scores that passed the uncorrected threshold with a gray dotted line denoting the uncorrected *p*-value of $p < 0.05$. Red bars indicated the hub scores that passed multiple comparisons and the red dashed line denotes the corrected *p*-value threshold (corrected $p < 0.05$). **A. Post-SA+ vs SA−:** Replication analysis examining participants with a history of suicide attempt vs. a matched control group. **B. Pre-SA+ vs. SA−:** Analysis examining participants with a future suicide attempt vs. a matched control group. **C. SI+ vs. SI−:** Analysis examining participants with current suicidal ideation vs. a matched control group without SI. The maximum number of connections for each hub score is 34 for the right amygdala and 25 for the right MTG. **SA−** = group without a history of suicide attempt but matched demographics to the Pre-SA+ and Post-SA+ groups, **Post-SA+** = group with a history of suicide attempt, neuroimaging after the reported suicide attempt, **Pre-SA+** = group with a future suicide attempt, neuroimaging before the reported suicide attempt, **SI−** = group without current suicidal ideation or history suicide attempt, with matched demographics and clinical symptom severity to the SI+ group, **SI+** = group with current suicidal ideation, and no history of suicide attempt. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

amygdala connectivity across the brain is indicative of a recent suicide attempt, but does not necessarily predict those who will attempt suicide in the next year or two. On the other hand, a subset of the right MTG connections to the prefrontal default mode network (DMN) differed between SA− from both the Pre-SA+ and Post-SA+ groups (Figs. 3 and 5) indicating this marker was present both before and 1–2 years after a SA. When we compared the same hubs in a sample with suicidal ideation but no SA (SI+) to a matched psychiatric control group (SI−), none of the connections from either hub significantly differed. This suggests that the right MTG and right amygdala connectivity is specific to suicidal behaviors rather than suicidal thoughts alone. Together, this study provides evidence that right MTG resting-state connectivity with the DMN could be a baseline, stable risk factor of SA, whereas a right amygdala connectivity pattern could reflect a more acute indicator of SA risk or history.

Our results potentially indicate both temporally stable and dynamic brain markers of suicide risk in resting-state connectivity, which corresponds to a conceptual model of temporal dynamics in suicide risk called the fluid vulnerability theory (FVT) (Rudd and Bryan, 2021; Rudd, 2006; Bryan et al., 2022). The FVT describes two distinct features of suicide risk: baseline and acute. Baseline risk includes temporally stable characteristics that increase vulnerability to experience acute risk (Rudd & Bryan, 2021). Examples of baseline risk include behavioral history (i.e., attempt history), life experiences (i.e., previous trauma), and cognitions like pervasive identify-based negative core beliefs about self (i.e., a suicidal belief system; Rudd & Bryan, 2021). On the other hand, acute suicide risk is time-limited, dynamic, and driven by situational and contextual characteristics like a life stressor (Rudd and Bryan, 2021; Rudd, 2006; Bryan et al., 2022) or the nature of suicidal thinking (Rudd & Bryan, 2021). Integrating FVT with the current results suggest that the right MTG connectivity may indicate baseline risk of suicide whereas the right amygdala connectivity may indicate more acute risk for suicide.

The amygdala has a well-documented involvement in stress and mood disorders (Roozendaal et al., 2009), but the amygdala has been less consistently implicated in SITBs (Schmaal et al., 2020; Wagner et al., 2012). We found that right amygdala connectivity was sensitive to a recent history of a suicide attempt but not to a future suicide attempt. One interpretation of these results is that the acute stressors or trauma that surround a SA (i.e., acute suicide risk) impact amygdala connectivity. However, if amygdala connectivity is related to acute risk, we might expect SI (another measure of acute suicide risk; Rudd & Bryan, 2021) to also be related to amygdala connectivity. Although current ideation was not associated with amygdala connectivity in this study, the link between SA history (a baseline risk factor) and SI (an acute risk factor) is often weak (Nock et al., 2008; Franklin et al., 2017; Li et al., 2019), and SA and SI often have divergent neural correlates (Schmaal et al., 2020). Thus it is plausible that amygdala connectivity and SI contribute independently to suicide risk, or that we were not powered to detect these modest relationships. Overall, the literature and the current results suggests that acute and baseline suicide risk are weakly related both behaviorally and neurobiologically. An alternative explanation is that the observed amygdala connectivity pattern is altered by the experience of a SA, which could itself be traumatic (Stanley et al., 2019). Any such changes in amygdala connectivity caused by a suicide attempt could increase baseline risk for suicide, and therefore this amygdala marker could become a predictor of multiple suicide attempts, although this would require future studies that track suicide risk in a sample with SA.

