

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Cortical thickness in parietal regions link perseverative thinking with suicidal ideation

Ana E. Sheehan^{*}, Emily Heilner, Nadia Bounoua, Rickie Miglin, Jeffrey M. Spielberg, Naomi Sadeh

Department of Psychological and Brain Sciences, University of Delaware, United States of America

ARTICLE INFO

Keywords:

Perseverative thinking
Suicidal ideation
Cortical thickness

ABSTRACT

Introduction: Suicide represents a major public health concern, as the tenth leading cause of death in the United States. Links between perseverative thinking (PT) and suicidal ideation have previously been examined, while their biological underpinnings remain understudied. The present study had two aims: 1) investigate whether cortical thickness varied as a function of PT, and 2) examine whether variation in thickness partially explained associations between PT and lifetime history of ideation. We hypothesized that cortical thickness would vary as a function of PT and PT would be positively associated with lifetime history of ideation.

Methods: A community sample of 73 adults (ages 18–55; 42.5% female) completed self-report measures examining PT and ideation, as well as a neuroimaging protocol. Mean scores on the Perseverative Thinking Questionnaire were entered as the explanatory variable in the analysis of cortical thickness clusters related to PT. The indirect effect of PT on ideation through thickness was tested cross-sectionally.

Results: PT was positively associated with i) thickness in three clusters bilaterally in the parietal cortex and ii) suicidal ideation. Follow-up analyses revealed a significant indirect effect of PT on suicidal ideation through left superior parietal thickness.

Limitations: Limitations of the study include the use of cross-sectional data and a modest sample size.

Conclusions: PT is associated with variations in cortical thickness, and increased thickness in the left parietal region may partially explain the link between PT and suicidal ideation, identifying a novel neurobiological mechanism of ideation.

Suicide represents a major public health concern, as the tenth leading cause of death overall in the United States and the second leading cause of death between the ages of 10–34 ([Centers for Disease Control and Prevention, 2020](#)). Despite substantial efforts towards prevention and intervention made in the last several decades, suicidal behaviors have remained virtually unchanged ([Centers for Disease Control and Prevention, 2020](#)). Recent events, such as the COVID-19 pandemic, have brought more attention to the rising rates of suicide, spurring a call to action from the U.S. Department of Health and Human Services along with the Office of the Surgeon General's to increase the identification of individuals at risk ([Office of the Surgeon General, 2021](#)). Previous literature has identified suicidal ideation as a robust risk factor associated with future suicide attempts, however the accuracy of suicidal ideation alone in predicting future attempts is only slightly higher than chance ([Franklin et al., 2017](#)). Given that the transition from suicidal ideation to plans and attempts takes place within a short temporal

window, it has been suggested that the identification of factors conferring unique risk for ideation, such as cognitive or biological vulnerabilities, should be prioritized, rather than the transition from ideation to action ([Borges et al., 2014](#)). The present study sought to advance research on neurocognitive vulnerabilities related to suicidal ideation by examining a key cognitive process, perseverative thinking (PT), along with a biological indicator, cortical thickness, in an at-risk sample of community adults.

PT is a cognitive style characterized by repetitive negative thinking, intrusive thoughts, and difficulty disengaging with intrusive negative thoughts, all of which impair mental capacity ([Ehring et al., 2011](#)). It is conceptually related to cognitive inflexibility, because it is characterized by difficulty disengaging from repetitive negative thoughts and exacts a toll on cognitive resources ([Ehring et al., 2011](#)). However, it does not completely overlap with the construct of cognitive inflexibility, as PT is characterized by unpleasant thoughts in particular, and also includes the

^{*} Corresponding author at: University of Delaware, Department of Psychological and Brain Sciences, 108 Wolf Hall, Newark, DE 19176, United States of America.
E-mail address: ansheeha@udel.edu (A.E. Sheehan).

<https://doi.org/10.1016/j.jad.2022.03.019>

Received 19 July 2021; Received in revised form 17 December 2021; Accepted 10 March 2022

Available online 15 March 2022

0165-0327/© 2022 Elsevier B.V. All rights reserved.

tendency to experience negative thoughts as intrusive. Notably, PT has been identified as a transdiagnostic risk factor for psychopathology and demonstrates consistent associations with symptoms of generalized anxiety disorder, obsessive compulsive disorder, and depression (Ehring et al., 2011; Nolen-Hoeksema et al., 2008; Sorg et al., 2012). It can manifest in different ways across psychiatric diagnoses, and encompasses features of rumination about past negative events and worry about the future. In addition to specific psychiatric disorders, certain forms of PT, like rumination and worry, have been implicated in the severity, intensity and maintenance of suicidal ideation (Miranda et al., 2013; Rogers and Joiner, 2017; Smith and Alloy, 2009). Considerably less research has examined how superordinate measures of PT that encompass aspects of both rumination and worry relate to suicidal ideation (Law and Tucker, 2018; Miranda et al., 2013; Rogers and Joiner, 2017), underscoring the need to further study relations between broad measures of PT and suicidal ideation (Law and Tucker, 2018).

