Suicidal thoughts and behaviours among military veterans: protocol for a prospective, observational, neuroimaging study

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ABSTRACT

Introduction This study’s overarching goal is to examine the relationship between brain circuits and suicidal thoughts and behaviours (STBs) in a transdiagnostic sample of US military veterans. Because STBs have been linked with maladaptive decision-making and disorders linked to impulsivity, this investigation focuses on valence and inhibitory control circuits.

Methods and analysis In this prospective, observational study, we will collect functional MRI (fMRI), cognitive and clinical data from 136 veterans (target sample size) recruited from the Providence VA Health System (PVaHS): 68 with STBs and 68 matched controls. Behavioural data will be collected using standardised measures of STBs, psychiatric symptoms, cognition, functioning and medical history. Neuroimaging data will include structural, task and resting fMRI. We will conduct follow-up interviews and assessments at 6, 12 and 24 months post-enrolment. Primary analyses will compare data from veterans with and without STBs and will also evaluate whether activation and connectivity within circuits of valence and inhibition covary with historical and prospective patterns of suicidal ideation and behaviour.

Ethics and dissemination The PVaHS Institutional Review Board approved this study (2018–051). Written informed consent will be obtained from all participants. Findings from this study will be published in peer-reviewed journals and presented at local, regional, national and international conferences. Nauder Namaky, Ph.D.* nauder_namaky@brown.edu

INTRODUCTION

Suicide is a significant problem among veterans. Approximately 30,000 veterans have died by suicide since 11 September 2001, which is more than four times the number of combat deaths in the same period. Suicide rates are 1.5 times higher in veterans than the general population. Almost 50% of veterans report exposure to suicide, which roughly doubles the risk of suicidal ideation, and diagnosable depression and anxiety. With suicide rates rising over the past 20 years, there is a crucial need for a better understanding of suicidal thoughts and behaviours (STBs) to improve prevention and intervention.

Functional MRI (fMRI) of STB is a growing subfield of suicide research (for a comprehensive review, see a study conducted by Schmaal et al.). Risk and value-based decision-making task paradigms have been widely used in fMRI studies of STBs, particularly in individuals diagnosed with depression with histories of suicidal ideation or attempt. This focus on decision-making is motivated by the long-standing association of STBs with maladaptive choice behavior and risky behaviors including gambling and excessive substance use. STBs are associated with decreased activation in the orbitofrontal cortex (OFC) when making risky choices and in the ventromedial prefrontal cortex (VMPFC) during value-based choice paradigms. Studies using the ‘delay discounting’ reward devaluation task have observed more pronounced discounting in individuals with suicide attempt histories, a characteristic negatively correlated with striatal volume in fMRI studies of STBs. These

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Recruitment from both inpatient psychiatric units and outpatient mental health settings permits the evaluation of transdiagnostic biomarkers across the spectrum of suicidal ideation and behaviour.
⇒ Two-year follow-up phase permits investigation of predictors of longitudinal outcomes.
⇒ The use of individualised imaging methods reduces intraindividual noise due to individual differences in anatomical and functional brain organisation.
⇒ Limiting enrolment to veterans receiving care at Veterans Affairs may limit generalisation to a lower-risk veteran population or a non-veteran population.
⇒ Reliance on prescreening medical charts as an enrolment strategy is limited to information as it is reported in clinical notes.
three regions—OFC, VMPFC and striatum—contribute to various aspects of valence, that is, reward or feedback processing, recommending valence circuits for additional study.

Top–down inhibitory control and related neural correlates have also been associated with STBs in the extant literature. Among high-risk populations for STBs, self-reported weak response inhibition is predictive of suicide risk, even when controlling for internalising and externalising psychopathology. Moreover, individuals with a previous suicide attempt exhibit further behavioural inhibition impairments when compared with individuals with suicidal ideations who have not attempted suicide. Differences in inhibitory circuit response during behavioural inhibition tasks are associated with the presence of STBs in psychiatric patients (see a study conducted by Schmaal et al. for a comprehensive review), further suggesting that investigating these circuits is critical for understanding the neurological bases of suicidal ideation and the conversion of ideation to suicidal behaviours.