Previous work has implicated the MTG with baseline suicide risk. For example, there have been multiple studies that have linked the MTG to suicide-related behavioral history (e.g., prior history of SA; Chen et al., 2022; Pan et al., 2015; Stumps et al., 2021; Vidal-Ribas et al., 2021) and suicide cognitions (e.g., implicit associations between self and death; Ballard et al., 2019, 2020). The MTG may also contribute to negative core beliefs about self and a suicidal belief system since it is also involved in self-referential thoughts, including making self versus other judgements (Frewen et al., 2020; Fuentes-Claramonte et al., 2019; Benoit et al., 2010; Kim, 2012; Morel et al., 2014). The previous literature has also implicated the prefrontal DMN in suicidal thoughts and behaviors (Just et al., 2017; Reisch et al., 2010; Jollant et al., 2010) and self-referential thoughts (Andrews-Hanna et al., 2014; Wagner et al., 2012; Dixon et al., 2017; Murray et al., 2012). Importantly, in this study, it was the right MTG's connectivity with the prefrontal DMN that differentiated individuals both after and 1–2 year before a reported SA. Since both the MTG and prefrontal DMN are implicated in both suicidal thoughts and behaviors, as well as self-referential thoughts, it is possible that the connectivity between these regions may partially contribute to a heightened suicidal belief system and consequently higher baseline suicide risk.

While strengths of this study include partially replicating our previous work and using longitudinal data in an at-risk population, there are several limitations. Our analyses were dependent upon self-disclosure of SA, limiting our group assignments to only those willing to report a SA. Also, we had no means to verify a SA via medical records, determine the time since a SA (could range from days to 1–2 years), or include analysis on the lethality, means, or circumstances of the attempt. Further, our relatively small sample size was conducted in a primarily white male veteran sample, therefore our results may not be generalizable, or be representative of, other gender identities, races, ethnicities, or civilian backgrounds. Another limitation of our study is that we were not able to assess the impact of SI on connectivity markers of future suicide attempts because the study protocol had not yet included an SI measurement. Although we did not find connectivity differences related to SI in a group without suicide attempt, it remains possible that ideation preceding attempt could contribute to these brain signatures. Importantly, not all brain connections from our previous study replicated, and thus this work points the field toward the most replicable brain connections associated with suicide.

Based on our results and current limitations, future work on brain markers of suicide risk should focus on generalizing the results to other populations (e.g., more diverse, non-Veteran, developmental, or high-risk, hospitalized patients). Further, replicating resting-state results in small sample sizes is challenging (Marek et al., 2022), and even large sample sizes may not be sufficient to identify reliable effects related to suicide (Thompson et al., 2022). Therefore, applying alternative analytical techniques, like those used in this study, may be more sensitive to group differences in resting-state brain networks related to suicide risk. Our results related to SA did not extend to other suicidal thoughts and behaviors (i.e. suicidal ideation), and thus additional investigation into the brain markers related to ideation will help us