Traditionally, research on risk for psychopathology has emphasized the utility of stable trait-level influences, such as personality, for predicting individuals at risk for developing mental health problems (Clark, 2005). Although less widely studied, cortical thickness is a relatively stable and reliable marker of individual differences (Han et al., 2006; Noble et al., 2017) that may convey unique information about trait-level differences in risk for psychopathology not captured by self-report or diagnostic interviews. Given that PT is also considered to be trait-like (Hijne et al., 2020), individual differences in cortical thickness might instantiate PT patterns, and in turn, confer risk for suicidal ideation. In terms of neuroanatomical studies, no research to our knowledge has examined brain structure variation as a function of PT broadly defined. However, a relatively large literature has examined the structural correlates of more specific manifestations of PT, like rumination and worry. For example, a meta-analysis of 64 structural imaging studies found that, among depressed patients with high levels of rumination, reliable reductions in brain volumes were observed in the anterior cingulate cortex and orbitofrontal cortex (Koolschijn et al., 2009). Most of these prior studies, however, focused selectively on gray matter volume, limiting our knowledge of other auxiliary measures of neuroanatomical structure, such as cortical thickness, that might unveil novel neural mechanisms of PT. An exception to this pattern are two studies that reported reduced thickness in the left superior frontal, right superior temporal, and medial orbitofrontal regions among depressed and anxious individuals, elevated in worry and rumination, compared to healthy controls (Kühn et al., 2011; Zhao et al., 2017). Continued examination of structural alterations related to PT, including variations in thickness of the cortical mantle, could be important for identifying brain regions involved in perseverative negative thinking, and the development and persistence of suicidal ideation.

The goal of this study was to advance research on PT and suicidal ideation by examining their relations with cortical thickness, an understudied biological substrate with potential implications for understanding trait-like risk for PT and, in turn, suicidal ideation. Our first aim was to examine the association between PT and variations in cortical thickness across the entire cortex, and our second aim was to examine whether observed differences in cortical thickness (the mediator) partially explain the relationship between PT (the independent variable), and suicidal ideation (the dependent variable).

We hypothesized that PT would be associated with variations in cortical thickness and lifetime history of suicidal ideation. Further, we expected that PT-related alterations in cortical thickness would be associated with suicidal ideation. Given the relative stability and trait-like nature of PT (Ehring et al., 2011) and cortical thickness (Han et al., 2006; Noble et al., 2017), we also hypothesized that PT-related variations in cortical thickness would partially explain the relationship between perseverative thinking styles and suicidal ideation.

1. Methods

1.1. Participants

A total of 77 adults completed a battery of questionnaires and a neuroimaging protocol. Four participants were excluded from the present analysis due to incidental magnetic resonance imaging (MRI) findings or excessive motion (all images were inspected for quality), resulting in a final sample of 73 adults aged 18–55 (M/SD 30.3/8.1, 42.5% female). Participants were recruited through the use of online postings and community flyers. The population was diverse in terms of racial and socioeconomic background (see Table 1), with participants identifying primarily as White (49.3%) and Black/African American (38.4%), followed by Hispanic/Latino (17.8%), Asian, Hawaiian, or Pacific Islander (6.9%), and Other (4.1%). The average household income for participants in the sample was \$40,438/year ($SD = \$39,037$). Participants were compensated with a financial incentive for their time and effort.

Individuals between the ages of 18 and 55 who were fluent in English were eligible to be recruited for participation in this study. Criteria for exclusion included serious medical or neurological conditions, current psychosis, past head injury with lasting impact, or any magnetic resonance imaging (MRI) contradictions.

1.2. Procedures

All participants gave both oral and written consent before participating in the study. Procedures were approved by the University of Delaware's Institutional Review Board.

1.3. Measures

1.3.1. Perseverative thinking

This study utilized the 15-item self-report Perseverative Thinking Questionnaire (PTQ) to assess for frequency and severity of ruminative negative thinking (Ehring et al., 2011). Repetitive negative thinking is characterized by thought patterns that are repetitive and intrusive in nature. Participants were presented with a series of statements about rumination (e.g., “*The same thoughts keep going through my mind again and again*”) and were asked to self-report their accuracy on a scale of 0–4 (0 = *Never*, 4 = *Almost Always*). The scale has been shown to have good internal consistency (Cronbach's alpha = 0.93; Ehring et al., 2011). A total PTQ score was calculated by averaging responses to all 15 items, and it demonstrated excellent internal consistency in the present sample (Cronbach's alpha = 0.95; $M/SD = 1.8/1.0$).

1.3.2. Suicidal ideation

The 38-item self-report Risky, Impulsive, and Self-destructive Behavior Questionnaire (RISQ; Sadeh and Baskin-Sommers, 2017) was used to assess the frequency of suicidal ideation across the lifespan.

Table 1
Sample characteristics.

Demographics	
Age (M/SD)	30.3/8.1
Biological sex ($n, \%$)	
Female	31/42.5%
Male	42/57.5%
Race/ethnicity ($n, \%$)	
Caucasian	36/49.3%
Black/African American	28/38.4%
Hispanic/Latino	13/17.8%
Asian/Hawaiian/Pacific Islander	5/6.9%
Other	3/4.1%
Household income (M/SD)	\$40,438/\$39,037

Note: $N = 73$.

Suicidal ideation was assessed with a single item asking participants how many times they had “Thought about killing myself” in their lives using this scale: 0 = 0, 1 = 1 to 10, 2 = 11 to 50, 3 = 51 to 100, and 4 ≥ 100 acts. Binned options were used to reduce the skewness of the item based upon those employed in the validation study of this measure. To further reduce skewness and the impact of outliers at the high end of the distribution, we employed Blom's transformation given its utility in dealing with asymmetric distributions (Ayán and Díaz, 2008). Following this transformation, values for asymmetry fell in the acceptable range (George and Mallery, 2019). The RISQ has demonstrated reliability and convergent validity with other self-report measures of risky behavior (Bounoua et al., 2020; Estrada et al., 2020; Miglin et al., 2019).