Importantly, suicide is a transdiagnostic phenotype and highly heterogenous psychiatric presentations drive STBs. While earlier suicide research has often taken a focused approach towards operationalising STBs (eg, focusing on one diagnosis, categorising all STBs as one phenotype), there are empirical and theoretical justifications for more fine-grained measurement and analysis. Transdiagnostic approaches to studying neural correlates of STBs can help differentiate which biological associations are universal, related to specific suicide subtypes and driven by individual heterogeneity. This information will be critical in helping to refine our understanding of the various causes of suicide and identifying potential biological targets for intervention.

The goal of this prospective, observational, neuroimaging study is to examine the relationship between STBs and positive valence and inhibitory control circuits. We will compare data from veterans with and without STBs and evaluate whether circuit activation and connectivity predict different historical and prospective patterns of STBs. We will use neuroimaging, cognitive and clinical data to evaluate collected from veterans over 48 months for hypothesis testing.

METHODS AND ANALYSIS

Overview

The current study consists of five sessions: a baseline interview, a cognitive testing and MRI session and three follow-up interview sessions (at 6, 12 and 24 months post-baseline) (figure 1). All procedures will take place at the Providence VA Health System (PVAHS) located in Providence, Rhode Island, USA. Procedures have been approved by the Institutional Review Board and abide by the Declaration of Helsinki principles and the Medical Research Involving Human Subjects Act. The PVAHS Center for Neurorestoration and Neurotechnology Veteran Research Engagement Committee made recommendations for recruitment strategies and broader engagement of the veteran population.

Study population and recruitment

We aim to recruit 136 veterans aged 18–70 receiving care at PVAHS. Two groups of participants will be recruited: (1) Veterans that have attempted suicide in the last 30 days (n=34) or with suicidal ideation in the past 2 weeks (n=34) and (2) veterans (n=68) without current STBs. This recruitment target was set based on the minimum sample size required for our planned, prospective, regression analyses assuming a medium effect size (f2=0.15, see Hypothesis testing below for descriptions of our planned analyses and required sample sizes). Exclusion criteria will be: (1) a primary psychotic disorder (B/C module of the Structured Clinical Interview for Diagnostic Statistical Manual-5 (DSM-5)), (2) MRI contraindications, (3) history of moderate-to-severe traumatic brain injury.

Figure 1 Study workflow. FT, Flanker Task; IGT, Iowa Gambling Task; MCQ, Monetary Choice Questionnaire.
from each participant, we will collect electronic health record data. We will collect electronic health record data from each participant, we will obtain written informed consent from all participants. See Table 1 for full inclusion and exclusion criteria. Recruitment and data collection for the study is currently underway. We anticipate that MRI data collection will be completed by 01 December 2023. Follow-up visits will continue until 24 months after the recruitment of the final study participant.

**Electronic health record data**

After obtaining a signed Health Insurance Portability and Accountability Act of 1996 (HIPAA) release form from each participant, we will collect electronic health record (EHR) data from the Providence VA Computerised Patient Record System. EHR data will be collected for the 3-year period beginning 12 months before baseline and ending 24 months after baseline. The total number of mental health encounters and hospitalisations will be manually recorded by study staff in 12, 3-month increments.

Mental health encounters are defined as an in-person or remote interaction with a licensed mental health clinician lasting 10 or more minutes in which participants receive individual or group psychotherapy, individual or group counselling and/or psychiatric medication management. Mental health hospitalisations are defined as an admission for which the primary diagnosis is psychiatric.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
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<tr>
<td>All participants</td>
<td>► Veteran status.</td>
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<td>► 18–70 years.</td>
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<td>► Capable of providing written informed consent.</td>
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<td>► Primary psychotic disorder.</td>
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<td>► MRI contraindications.</td>
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<td>► Unstable medical conditions.*</td>
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<td>► Neurological disorder.</td>
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<td>► Lifetime history of seizures, CNS tumours, stroke, cerebral aneurysm.</td>
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<td>► Active moderate-to-severe substance use disorder.</td>
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*Any medical condition that has not been treated within the last month.