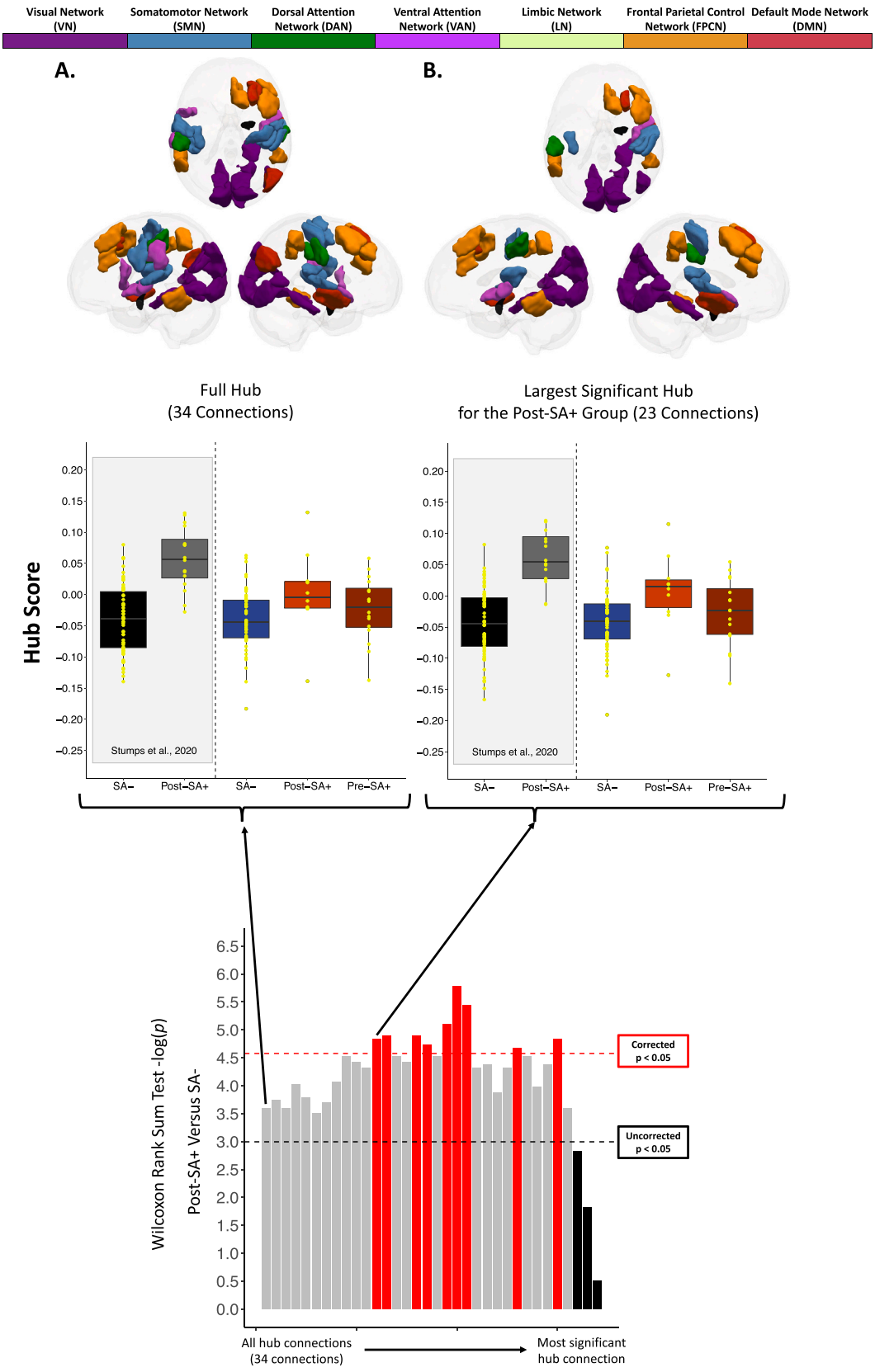


Fig. 4. Right amygdala hubs of dysfunction results. Hub scores from previous independent study (Stumps et al., 2020; Post-SA+ vs SA−) displayed next to the data from the current study (SA−, Post-SA+, Pre-SA+). **A.** Results for all hub connections (34), which are distributed throughout the whole brain. **B.** Results for Post-SA+ vs. SA− comparison at the hub threshold with the maximum number of connections (23) that survived multiple comparisons correction. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