1.3.3. Cortical thickness

Data was collected at the University of Delaware using a Siemens 3 T Magnetom Prisma scanner with a 64-channel head coil. A T1 weighted multi-echo MPRAGE anatomical scan (resolution = 1 mm³, TR = 2530 ms, Tes = 1.69, 3.55, 5.41, 7.27 ms) was performed to show distinction between gray matter and white matter. Compared to standard MPRAGE sequences, the multi-echo MPRAGE scan provides minimized distortion and enhanced contrast, which results in more reliable cortical models. A T2-weighted variable flip-angle turbo spin echo scan (resolution = 1 mm³, TR = 3200 ms, TE = 564 ms) was collected, and was used in FreeSurfer to better differentiate the gray matter-dura boundary. The standard FreeSurfer v6 morphometric pipeline was used in calculation of the segmentation and thickness of the cortical mantle at each vertex. The surface-based cortical thickness measurement data were spatially smoothed using a Gaussian kernel of 10 mm full width at half maximum (FWHM), ensuring that the data approximate a continuous field of random values.

1.4. Data analysis

All analyses were conducted using cross-sectional data. To investigate our first aim and hypothesis, we examined the association between PT and cortical thickness using vertex-wise analysis of the entire cortex conducted separately by hemisphere. More specifically, general linear models with the total PTQ score entered as the explanatory variable were conducted separately for each cortical hemisphere using FreeSurfer's QDEC software. The vertex wise threshold was set to $p < 0.01$. Covariates of no interest, specifically biological sex, age, body mass index (BMI) and education level, were included based on their previous associations with cortical thickness (Medic et al., 2016; Miglin et al., 2019; Veit et al., 2014). To correct for multiple comparisons, we utilized a Monte Carlo simulation with 10,000 iterations and a cluster-based threshold of $p < 0.05$, correcting for the comparisons across both hemispheres.

To test our second aim, we extracted mean thickness for the clusters associated with PT in the aforementioned analyses and used linear regressions in SPSS v26 to examine whether mean thickness in any of the clusters were related to the frequency of lifetime suicidal ideation. To test the indirect effect of PT on lifetime suicidal ideation through cortical thickness, we used maximum likelihood estimation with robust standard errors (MLR) in Mplus with the “model indirect” procedure. We included lifetime history of major depressive disorder as a covariate of no interest in this analysis to test whether results were specific to suicidal ideation, given the robust link between major depressive disorder and ideation.

All of the variables, except biological sex, were continuous and met the distributional assumptions for the indirect effect and regression models. Furthermore, the self-report and neuroimaging variables entered into analyses were normally distributed and did not evidence excessive skewness or kurtosis. All tests were two-tailed and included age, biological sex, BMI as covariates (unless otherwise noted). As a measure of effect size, we included R^2 or ΔR^2 to describe the amount of variance in the dependent variable explained by the independent variables above that accounted for by the covariates of no interest (where

applicable). We conducted a post-hoc sensitivity power analysis in G*Power (version 3.1; Faul et al., 2007) to evaluate the minimum effect size detectable based on our sample size. With our sample of 73 participants, this analysis indicated we were powered to detect small effect sizes (0.15) at 90% power.

2. Results

2.1. Descriptive statistics

Participants reported a range of suicidal ideation in their lifetime, with 52% reporting at least some suicidal ideation and 33.3% reporting between 1 and 10 instances of suicidal ideation. As described in the bivariate correlations in Table 2, PT was positively associated with suicidal ideation, and PT scores were higher in women than men. In addition, lifetime suicidal ideation was reported more commonly in women than men.

2.2. Perseverative thinking associations with cortical thickness

PT scores were significantly positively related to cortical thickness in three clusters, such that individuals who engaged in more PT had greater thickness in these regions (see Table 3 and Fig. 1). The first cluster peaked in the right superior parietal region and spanned the supra marginal region. The second cluster also peaked in the right hemisphere superior parietal region and included the cuneus and precuneus regions. Finally, the third cluster peaked in the left hemisphere superior parietal region, spanning the inferior parietal and supra marginal regions.

2.3. Cortical thickness associations with suicidal ideation

Greater thickness in the left superior parietal region was related to increased frequency of suicidal ideation across the lifespan ($\beta = 0.33$, $p = 0.01$, $\Delta R^2 = 0.09$), and the model explained 17% of the variance in suicidal ideation ($F_{(4, 68)} = 3.53$, $p = 0.01$). However, suicidal ideation was not significantly related to thickness in the right superior parietal region spanning the supramarginal and inferior parietal regions ($\beta = 0.18$, $p = 0.13$, $\Delta R^2 = 0.03$), and the model explained 12% of the variance in suicidal ideation ($F_{(4, 68)} = 2.25$, $p = 0.07$). Finally, suicidal ideation was not significantly related to thickness in the right superior parietal spanning the cuneus and precuneus ($\beta = 0.18$, $p = 0.15$, $\Delta R^2 = 0.03$), and the model explained 11% of the variance in suicidal ideation ($F_{(4, 68)} = 2.18$, $p = 0.08$).

2.4. Modeling links between perseverative thinking, cortical thickness, and suicidal ideation

We tested the indirect effect of PT on suicidal ideation through cortical thickness. First, the direct effects of PT on left superior parietal thickness ($\beta = 0.47$, $p < 0.001$) and left superior parietal thickness on lifetime frequency of suicidal ideation ($\beta = 0.31$, $p = 0.02$) were both

Table 2

Bivariate correlations among suicidal ideation, perseverative thinking, and covariates.