CNS, central nervous system; C-SSRS, Columbia-Suicide Severity Rating Scale, Baseline and Screening Version; DSM-5, Diagnostic and Statistical Manual-5; SA, Suicide Attempt; SI, Suicidal Ideation; STBs, suicidal thoughts and behaviours; TBI, traumatic brain injury.

**Clinical and cognitive assessments**

Following consent, all participants will undergo an eligibility evaluation (Figure 1). Eligible participants will complete a battery of structured interviews and self-report instruments assessing psychiatric diagnoses and symptoms, cognition, suicidal ideation or behaviour, trauma exposure, sleep and impulsivity. Participants will complete an abbreviated version of the battery at 6-month, 12-month and 24-month follow-up visits. Staff administering structured interviews and self-report instruments will be trained and supervised by a licensed clinical psychologist. Interviews will be recorded and evaluated during reliability meetings. See Table 2 for the complete assessment schedule.

**MRI data collection procedures**

Scanning will occur within 2 weeks of the baseline interview. We will brief participants on MRI safety and procedures prior to scanning. Images will be collected using a Siemens (Erlangen, Germany) Prisma 3T MRI scanner and a 64-channel head coil. Visual stimuli will be presented on an MRI-safe display screen positioned behind the scanner that can be viewed using a mirror affixed to the head coil. Task responses will be collected using an MRI-compatible fibre optic response pad (Current Designs) connected to the MacBook Pro.

**Structural MRI**

We will collect a high-resolution T1-weighted multi-echo MPRAGE from each participant (voxel=1.0mm³, in-plane matrix=256x256, slices=176, sagittal orientation, echo time (TE)=1.69, 3.55, 5.41, 7.27 ms, repetition time (TR)=2530 ms, flip angle=7 degrees).
Functional MRI

All fMRI runs will be collected using a gradient echo echo-planar imaging sequence (68 transverse slices, voxel=2.0 mm³, TR=1110 ms, TE=27 ms, field-of-view=104 mm², flip angle=62, echo spacing=0.74, multiband factor=4, GeneRalized Autocalibrating Partial Parallel Acquisition, GRAPPA=2).

Each task run will be acquired twice in opposing phase-encoding directions which are aligned using a non-linear registration procedure to distribute directional susceptibility artefacts to enable correction for magnetic field susceptibilities. Participants complete the two runs consecutively, performing half of each tasks’ trials in each run.

Functional MRI

Resting state

Two, 6 min runs of resting state fMRI will be obtained while participants rest quietly while visually fixating on a white crosshair rendered on a black screen.

The Stop Signal Reaction Time task

The Stop Signal Reaction Time (SSRT) task is an experimental paradigm used to study response inhibition, that is, the ability to stop an action in progress. The SSRT task is readily adapted to the MRI environment and has been widely used to study response inhibition in various clinical populations (eg, obsessive compulsive, bipolar, substance use and attention deficit hyperactivity disorders).

On each trial of the SSRT task, participants rapidly indicate the direction of a white arrow (left or right, 50/50 probability), but withhold responses if a visual cue (the arrow turning red, ‘stop signal’) is presented. Non-responses on Go trials and responses on Stop trials are considered performance errors. The latency between the go and stop cues (‘stop signal delay’) will increase after stop failures and decrease after successful inhibition. The task is divided into two, 128 trial scanner runs, (96 Go, 32 Stop). See figure 2 for task schematic. We will estimate SSRT according to the quantile method.