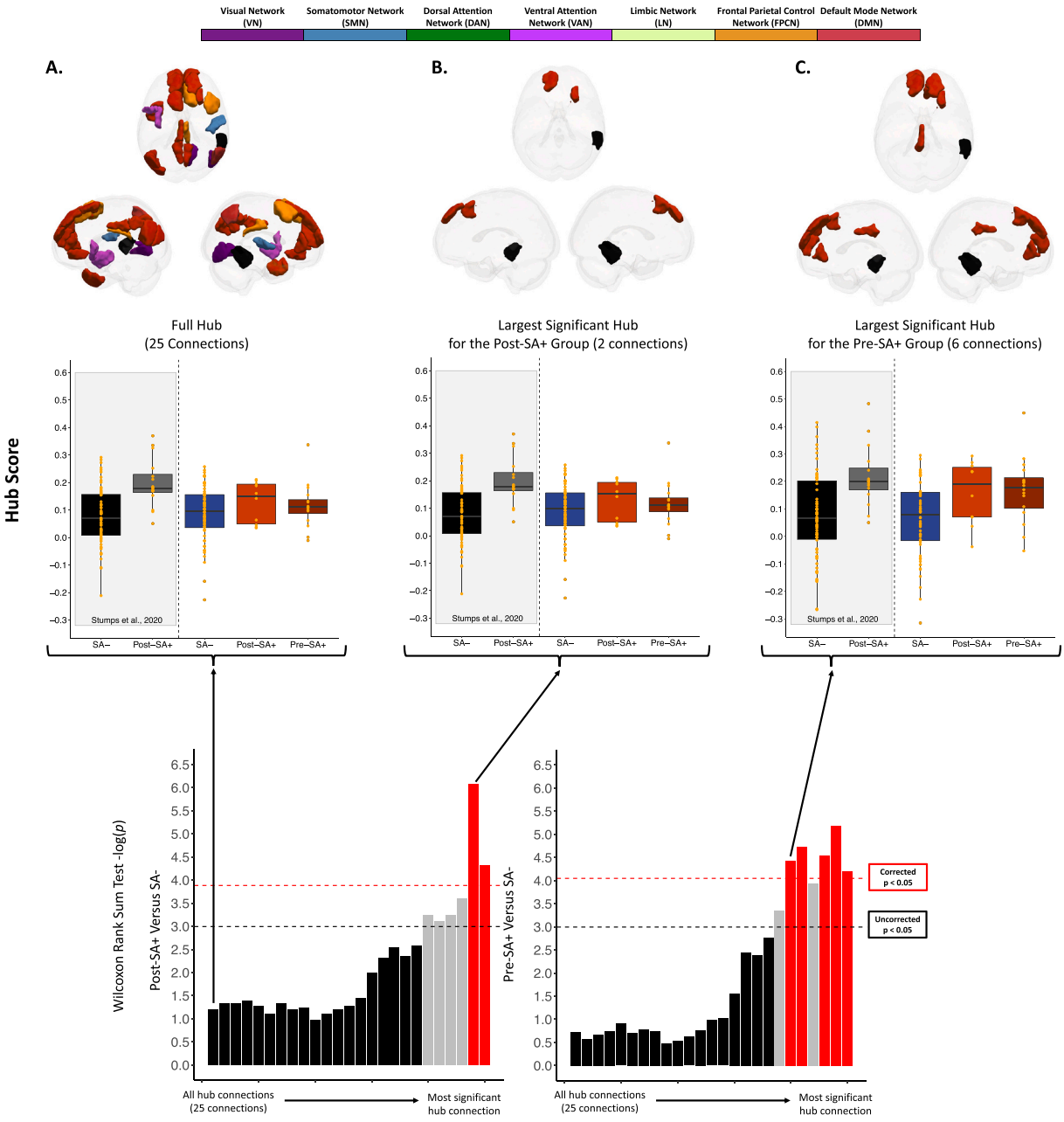


Fig. 5. Right middle temporal gyrus hubs of dysfunction results. Hub scores from previous independent study (Stumps et al., 2020; Post-SA+ vs SA−) displayed next to the data from the current study (SA−, Post-SA+, Pre-SA+). **A.** Results for all hub connections (25), which are primarily with the default mode network and the frontoparietal control network. **B.** Results for Post-SA+ vs. SA− comparison at the hub threshold with the maximum number of connections (2) that survived multiple comparisons correction. Both connections were to default mode network. **C.)** Results for Pre-SA+ vs. SA− comparison at the hub threshold with the maximum number of connections (6) that survived multiple comparisons correction. All 6 connections were to default mode network. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

further uncover neurobiological markers of suicide risk. Additionally, investigating the role of the right amygdala and right MTG in cognitions and behaviors related to suicide vulnerability (i.e. core beliefs about oneself; Brown et al., 2000) may help us develop treatments for those at heightened risk for suicide or identify those at greatest risk for suicide without self-disclosure.

Overall, this study is one of the first to identify replicable resting-state brain connectivity markers present both before and after a suicide attempt, laying important groundwork for understanding the temporal brain dynamics related to suicide risk.

CRediT authorship contribution statement

AJR: Conceptualization, Formal analysis, Visualization, Writing—Original draft, reviewing and editing subsequent drafts, Funding Acquisition; AS: Methodology, Writing-Reviewing and Editing; DR: Software, Writing-Reviewing and Editing; TCE: Writing-Reviewing and Editing; DL: Writing—Reviewing and Editing; RM: Funding Acquisition, Resources; JD: Methodology, Supervision, Writing—Reviewing and Editing; ME: Conceptualization, Methodology, Supervision, Writing—Reviewing and Editing, Funding Acquisition, Resources.