	1	2	3	4	5
1. Suicidal ideation					
2. Perseverative thinking	0.30*				
3. Age	-0.14	-0.18			
5. Male sex	-0.26*	-0.33**	0.14		
6. BMI ^a	0.06	0.05	0.12	0.07	
7. Lifetime history of depression	0.27*	0.08	-0.13	-0.15	0.67

Values represent Pearson correlation coefficients.

* $p < 0.05$.

** $p < 0.01$.

^a Body Mass Index.

Table 3
Regions of significant correlation between perseverative thinking and cortical thickness.

Cluster no.	Hemisphere	Annotation	Peak F-value	Peak MNI (x, y, z)	No. of vertices	Cluster size (mm ²)
1	RH	Superior parietal Supramarginal Inferior parietal	3.16	34.0, -40.0, 50.8	3973	1621.57
2	RH	Superior parietal Cuneus Precuneus	4.37	19.1, -74.8, 41.6	2562	5023.73
3	LH	Superior parietal Inferior parietal Supra marginal	3.26	-22.0, -59.4, 49.1	8438	4036.38

Note. All clusters survived Monte Carlo Simulation correction for multiple comparisons. RH = right hemisphere; LH = left hemisphere.

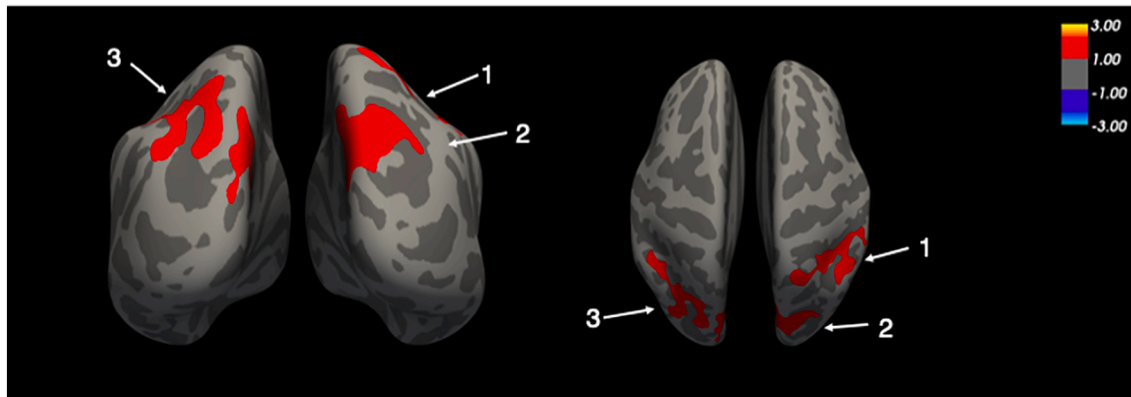


Fig. 1. PT is associated with increased thickness bilaterally in parietal regions.

Note. PT is linked to greater cortical thickness in three clusters, adjusting for age, sex, and BMI. 1) Right superior parietal, supra marginal, and inferior parietal regions. 2) Right superior parietal, cuneus, and precuneus regions. 3) Left superior parietal, inferior parietal, and supra marginal regions.

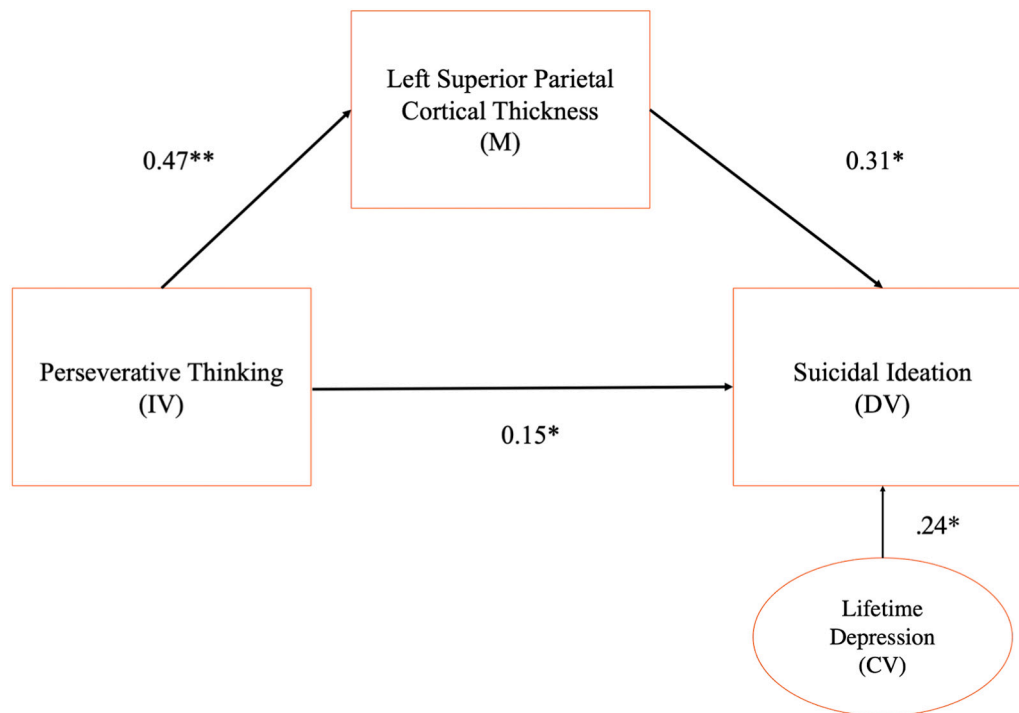


Fig. 2. Indirect effect model of PT on suicidal ideation through left superior parietal thickness.