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### Table 2

<table>
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Continued
The incentive processing task

This incentive processing task indexes brain activity associated with processing reward and punishment and is adapted from the version used by the Human Connectome Project. The incentive processing task has been used to study reward processing in clinical populations including those with mood disorders, schizophrenia and eating disorders. On each trial, the participant is prompted (?) to guess whether the value of a subsequent card cue (range=1–9) is higher or lower than five via button press. After a brief, variable delay (mean=0.5 s), participants are presented with a feedback screen (1.0 s) showing either: (1) a green arrow with a '$1' reward for correct guesses, (2) a red arrow and a ‘−$0.75’ loss for incorrect guesses; or (3) a grey arrow for neutral (no reinforcement) trials wherein the card's value is 5. The monetary value of rewards and punishments was chosen to match those used by Chase and colleagues, and matching the US$0.25 difference used in previous studies with clinical populations. Feedback is predetermined and standardised across participants. The task is presented as a series of six-trial blocks composed of mostly reward or loss trials, with interleaved 15 s fixation blocks. The task is divided into two, 48 trial scanner runs (see figure 3).

Experimental task procedures

Outside of the scanner, all participants will complete a battery of decision-making and executive function tests derived from the PhenX Toolkit (www.phenxtoolkit.org) and the NIH Toolbox (www.healthmeasures.net).

The Monetary Choice Questionnaire

The Monetary Choice Questionnaire (MCQ) measures how a reward’s size and immediacy influence its perceived value and impact on decision-making. The MCQ has been used to examine decision-making in individuals with STBs. During MCQ trials, participants choose between a hypothetical small, immediate reward and a larger, delayed option. We will calculate subjects' delay discounting rate following the guidelines in Kirby using the following equation:

\[ V = \frac{A}{1+kD} \]

where \( V \) is the delayed reward’s (A) present value at delay (D), and \( k \) is the rate of discounting.

The Iowa gambling task

The lowa gambling task (IGT) examines how risk influences decision-making and has been used in numerous clinical populations, including those with suicidal behaviour. During each trial of the IGT, participants select a card from one of four decks with varying reward probabilities. Two ‘high-risk’ decks yield large wins and losses, whereas the ‘low-risk’ decks yield smaller rewards and punishments. Participants that learn to avoid the high-risk decks will accrue a small profit, whereas favouring high-risk decks will incur a large loss, across trials. Risk tolerance is operationalised as the proportion of high versus low-risk gambles across the experiment. This proportion will be used to estimate individuals’ risk tolerance.

Figure 2 Stop-signal reaction time task. On each trial of the SSRT, participants report whether a white arrow points right or left by keypress. During Stop trials, the white arrow turns red (stop-signal) after a brief ‘stop signal delay’ (SSD), signalling the participant to withhold their response. The SSD adapts to performance changing ±50 ms between stop trials. Fixation events are interspersed between trials. Left. SSRT Go-Trial timing. Right. SSRT Stop-Trial timing. SSRT, Stop Signal Reaction Time.

Figure 3 Incentive processing task. On each trial of this modified card guessing task, participants make a 50/50 guess about whether the number on a card is higher or lower than 5 (range=1–9). Correct guesses are rewarded with a green up arrow and US$1.00 added to their total winnings, incorrect guesses are punished with a red down arrow and US$0.75 removed from their total winnings and neutral guesses, in which the number on the card was five, receive a grey double-sided arrow and no change to total winnings. The example trial above shows all three feedback options with total winnings at US$1.00.
The flanker task

The flanker task[^67][^68] has been used to study attention and inhibitory control in mood disorders,[^69][^70] borderline personality disorder[^71] and TBI.[^72] Participants report the direction a central arrow points in trials of the flanker task. This central arrow is surrounded by others pointing in the same (congruent) or opposite (incongruent) direction. Incongruence between the central and surrounding stimuli introduces interference and taxes inhibitory control.[^73][^74] Accuracy and reaction time are calculated over each trial. Overall task score is computed on a combination of accuracy and reaction times. Lower scores are associated with decreased ability to attend to important stimuli and inhibit attention from unimportant stimuli. The flanker task will be scored using the NIH Toolbox algorithm, which calculates a normalised standard score and an age-corrected standard score following the procedures of Casaletto et al.[^75]

**Data analysis**

**MRI analysis**

MRI quality control, pre-processing and statistical modelling will be carried out using community developed and vetted, open-source software.