Conflict of interest

All authors have no conflicts of interest.

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References

Allaire, J., 2012. In: RStudio: Integrated Development Environment for R, 770(394), pp. 165–171. Boston, MA.

Andrews-Hanna, J.R., Smallwood, J., Spreng, R.N., 2014. The default network and self-generated thought: component processes, dynamic control, and clinical relevance. Ann. N. Y. Acad. Sci. 1316 (1), 29–52. https://doi.org/10.1111/nyas.12360.

Auerbach, R.P., Stewart, J.G., Johnson, S.L., 2017. Impulsivity and suicidality in adolescent inpatients. J. Abnorm. Child Psychol. 45 (1), 91–103. https://doi.org/10.1007/s10802-016-0146-8.

Auerbach, R.P., Chase, H.W., Brent, D.A., 2021. The elusive phenotype of preadolescent suicidal thoughts and behaviors: can neuroimaging deliver on its promise? Am. J. Psychiatr. 178 (4), 285–287. https://doi.org/10.1176/appi.ajp.2020.21010022.

Ballard, E.D., Reed, J.L., Szczepanik, J., et al., 2019. Functional imaging of the implicit association of the self with life and death. Suicide Life Threat Behav. 49 (6), 1600–1608. https://doi.org/10.1111/sltb.12543.

Ballard, E.D., Gilbert, J.R., Fields, J.S., Nugent, A.C., Zarate, C.A., 2020. Network changes in insula and amygdala connectivity accompany implicit suicidal associations. Front.Psychiatry 11. https://doi.org/10.3389/fpsyt.2020.577628.

Banks, S.J., Eddy, K.T., Angstadt, M., Nathan, P.J., Luan, Phan K., 2007. Amygdala-frontal connectivity during emotion regulation. Soc. Cogn. Affect. Neurosci. 2 (4), 303–312. https://doi.org/10.1093/scan/nsm029.

Beck, A.T., Steer, R.A., 1991. In: Manual for the Beck Scale for Suicide Ideation. Psychological Corporation, San Antonio, TX, p. 63.

Benoit, R.G., Gilbert, S.J., Volle, E., Burgess, P.W., 2010. When I think about me and simulate you: medial rostral prefrontal cortex and self-referential processes. NeuroImage 50 (3), 1340–1349. https://doi.org/10.1016/j.neuroimage.2009.12.091.

Ben-Zion, Z., Spiller, T.R., Keynan, J.N., et al., 2023. Evaluating the evidence for brain-based biotypes of psychiatric vulnerability in the acute aftermath of trauma. Am. J. Psychiatry, appi.ajp.20220271. https://doi.org/10.1176/appi.ajp.20220271. Published online January 11.

Black, S.A., Gallaway, M.S., Bell, M.R., Ritchie, E.C., 2011. Prevalence and risk factors associated with suicides of army soldiers 2001–2009. Mil. Psychol. 23 (4), 433–451. https://doi.org/10.1037/h0094766.

Brown, G.K., Beck, A.T., Steer, R.A., Grisham, J.R., 2000. Risk factors for suicide in psychiatric outpatients: a 20-year prospective study. J. Consult. Clin. Psychol. 68 (3), 371–377. https://doi.org/10.1037/0022-006X.68.3.371.

Bryan, C.J., Rozek, D.C., 2018. Suicide prevention in the military: a mechanistic perspective. Curr. Opin. Psychol. 22, 27–32. https://doi.org/10.1016/j.copsyc.2017.07.022.

Bryan, C.J., Thomsen, C.J., Bryan, A.B.O., Baker, J.C., May, A.M., Allen, M.H., 2022. Scores on the suicide cognitions scale-revised (SCS-R) predict future suicide attempts among primary care patients denying suicide ideation and prior attempts. J. Affect. Disord. 313 (March), 21–26. https://doi.org/10.1016/j.jad.2022.06.070.

Campos, A.I., Thompson, P.M., Veltman, D.J., et al., 2021. Brain correlates of suicide attempt in 18,925 participants across 18 international cohorts. Biol. Psychiatry 90 (4), 243–252. https://doi.org/10.1016/j.biopsych.2021.03.015.