Note. Standardized coefficients are displayed. The lines represent the paths of interest. IV, independent variable; M, mediator; DV, dependent variable; CV, covariate. * $p < 0.05$, ** $p < 0.001$.

significant. Of note, the indirect effect of PT on suicidal ideation through left superior parietal thickness was significant ($\beta = 0.15$, $p = 0.04$), suggesting the left superior parietal thickness partially accounted for variance in the relationship between PT on the frequency of suicidal ideation. Further, the direct effect of PT on frequency of suicidal ideation was no longer significant in this model ($\beta = 0.09$, $p = 0.48$). In addition, the effect of lifetime history of depression entered as a covariate on frequency of suicidal ideation was significant ($\beta = 0.24$, $p = 0.02$). In sum, the model explained 22.0% of the variance in cortical thickness in the left superior parietal cluster ($p = 0.006$), and 24.4% of the variance in lifetime frequency of suicidal ideation ($p = 0.003$) (Fig. 2).

Given the cross-sectional nature of the data, we examined an alternative model testing the indirect effect of thickness in the parietal cluster on ideation through PT. With this alternative model, the direct effect of left superior parietal thickness on PT ($\beta = 0.45$, $p < 0.001$) was significant. In contrast, the direct effect of PT on frequency of suicidal ideation was not significant ($\beta = 0.09$, $p = 0.48$), and the indirect effect from cortical thickness to suicidal ideation by way of PT was not significant ($\beta = 0.04$, $p = 0.48$). Finally, the partial effect of the covariate lifetime history of depression on suicidal ideation was significant ($\beta = 0.24$, $p = 0.02$). The model explained 22.0% of the variance in PT ($p = 0.008$), and 22.7% of the variance in lifetime frequency of suicidal ideation ($p = 0.004$).

3. Discussion

Prior research has supported the link between repetitive negative thinking patterns and suicidal ideation. However, considerably less work has directly examined the link between PT broadly defined and suicidal ideation. Further, this is the first published study to examine the neuroanatomical basis of this link. In order to gain further insight into the neurobiological mechanisms underlying this relationship, we examined whether cortical thickness and suicidal ideation varied as a function of PT, and furthermore if there was an indirect effect of PT on suicidal ideation through cortical thickness. Our findings revealed that scores on the PTQ demonstrated positive direct associations with cortical thickness in three clusters that survived correction for multiple comparisons bilaterally in the parietal region. Namely, PT was positively associated with thickness in the left superior parietal region, right superior parietal and cuneus, and right superior parietal and supra marginal regions. In addition, increased cortical thickness in the left parietal region was associated with greater frequency of suicidal ideation. Finally, there was a significant indirect effect of PT on suicidal ideation through thickness in the left parietal region with lifetime history of depression entered as a covariate. Overall, these results provide greater clarity into cortical thickness vulnerabilities linked to PT that might contribute to the emergence and maintenance of suicidal ideation.

Despite an extensive literature confirming the transdiagnostic risk posed by PT, much less is known about the biological instantiations of these cognitive patterns. Our study adds to this literature by identifying a positive association between PT scores and thickness bilaterally in parietal areas spanning the left and right superior and inferior parietal, and supra marginal regions along with the right cuneus, precuneus. Prior work has implicated greater activation in the right inferior parietal region with processes related to empathy and perspective taking (Decety and Moriguchi, 2007; Decety and Sommerville, 2003). Furthermore, greater activity in these regions has been found when individuals are reflecting on the past and future selves, than when focusing on the present self (D'Argembeau et al., 2010). Consistent with these findings, increased thickness in these regions found in the present work may reflect over-activation of neuroanatomical areas sustaining rumination about the past and thus maintaining perseverative thought patterns. In addition, some of the regions we identified in the present study, including the inferior parietal and precuneus regions, are involved in the default mode network (DMN), a functional network linked with self-

referential processing (Nejad et al., 2013) and mind wandering (Poerio et al., 2017). A converging body of evidence suggests that abnormalities in the DMN have been associated with diagnoses of major depressive disorder (Yan et al., 2019) and generalized anxiety disorder (Sylvester et al., 2012), which are also characterized by PT (McEvoy et al., 2018). In line with this, the synchronous increases in cortical thickness across the bilateral parietal regions identified in the present work may reflect a functional relationship, which when altered could promote perseverative and ruminative thinking. Our findings provide additional structural evidence supporting the association between atypicalities within the DMN and PT. Future work should aim to examine the functional relationship between these regions to provide clarity to the neural mechanisms underlying perseverative thought.

Findings from the present study also replicated previous work identifying a positive association between a superordinate measure of PT and suicidal ideation. Our work expanded upon these findings by determining that thickness clusters associated with PT, specifically the left superior parietal region, spanning the inferior parietal and supra-marginal regions was also positively associated with suicidal ideation. The left superior parietal region is primarily involved with aspects of attention and visuospatial perception, while the left inferior parietal region is concerned with the interpretation of language through visual and auditory stimuli (Barbeau et al., 2017; Yue et al., 2019). Although speculative, this finding suggests that perhaps thickness within this left parietal cluster may differentiate individuals with PT styles with and without suicidal ideation. In light of the functions of this region, increased thickness may reflect over-activation of attention processes supporting ruminative thinking, which might confer additional risk for suicidal ideation. Previous work examining neural contributors to suicidality have identified reduced gray matter and cortical thickness in parietal regions differentiating individuals at high risk or with a history of suicidality from those without (Hwang et al., 2010; Taylor et al., 2015; Wagner et al., 2012). However, the present study provides contrasting evidence supporting a positive relationship between cortical thickness in the left parietal region and suicidal ideation. Work by Peng et al. (2014) identified larger gray matter volumes in the parietal region among adults with a history of suicide compared to age-matched healthy controls. Our findings provide additional evidence supporting the positive relationship between abnormalities in the parietal region and suicidal ideation. However, future research using functional imaging methods is necessary in order to further explore this relationship.