**Organisation and initial quality control**

Raw MRI data will be converted to the NiTi-1 file format using the Python-based HeuDiConv[^76] (V.0.9.0). Imaging data will be named and organised following the Brain Imaging Data Structure framework (V.1.7.0).[^80] Images will be visually inspected for artefacts using FSLeyes[^81] (V.6.0.5.1). MRIQC[^80] (SINGULARITY V.22.0.6), will be used to extract image quality metrics (IQMs) from fMRI data. Images that fall outside 1.5 times IQR of the upper or lower quartile on at least three IQMs will be flagged for further individual evaluation. We will also apply the exclusion threshold of mean framewise displacement >0.55 mm full-width, half max Gaussian kernel. Next, simultaneous bandpass filtering (0.008–0.15 Hz) and nuisance regression will be applied to remove estimated artefacts.[^90] Though controversial[^91], we will perform global signal regression, as it is the most effective method for removing globally consistent, non-neural signals (eg, motion, respiratory).[^83] Then, non-aggressive de-noising with the first 100 estimated ICA-AROMA noise components will be performed.[^90]

**Defining individualised regions of interest**

Functional regions-of-interest (ROIs) will be located for each participant using procedures adapted from Wang et al.[^86] We will obtain group-level functional-anatomical labels from the 400 region parcellation of Schaefer et al and will map them to each subject using an iterative parcellation algorithm. This procedure involves projecting the group-level atlas onto each participant’s respective cortex image and subsequent refinement of parcellation boundaries through an iterative validation procedure (see[^92] for details). The algorithm weights intraindividual activation patterns more heavily than the initial functional atlas, maximising the contribution of each participant’s unique data. For each participant, masks consisting of selected individualised ROIs will be used for the analyses of activations and functional connectivity outlined below.

**Task-based univariate models**

SSRT and the incentive processing tasks data will be analysed with FMRI Software Library FSL V.6.0.5,[^93] and MATLAB R2021a.[^94] Subject-level design matrices will be built using FSL. Matrix condition vectors (defined by event onsets and durations) will be convolved with a double-gamma haemodynamic response function and its first and second derivatives. Matrices will also include confound regressors for six translational/rotational motion parameters and framewise displacement. Task models (detailed below) will be estimated with FSL’s FILM.[^95]

**Stop Signal Reaction Time task**

Design matrix will include regressors for Go, Stop Inhibit and Stop Fail trials. Go Errors and intertrial intervals will be treated as nuisance events. We will compute two contrasts for hypothesis testing, (Stop Inhibit-Go) and (Stop Inhibit-Stop Fail).

**Incentive processing task**

The design matrix will contain regressors for Reward, Punishment and Baseline blocks (16s null inter-block intervals). We will compute two contrasts for hypothesis testing, (Reward-Punish) and (Punish-Reward).
Group-level ROI models
FSL tools will be used to extract data from subject-level z-statistic maps for critical task contrasts. For each participant, we will compute the average contrast estimate for each ROI and critical contrast.

Functional connectivity models
Following preprocessing, unsmoothed, resting-state preprocessed MRI data will be warped to individual-space and the mean time series will be extracted from a subset of ROIs from subjects’ individualised Schaefer parcellation. ROIs will include regions of the valence network: bilateral striatum, OFC, VMPFC and insula and regions involved in response inhibition: right pars triangularis and opercularis, bilateral pre-supplementary motor area (pre-SMA), bilateral insula and bilateral dorsal anterior cingulate. Extracted time courses will be cross-correlated and correlation coefficients converted to z-scores using Fisher’s r-to-z transformation. The resulting ROI-to-ROI connectivity scores will be entered into SPSS statistical models for hypothesis testing.