Chen, C.feng, Chen, W.ni, Zhang, B., 2022. Functional alterations of the suicidal brain: a coordinate-based meta-analysis of functional imaging studies. Brain Imaging Behav. 16 (1), 291–304. https://doi.org/10.1007/s11682-021-00503-x. Boston, MA.

Cox, R., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput. Biomed. Res. 29 (3), 162–173. https://doi.org/10.1006/cbmr.1996.0014.

Crawford, B., Muhlert, N., MacDonald, G., Lawrence, A.D., 2020. Brain structure correlates of expected social threat and reward. Sci. Rep. 10 (1) https://doi.org/10.1038/s41598-020-74334-z.

David Blake, D., Weathers, F.W., Nagy, L.M., et al., 1995. The Development of a Clinician-Administered PTSD Scale, Vol 8.

Dixon, M.L., Thiruchselvam, R., Todd, R., Christoff, K., 2017. Emotion and the prefrontal cortex: an integrative review. Psychol. Bull. 143 (10), 1033–1081. https://doi.org/10.1037/bul0000096.

Esterman, M., Stumps, A., Jagger-Rickels, A., et al., 2020. Evaluating the Evidence for a Neuroimaging Subtype of Posttraumatic Stress Disorder, Vol 12. http://stm.sciencemag.org/.

Feng, C., Luo, Y.J., Krueger, F., 2015. Neural signatures of fairness-related normative decision making in the ultimatum game: a coordinate-based meta-analysis. Hum. Brain Mapp. 36 (2), 591–602. https://doi.org/10.1002/hbm.22649.

First, M., Spitzer, R.L., Gibbon, M.L., Williams, J., 2002. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-patient Edition (SCID-I/P).

Franklin, J.C., Ribeiro, J.D., Fox, K.R., et al., 2017. Risk factors for suicidal thoughts and behaviors: a meta-analysis of 50 years of research. Psychol. Bull. 143 (2), 187–232. https://doi.org/10.1037/bul0000084.

Frewen, P., Schroeter, M.L., Riva, G., et al., 2020. Neuroimaging the consciousness of self: review, and conceptual-methodological framework. Neurosci. Biobehav. Rev. 112, 164–212. https://doi.org/10.1016/j.neubiorev.2020.01.023.

Fuentes-Claramonte, P., Martín-Subero, M., Salgado-Pineda, P., et al., 2019. Shared and differential default-mode related patterns of activity in an autobiographical, a self-referential and an attentional task. PLoS One 14 (1). https://doi.org/10.1371/journal.pone.0209376.

Godwin, C.A., Hunter, M.A., Bezdek, M.A., et al., 2017. Functional connectivity within and between intrinsic brain networks correlates with trait mind wandering. Neuropsychologia 103, 140–153. https://doi.org/10.1016/j.neuropsychologia.2017.07.006.

Gutierrez, P.M., Joiner, T., Hanson, J., Stanley, I.H., Silva, C., Rogers, M.L., 2019. Psychometric properties of four commonly used suicide risk assessment measures: applicability to military treatment settings. Mil. Behav. Health 7 (2), 177–184. https://doi.org/10.1080/21635781.2018.1562390.

Henry, J.D., Crawford, J.R., 2005. The short-form version of the Depression Anxiety Stress Scales (DASS-21): construct validity and normative data in a large non-clinical sample. Br. J. Clin. Psychol. 44 (Pt 2), 227–239. https://doi.org/10.1348/014466505X29657.

Ho, D.E., Imai, K., King, G., Stuart, E.A., 2007. Matching as nonparametric preprocessing for reducing model dependence in parametric causal inference. Polit. Anal. 15 (3), 199–236. https://doi.org/10.1093/pan/mpl013.

Huang, X., Rootes-Murdy, K., Bastidas, D.M., Nee, D.E., Franklin, J.C., 2020. Brain differences associated with self-injurious thoughts and behaviors: a meta-analysis of neuroimaging studies. Sci. Rep. 10 (1) https://doi.org/10.1038/s41598-020-59490-6.

Jagger-Rickels, A., Stumps, A., Rothlein, D., Park, H., Fortenbaugh, F., Zuberer, A., Fonda, J.R., Fortier, C.B., DeGutis, J., Milberg, W., McGlinchey, R., Esterman, M., 2021. Impaired executive function exacerbates neural markers of posttraumatic stress disorder. Psychol. Med. 52 (16), 1–14. https://doi.org/10.1017/S0033291721000842.