Subsequently, follow up analyses revealed an indirect effect of PT on frequency of suicidal ideation through thickness in the left parietal region after controlling for depressive symptoms. These findings provide preliminary evidence suggesting increased thickness in this cluster plays a critical role in maintaining the relationship between PT and suicidal ideation, above and beyond shared associations with depressive symptoms. The specificity of this finding is intriguing given the considerable overlap between suicidal ideation and depression, suggesting that the observed indirect effect cannot be attributed to this region's association with psychopathology more broadly, including mental disorders that commonly co-occur with suicidal ideation. Although it is still unknown whether this abnormality in the left superior parietal region precedes PT or vice versa, future research should examine the temporal order of these associations by way of longitudinal designs and explore associations between this region and other suicide-related phenotypes.

Furthermore, our findings offer important and unexplored potential for clinical application. First, given that as a field we are no better than chance at predicting suicide attempts, exploration of novel avenues for improving evaluation, like neuroanatomical vulnerabilities, remains critical. Our findings, although preliminary, shed light on an unexplored and potentially important line of study to enhance our understanding of suicide. Second, this work identifies neural structures and mechanisms that may help maintain suicidal ideation. This points to the need for interventions that target repetitive negative thinking patterns and disrupt these cycles before individuals act on their ideations. Finally, in

light of increased accessibility and feasibility of neuroimaging methodologies, clinical settings including inpatient hospitals where rates of suicidal ideation are elevated, may consider implementing structural scanning as part of a routine assessment procedure in order to evaluate the predictive utility of these measures over time. Unlike functional imaging, anatomical scans do not require additional training for technicians nor do they burden participants with behavioral tasks. At this time, a recommendation for implementing neuroimaging assessment tools is premature, but it holds promise as the field continues to identify links between biomarkers and suicide risk factors.

Findings from the present study should be understood within the context of several limitations. First, data from the present study, including measures of cortical thickness, PT, and frequency of suicidal ideation, were all assessed cross-sectionally. As such, this limits our ability to make inferences about the temporal relationship between these factors. Despite this limitation, our models are based in a theoretical framework that allow us to make informed conjectures about temporality, with a breadth of research conceptualizing PT as a relatively stable cognitive pattern (Everaert and Joormann, 2020; Hijne et al., 2020; Smith and Alloy, 2009) and thus influencing the course and severity of suicidal ideation. Similarly, cortical thickness is thought to be largely unvarying with greater temporal stability and reliability compared to functional neuroimaging measures (Han et al., 2006; Noble et al., 2017). In this way cortical thickness may represent a stable trait-like neurobiological mechanism underlying suicidal ideation rather than the reverse. Although this was not within the scope of our project, future work should prioritize longitudinal designs, which could illuminate the causal mechanisms driving suicidal ideation. A second limitation of the present study is that our measures of PT and suicidal ideation were assessed using self-report measures, inherently introducing the possibility of reporter biases. However, systematic reviews have demonstrated that adults can recall past information with a high degree of accuracy and these reports are useful when prospective data is not available (Hardt and Rutter, 2004). Future work should aim to obtain more accurate assessment of suicidal ideation through methods including ecological-momentary assessment along with replication studies. It should be noted that although the present study included symptoms of depression as a variable of no-interest, there may be other factors including lifetime history of anxiety or experiences of trauma which could account for our findings. Thus, future work should aim to rule-out other third variables of interest that could be accounting for the relationship between PT and suicidal ideation. Finally, our analyses were limited to a structural risk factor of cortical thickness and its associations with PT and suicidal ideation. Given that other structural candidates for risk exist including gray matter volume, cortical surface area, and subcortical volumes, these should be further explored in future work.

Notable strengths of our study should also be highlighted. Namely, the community sample was an ethnically and socioeconomically diverse group of adults that reported relatively high rates of lifetime suicidal ideation (52.0%), making them uniquely suited to answer the questions posed by our study. Given, these populations are historically under-represented in the literature to date, our findings provide a more accurate representation of the relationship between perseverative thinking and suicide within a diverse population. Another area of strength in our study was the multidimensional approach testing both biological and cognitive risk related to suicidal ideation. Although prior research has examined these factors separately, relatively less work has synthesized these components within models of risk. Finally, while prior neuroimaging work has mainly emphasized a region of interest analytic approach, our study used a whole-cortex analysis with a conservative correction for multiple comparisons, which strengthened the replicability of our findings and allowed for an exploratory identification of regions not previously identified in the literature.

Altogether, these results provide new insight on the neuroanatomical correlates of PT and suggest that variability in cortical thickness in the

left superior parietal region partially explains the link between PT and suicidal ideation. Understanding these mechanisms could have important implications for informing models of risk for suicidal ideation and improving early detection of risk.

Data availability statement

The data that support the findings of this study are available from the corresponding author (A.E.S), upon request.

CRediT authorship contribution statement

Ana E. Sheehan: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing, Visualization, Project administration, Funding acquisition, Validation. **Emily Heilner:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing, Visualization, Validation. **Nadia Bounoua:** Data curation, Writing – review & editing, Supervision, Funding acquisition, Validation. **Rickie Miglin:** Writing – review & editing, Supervision, Validation. **Jeffrey M. Spielberg:** Conceptualization, Writing – review & editing, Supervision, Validation. **Naomi Sadeh:** Conceptualization, Investigation, Methodology, Writing – review & editing, Visualization, Supervision, Funding acquisition, Validation.