Experimental tasks’ scoring and analyses
All analyses will be conducted using MathWorks MATLAB R2021a, except for the NIH Toolbox flanker task for which summary statistics are automatically computed by the application.

Hypothesis testing
Outcomes
This study will examine the relationship between STBs and positive valence and inhibitory control circuits in a veteran population. The Columbia-Suicide Severity Rating Scale (C-SSRS), administered during the baseline interview, assess suicidal ideation with five, yes/no items. These items ask if individuals have experienced a wish to be dead, non-specific suicidal thoughts, active suicidal ideation without intent to act, active suicidal ideation with some intent to act and/or active suicidal ideation with a specific plan and intent, respectively, in the 2 weeks prior to assessment.

We will define current ideation as any ‘yes’ response to ideation items of the C-SSRS and current suicidal behaviour as endorsement of an actual, interrupted or aborted lifetime suicide attempt. We will explore the potential effects of ideation severity, defined as the maximum ideation items endorsed on C-SSRS, impulsivity, depression, anxiety, sleep and Montreal Cognitive Assessment scores on primary outcomes in post hoc sensitivity analyses.

Given that females comprise approximately 8% of the total veteran population of Rhode Island, we anticipate being underpowered to address biological sex differences statistically. Our a priori statistical power estimates below were computed with G*Power V.3.0. Unless stated otherwise, estimates assume medium sized effects (d=0.5), per Cohen’s effect size taxonomy (1988), with alpha=0.05 and power=0.8.

Hypothesis 1
Greater risk tolerance, biases toward immediate reward, and hyper or hypo fMRI activation to reward feedback will differentiate veterans with and without STBs (both ideation and attempts), at baseline. Groups will be delineated by (1) the absence of STBs, (2) current ideation only or (3) suicidal behaviour, within 2 weeks of the baseline interview. We define the valence network as bilateral striatum, OFC, VMPFC and insula. Separate analysis of variance (ANOVA) models will evaluate risk tolerance (propensity of risky IGT choices), preference for immediate reward (delay discounting rate), valence network functional connectivity or ROI activation during the incentive processing task. A minimum sample size of 42 is required for all models, except for task activation models which require 66, after Bonferroni adjustment for 8 ROIs.

Hypothesis 2
Greater susceptibility to interference, less efficient inhibition and weaker circuit engagement during inhibition, will differentiate veterans with and without STBs, at baseline. We define the inhibitory circuit as right pars triangularis and opercularis, and bilateral pre-SMA, insula and dorsal anterior cingulate. Separate ANOVA models will be used to evaluate the effect of a group on susceptibility to interference (incongruent flanker errors), response inhibition efficiency (stop signal reaction time), inhibitory network functional connectivity or ROI activation during the SSRT task. A minimum sample size of 42 is required for all models, except for task activation models which require 66, after Bonferroni adjustment.

Hypothesis 3
Within veterans with STBs, greater valence circuit disruption will be associated with more frequent attempts and hospitalisations, and heavier usage of mental health services, historically and prospectively. We speculate that circuit dysfunction underlies cognitive distortions (eg, hopelessness, negative self-evaluations) contributing to suicidal thoughts and undermines more adaptive problem solving and coping strategies. Regression models will be used to evaluate the effect of the independent variables of (1) valence network connectivity and (2) incentive task activation on three separate outcomes: (1) attempt frequency, defined as the sum of all actual, interrupted or aborted suicide attempts, (2) total mental-health hospitalisations and (3) usage defined as total number of mental health encounters. Historical attempts will be derived from total number of lifetime suicidal behaviours reported on the C-SSRS during the baseline interview. Prospective attempts will be total number of suicidal behaviours disclosed since baseline during the 24-month follow-up interview. Mental health hospitalisations will be derived from interviews and EHRs. Usage will be derived from the total number of mental health encounters documented in electronic records. Hospitalisation and usage will be computed for the 12 months preceding baseline (historical) and for the 6-month, 12-month and 24-month.
follow-up time points (prospective). Assuming a medium effect size ($f^2=0.15$), a minimum sample size of 68 is required for a two-predictor regression model.