Jollant, F., Lawrence, N.S., Olie, E., et al., 2010. Decreased activation of lateral orbitofrontal cortex during risky choices under uncertainty is associated with disadvantageous decision-making suicidal behavior. NeuroImage 51 (3), 1275–1281. https://doi.org/10.1016/j.neuroimage.2010.03.027.

Jollant, F., Lawrence, N.L., Olié, E., Guillaume, S., Courtet, P., 2011. The suicidal mind and brain: a review of neuropsychological and neuroimaging studies. World J. Biol. Psychiatry 12 (5), 319–339. https://doi.org/10.3109/15622975.2011.556200.

Just, M.A., Pan, L., Cherkassky, V.L., et al., 2017. Machine learning of neural representations of suicide and emotion concepts identifies suicidal youth. Nat. Hum. Behav. 1 (12), 911–919. https://doi.org/10.1038/s41562-017-0234-y.

Kim, H., 2012. A dual-subsystem model of the brain's default network: self-referential processing, memory retrieval processes, and autobiographical memory retrieval. NeuroImage 61 (4), 966–977. https://doi.org/10.1016/j.neuroimage.2012.03.025.

Li, J., Kong, R., Liégeois, R., et al., 2019. Global signal regression strengthens association between resting-state functional connectivity and behavior. NeuroImage 196 (April), 126–141. https://doi.org/10.1016/j.neuroimage.2019.04.016.

Liberzon, I., Abelson, J.L., 2016. Context processing and the neurobiology of post-traumatic stress disorder. Neuron 92 (1), 14–30. https://doi.org/10.1016/j.neuron.2016.09.039.

Lippard, E.T., Johnston, J.A.Y., Blumberg, H.P., 2014. Neurobiological risk factors for suicide: insights from brain imaging. Am. J. Prev. Med. 47 (3 Suppl 2), S152–S162. https://doi.org/10.1016/j.amepre.2014.06.009.

Lovibond, P.F., Lovibond, S.H., 1995. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav. Res. Ther. 33 (3), 335–343. https://doi.org/10.1016/0005-7967(94)00075-U.

Marek, S., Tervo-Clemmens, B., Calabro, F.J., et al., 2022. Reproducible brain-wide association studies require thousands of individuals. Nature 603 (7902), 654–660. https://doi.org/10.1038/s41586-022-04492-9.

McGlinchey, R.E., Milberg, W.P., Fonda, J.R., Fortier, C.B., 2017. A methodology for assessing deployment trauma and its consequences in OEF/OIF/OND veterans: the TRACTS longitudinal prospective cohort study. Int. J. Methods Psychiatr. Res. 26 (3) https://doi.org/10.1002/mpr.1556.

McNorgan, C., Joanisse, M.F., 2014. A connectionist approach to mapping the human connectome permits simulations of neural activity within an artificial brain. Brain Connect. 4 (1), 40–52. https://doi.org/10.1089/brain.2013.0174.

Morawetz, C., Bode, S., Baudewig, J., Heekeren, H.R., 2017. Effective amygdala-prefrontal connectivity predicts individual differences in successful emotion regulation. Soc. Cogn. Affect. Neurosci. 12 (4), 569–585. https://doi.org/10.1093/scan/nsw169.

Morel, N., Villain, N., Rauchs, G., et al., 2014. Brain activity and functional coupling changes associated with self-reference effect during both encoding and retrieval. PLoS One 9 (3). https://doi.org/10.1371/journal.pone.0090488.

Murray, R.J., Schaer, M., Debbané, M., 2012. Degrees of separation: a quantitative neuroimaging meta-analysis investigating self-specificity and shared neural activation between self- and other-reflection. Neurosci. Biobehav. Rev. 36 (3), 1043–1059. https://doi.org/10.1016/j.neubiorev.2011.12.013.

Nock, M.K., Borges, G., Bromet, E.J., Cha, C.B., Kessler, R.C., Lee, S., 2008. Suicide and suicidal behavior. Epidemiol. Rev. 30 (1), 133–154. https://doi.org/10.1093/epirev/mxn002.

Pan, L.A., Ramos, L., Segreti, A.M., Brent, D.A., Phillips, M.L., 2015. Right superior temporal gyrus volume in adolescents with a history of suicide attempt. Br. J. Psychiatry 206 (4), 339–340. https://doi.org/10.1192/bjp.bp.114.151316.