Declaration of competing interest

The authors report no conflicts of interest.

Acknowledgements

This research was supported by the National Science Foundation Graduate Research Fellowship Award, a National Institute of General Medical Sciences grant (2P20GM103653-06-6527) and National Institute of Mental Health grant (1F31MH120936-01A2). These institutes had no role in the study design; collection, analysis or interpretation of the data; writing the manuscript or the decision to submit the paper for publication.

References

- Ayán, María Noel, Díaz, Miguel Ángel, 2008. Atenuación de la asimetría y de la curtosis de las puntuaciones observadas mediante transformaciones de variables: Incidencia sobre la estructura factorial. *Psicológica*, 29 (2), 205–227.
- Barbeau, E.B., Chai, X.J., Chen, J.-K., Soles, J., Berken, J., Baum, S., Klein, D., 2017. The role of the left inferior parietal lobule in second language learning: an intensive language training fMRI study. *Neuropsychologia* 98, 169–176.
- Borges, Guilherme, Chiu, Wai Tai, Irving, Hwang, Panchal, Bharat N., Ono, Yutaka, Sampson, Nancy A., Kessler, Ronald C., Nock, Matthew K., 2014. Prevalence, onset, and transitions among suicidal behaviors. *Suicide: Global Perspectives from the WHO World Mental Health Surveys*, 1st ed. Cambridge University Press, pp. 65–74.
- Bounoua, N., Miglin, R., Spielberg, J.M., Sadeh, N., 2020. Childhood assaultive trauma and physical aggression: links with cortical thickness in prefrontal and occipital cortices. *Neuroimage: Clinical* 27, 102321.
- Centers for Disease Control and Prevention, 2020. WISQARS Injury Mortality Report. Web-based Injury Statistics Query and Reporting System (WISQARS). (Accessed 18 June 2021).
- Clark, L.A., 2005. Temperament as a unifying basis for personality and psychopathology. *J. Abnorm. Psychol.* 114 (4), 505.
- D'Argembeau, A., Stawarczyk, D., Majerus, S., Collette, F., Van der Linden, M., Salmon, E., 2010. Modulation of medial prefrontal and inferior parietal cortices when thinking about past, present, and future selves. *Soc. Neurosci.* 5 (2), 187–200.
- Decety, J., Moriguchi, Y., 2007. The empathic brain and its dysfunction in psychiatric populations: implications for intervention across different clinical conditions. *BioPsychoSocial Medicine* 1 (1), 1–21.
- Decety, J., Sommerville, J.A., 2003. Shared representations between self and other: a social cognitive neuroscience view. *Trends Cogn. Sci.* 7 (12), 527–533.
- Ehring, T., Zetsche, U., Weidacker, K., Wahl, K., Schönfeld, S., Ehlers, A., 2011. The perseverative thinking questionnaire (PTQ): validation of a content-independent measure of repetitive negative thinking. *J. Behav. Ther. Exp. Psychiatry* 42 (2), 225–232.