Hypothesis 4
Within veterans with STBs, lesser inhibitory circuit disruption will be associated with fewer past attempts and hospitalisations, and prospectively with lower usage of mental health services. We speculate that better inhibitory control facilitates behavioural regulation reducing suicidal and other behaviours initiating mental health referrals, despite the presence of ideation. Testing follows hypothesis 3 procedures, substituting (1) inhibitory network connectivity and (2) SSRT task activation as the independent variables.

Exploratory hypothesis
Within veterans with STBs, distinct, longer-term patterns of STBs emerge from the combination of valence and inhibitory control signatures. More specifically, we hypothesise that strong inhibitory control coupled with blunted feedback sensitivity will be associated with a proposed chronic biotype, whereas poor inhibitory control and feedback hyperactivity will typify a distinct high variability biotype. For each participant, we will compute the average monthly variance in usage across historical and prospective time points and will median split the sample into high and low variability subgroups. We will then enter connectivity and activation metrics from both valence and inhibitory circuits, into regularised regressions predicting variability profile.

Patient and public involvement
None.

ETHICS AND DISSEMINATION
Ethics approval and consent
The PVaHS Institutional Review Board approved this study (2018–051). Written informed consent will be obtained from all participants.

Handling of data and documents
All interviews, self-reports, behavioural and fMRI data will be labelled with anonymised study identifiers. Only researchers involved directly with this study will have access to encoded data. All data handling and sharing procedures were reviewed and approved by the Providence VA Institutional Review Board (IRB), Privacy Officer and Information Security Officer. Data collected for this study cannot be shared without a prior Data Sharing Agreement approved by the Department of Veterans Affairs.

Dissemination
We will submit study results for publication in peer-reviewed journals and presentations at local, regional, national and international conferences.

DISCUSSION
Limitations
This study has several limitations. First, because we have limited enrolment to veterans receiving care at VA, we may be under sampling veterans at highest risk. Deaths from suicide are elevated in veterans receiving care outside, versus inside of the VA health system. We also note that because our enrolment strategy is built around prescreening charts, the degree to which our sample is representative of veterans is limited by the information in clinical notes. Initially, we planned to recruit participants in the STB group from the psychiatric inpatient unit. Due to the COVID-19-2019 pandemic, however, we expanded recruitment to outpatient locations as inpatient psychiatric beds were converted to medical use or used for COVID-19-positive psychiatric inpatients. Participants recruited from the outpatient units are typically approached within several days of reporting suicidal thoughts or behaviours to their providers, whereas approach on the inpatient unit is usually more rapid. We also acknowledge the known limitations of our sample size on reproducibility.

Strengths
As a 2-year study, the longer follow-up period will allow us to explore long-term patterns involving STBs and clinical symptoms. Additionally, as our study sample is obtained from a VA Health System, a closed system of healthcare, we can obtain a more comprehensive profile of participants’ health and healthcare usage. Finally, this study uses an individual-specific method for identifying functional connectivity networks of interest. This allows our analyses to account for individual differences in anatomical and functional brain organisation among participants, reducing the likelihood of detecting spurious associations driven by these differences. Further, given the heterogeneity of underlying psychiatric profiles related to suicide, it is theoretically appropriate to investigate the degree to which individualised brain processes contribute to STBs.

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Contributors JB designed the study protocol and is the principal investigator. HRS, JW, NN and JB wrote the initial manuscript draft. MB, JMP and NSP reviewed the draft critically for important intellectual content. NN, HRS, JW, MB, JMP, NSP and JB approved the final manuscript and accepted responsibility for the work’s accuracy and integrity.

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Data availability statement Data may be obtained from a third party and are not publicly available. All data handling and sharing procedures were reviewed and approved by the Providence VA IRB, Privacy Officer and Information Security Officer. Data collected for this study cannot be shared without a prior Data Sharing Agreement approved by the Department of Veterans Affairs.

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