Reisch, T., Seifritz, E., Esposito, F., Wiest, R., Valach, L., Michel, K., 2010. An fMRI study on mental pain and suicidal behavior. J. Affect. Disord. 126 (1–2), 321–325. https://doi.org/10.1016/j.jad.2010.03.005.

Roozendaal, B., McEwen, B.S., Chattarji, S., 2009. Stress, memory and the amygdala. Nat. Rev. Neurosci. 10 (6), 423–433. https://doi.org/10.1038/nrn2651.

Rudd, M.D., 2006. Fluid Vulnerability Theory: A Cognitive Approach to Understanding the Process of Acute and Chronic Suicide Risk. Published online.

Rudd, M.D., Bryan, C.J., 2021. The Brief Suicide Cognitions Scale: development and clinical application. Front. Psychiatry 12 (September), 1–10. https://doi.org/10.3389/fpsyt.2021.737393.

Schaefer, A., Kong, R., Gordon, E.M., et al., 2018. Local-global parcellation of the human cerebral cortex from intrinsic functional connectivity MRI. Cereb. Cortex 28 (9), 3095–3114. https://doi.org/10.1093/cercor/bhx179.

Schmaal, L., van Harmelen, A.L., Chatzi, V., et al., 2020. Imaging suicidal thoughts and behaviors: a comprehensive review of 2 decades of neuroimaging studies. Mol. Psychiatry 25 (2), 408–427. https://doi.org/10.1038/s41380-019-0587-x.

Soloff, P., White, R., Diwadkar, V.A., 2014. Impulsivity, aggression and brain structure in high and low lethality suicide attempters with borderline personality disorder. Psychiatry Res. Neuroimaging 222 (3). https://doi.org/10.1016/j.pscychresns.2014.02.006.

Stanley, I.H., Boffa, J.W., Joiner, T.E., 2019. PTSD from a suicide attempt: phenomenological and diagnostic considerations. Psychiatry 82 (1), 57–71. https://doi.org/10.1080/00332747.2018.1485373.

Stumps, A., Jagger-Rickels, A., Rothlein, D., et al., 2021. Connectome-based functional connectivity markers of suicide attempt. J. Affect. Disord. 283, 430–440. https://doi.org/10.1016/j.jad.2020.11.061.

Thomas Yeo, B.T., Krienen, F.M., Sepulcre, J., et al., 2011. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J. Neurophysiol. 106 (3), 1125–1165. https://doi.org/10.1152/jn.00338.2011.

Thompson, M.F., Ghahramanlou-Holloway, M., Murphy, M.A., et al., 2022. Resting-State Network Analysis of Suicide Attempt History in the UK Biobank. bioRxiv. Published online January 1. https://doi.org/10.1101/2022.01.04.474947, 2022.01.04.474947.

Tullo, S., Devenyi, G.A., Patel, R., Park, M.T.M., Collins, D.L., Chakravarty, M.M., 2018. Warping an atlas derived from serial histology to 5 high-resolution MRIs. Sci. Data 5 (1), 1–10. https://doi.org/10.1038/sdata.2018.107.

United States Department of Defense, 2018. Annual Suicide Report, Calendar Year 2018. Published online.

United States Department of the Army, 2010. Health Promotion Risk Reduction Suicide Prevention Report 2010. Published online.

Vidal-Ribas, P., Janiri, D., Doucet, G.E., et al., 2021. Multimodal neuroimaging of suicidal thoughts and behaviors in a U.S. population-based sample of school-age children. Am. J. Psychiatr. 178 (4), 321–332. https://doi.org/10.1176/appi.ajp.2020.20020120.

Wagner, D.D., Haxby, J.v., Heatherton, T.F., 2012. The representation of self and person knowledge in the medial prefrontal cortex. Wiley Interdiscip. Rev. Cogn. Sci. 3 (4), 451–470. https://doi.org/10.1002/wcs.1183.

Wiglesworth, A., Falke, C.A., Fiecas, M., Luciana, M., Cullen, K.R., Klimes-Dougan, B., 2021. Brain signatures in children who contemplate suicide: learning from the large-scale ABCD study. Psychol. Med. https://doi.org/10.1017/S0033291721004074. Published online.

Zhou, H.X., Chen, X., Shen, Y.Q., et al., 2020. Rumination and the default mode network: meta-analysis of brain imaging studies and implications for depression. NeuroImage 206. https://doi.org/10.1016/j.neuroimage.2019.116287.