- Estrada, S., Richards, C., Gee, D.G., Baskin-Sommers, A., 2020. Exposure to violence and nonassociative learning capability confer risk for violent behavior. *J. Abnorm. Psychol.* 129 (7), 748.
- Everaert, J., Joormann, J., 2020. Emotion regulation habits related to depression: a longitudinal investigation of stability and change in repetitive negative thinking and positive reappraisal. *J. Affect. Disord.* 276, 738–747.
- Faul, F., Erdfelder, E., Lang, A.G., Buchner, A., 2007. G* power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav. Res. Methods* 39 (2), 175–191.
- Franklin, J.C., Ribeiro, J.D., Fox, K.R., Bentley, K.H., Kleiman, E.M., Huang, X., Nock, M. K., 2017. Risk factors for suicidal thoughts and behaviors: a meta-analysis of 50 years of research. *Psychol. Bull.* 143 (2), 187.
- George, D., Mallery, P., 2019. IBM SPSS Statistics 26 Step by Step: A Simple Guide and Reference. Routledge.
- Hardt, J., Rutter, M., 2004. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *J. Child Psychol. Psychiatry* 45 (2), 260–273.
- Han, X., Jovicich, J., Salat, D., van der Kouwe, A., Quinn, B., Czanner, S., Fischl, B., 2006. Reliability of MRI-derived measurements of human cerebral cortical thickness: the effects of field strength, scanner upgrade and manufacturer. *NeuroImage* 32 (1), 180–194.
- Hijne, K., Penninx, B.W., van Hemert, A.M., Spinhoven, P., 2020. The association of changes in repetitive negative thinking with changes in depression and anxiety. *J. Affect. Disord.* 275, 157–164.
- Hwang, J.-P., Lee, T.-W., Tsai, S.-J., Chen, T.-J., Yang, C.-H., Lirng, J.-F., Tsai, C.-F., 2010. Cortical and subcortical abnormalities in late-onset depression with history of suicide attempts investigated with MRI and voxel-based morphometry. *J. Geriatr. Psychiatry Neurol.* 23 (3), 171–184. <https://doi.org/10.1177/0891988710363713>.
- Koolschijn, P.C.M., van Haren, N.E., Lensvelt-Mulders, G.J., Hulshoff Pol, H.E., Kahn, R. S., 2009. Brain volume abnormalities in major depressive disorder: a meta-analysis of magnetic resonance imaging studies. *Hum. Brain Mapp.* 30 (11), 3719–3735.
- Kühn, S., Schubert, F., Gallinat, J., 2011. Structural correlates of trait anxiety: reduced thickness in medial orbitofrontal cortex accompanied by volume increase in nucleus accumbens. *J. Affect. Disord.* 134 (1–3), 315–319.
- Law, K.C., Tucker, R.P., 2018. Repetitive negative thinking and suicide: a burgeoning literature with need for further exploration. *Curr. Opin. Psychol.* 22, 68–72.
- McEvoy, P.M., Hyett, M.P., Ehring, T., Johnson, S.L., Samtani, S., Anderson, R., Moulds, M.L., 2018. Transdiagnostic assessment of repetitive negative thinking and responses to positive affect: structure and predictive utility for depression, anxiety, and mania symptoms. *J. Affect. Disord.* 232, 375–384.
- Medic, N., Ziauddeen, H., Ersche, K.D., et al., 2016. Increased body mass index is associated with specific regional alterations in brain structure. *Int. J. Obes.* 40 (7), 1177–1182.
- Miglin, R., Bounoua, N., Goodling, S., Sheehan, A., Spielberg, J.M., Sadeh, N., 2019. Cortical thickness links impulsive personality traits and risky behavior. *Brain Sci.* 9 (12), 373.
- Miranda, R., Tsypes, A., Gallagher, M., Rajappa, K., 2013. Rumination and hopelessness as mediators of the relation between perceived emotion dysregulation and suicidal ideation. *Cogn. Ther. Res.* 37 (4), 786–795.
- Nejad, A.B., Fossati, P., Lemogne, C., 2013. Self-referential processing, rumination, and cortical midline structures in major depression. *Front. Hum. Neurosci.* 7, 666.
- Noble, S., Spann, M.N., Tokoglu, F., Shen, X., Constable, R.T., Scheinost, D., 2017. Influences on the test–retest reliability of functional connectivity MRI and its relationship with behavioral utility. *Cereb. Cortex* 27 (11), 5415–5429.
- Nolen-Hoeksema, Susan, Wisco, Blair E., Lyubormirsky, Sonja, 2008. Rethinking rumination. *Perspect. Psychol. Sci.* 3 (5), 400–424.
- Office of the Surgeon General, 2021. The Surgeon General’s Call to Action to Implement the National Strategy for Suicide Prevention: A Report of the U.S. Surgeon General and of the National Alliance for Suicide Prevention. Retrieved June 18th, 2021 from. <https://www.hhs.gov/sites/default/files/spre-call-to-action.pdf>.
- Peng, H., Wu, K., Li, J., Qi, H., Guo, S., Chi, M., Ning, Y., 2014. Increased suicide attempts in young depressed patients with abnormal temporal–parietal–limbic gray matter volume. *J. Affect. Disord.* 165, 69–73.
- Poerio, G.L., Sormaz, M., Wang, H.-T., Margulies, D., Jefferies, E., Smallwood, J., 2017. The role of the default mode network in component processes underlying the wandering mind. *Soc. Cogn. Affect. Neurosci.* 12 (7), 1047–1062.
- Rogers, M.L., Joiner, T.E., 2017. Rumination, suicidal ideation, and suicide attempts: a meta-analytic review. *Rev. Gen. Psychol.* 21 (2), 132–142.
- Sadeh, N., Baskin-Sommers, A., 2017. Risky, impulsive, and self-destructive behavior questionnaire (RISQ): a validation study. *Assessment* 24 (8), 1080–1094.
- Smith, J.M., Alloy, L.B., 2009. A roadmap to rumination: a review of the definition, assessment, and conceptualization of this multifaceted construct. *Clin. Psychol. Rev.* 29 (2), 116–128.
- Sorg, Sonja, Vögele, Claus, Furka, Nadine, Meyer, Andrea Hans, 2012. Perseverative thinking in depression and anxiety. *Front. Psychol.* 3, 20.
- Sylvester, C.M., Corbetta, M., Raichle, M.E., Rodebaugh, T.L., Schlaggar, B.L., Sheline, Y. I., Lenze, E.J., 2012. Functional network dysfunction in anxiety and anxiety disorders. *Trends Neurosci.* 35 (9), 527–535.
- Taylor, W.D., Boyd, B., McQuoid, D.R., Kudra, K., Saleh, A., MacFall, J.R., 2015. Widespread white matter but focal gray matter alterations in depressed individuals with thoughts of death. *Prog. Neuro-Psychopharmacol. Biol. Psychiatry* 62, 22–28.
- Veit, R., Kullmann, S., Heni, M., et al., 2014. Reduced cortical thickness associated with visceral fat and BMI. *NeuroImage: Clin.* 6, 307–311.
- Wagner, G., Schultz, C.C., Koch, K., Schachtzabel, C., Sauer, H., Schlösser, R.G., 2012. Prefrontal cortical thickness in depressed patients with high-risk for suicidal behavior. *J. Psychiatr. Res.* 46 (11), 1449–1455.
- Yan, C.-G., Chen, X., Li, L., Castellanos, F.X., Bai, T.-J., Bo, Q.-J., Chen, W., 2019. Reduced default mode network functional connectivity in patients with recurrent major depressive disorder. *Proc. Natl. Acad. Sci.* 116 (18), 9078–9083.
- Yue, Q., Martin, R.C., Hamilton, A.C., Rose, N.S., 2019. Non-perceptual regions in the left inferior parietal lobe support phonological short-term memory: evidence for a buffer account? *Cereb. Cortex* 29 (4), 1398–1413.
- Zhao, K., Liu, H., Yan, R., Hua, L., Chen, Y., Shi, J., Yao, Z., 2017. Cortical thickness and subcortical structure abnormalities in patients with major depression with and without anxious symptoms. *Brain Behav.* 7 (8), e00754.