Neuroanatomical Biomarkers for Suicidality in Dissociative Identity Disorder

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Abstract

This study investigated the potential of incorporating neuroanatomical biomarkers into suicidality research in those with Dissociative Identity Disorder (DID), more specifically variability in cortical thickness, to better provide a foundation in DID research that could lead to improved development of treatments, preventative measures, and better assessments for suicide and self-harm risk in those with DID. Ninety-seven participants were recruited with 24 controls and 73 patients diagnosed with Dissociative Identity Disorder and comorbid Post-Traumatic Stress Disorder (PTSD) via a psychiatric hospital in the northeastern United States. We used a standard set of qualitative assessments to measure characteristics such as PTSD, frequency of childhood maltreatment, dissociative disorder prevalence, dissociative symptom severity, depression severity, and suicidal tendancies in our patients. Patients were placed into a magnetic resonance imaging machine (MRI) for a structural image of their brains for no longer than ten minutes. We used machine learning to analyze the structural MRI images for abnormal cortical thickness in each patient and mine for patterns that correspond with the abnormal cortical thickness and their clinical assessment responses. We found nine regions with abnormal cortical thickness, all known to be associated with memory, visual processing, emotion regulation, language processing, social perception and cognition, and self-awareness. These regions have associations with both suicidality and DID symptomologies. Providing this neuroanatomical basis allows us to provide a foundation to suicidality and DID research that was previously unavailable, in the hopes that future research will build upon our results to better treatments and preventative measures for those with DID.

Keywords: Dissociative Identity Disorder, Suicidality, Neuroanatomical Biomarkers, Cortical Thickness, Machine Learning, Artificial Intelligence.

Neuroanatomical Biomarkers of Suicidality in Dissociative Identity Disorder

Dissociative Identity Disorder (DID) occurs when an individual has two or more separate identities (or personality states; DSM-5, 2013). While those who have DID are more likely to engage in self-harm, suicide attempts, and completed suicides (Kluft, 1995; Webermann et al., 2016; Foote et al., 2008; Galbraith & Neubauer, 2000; Tanner et al., 2017), much of the research to date on suicide has excluded individuals with DID from the research (Foote, et al., 2008). One reason for this exclusion is that it becomes difficult to identify and treat suicidal ideations and behaviors when an individual has multiple, often competing, identities. Moreover, traditional methods of studying suicidality (e.g., self-report and diagnostic measures) are less reliable when an individual completes it with one identity and then another identity emerges (see Rifkin, et al., 1998 for more on this issue). Given the limited research, the current study seeks to examine suicidality with individuals with DID. To account for the complexities of understanding suicidality with individuals with DID, we rely on structural MRI images which can help us assess the current suicide risk as well as past history of suicide based on cortical thickness (width of the gray matter in the brain) of associated regions (Tahedl, 2020). Thus, this study aims to develop a neuroanatomical foundation of suicidality in DID to be used towards achieving a better understanding of the neural mechanisms behind suicidality for those with DID, to improve suicide and self-harm risk assessment, as well as improve preventative measures and treatments. More specifically, this study aimed to use abnormal cortical thickness in order to highlight regions of interest that may be associated with suicidality in those with DID. Past research shows that abnormal cortical thickness has significant associations to both intellectual ability, social cognition, and other aspects of cognition including verbal recall and visuospatial functioning (Menary et al., 2013; Serra et al., 2020; Sowell et al., 2008).

Dissociative Disorders are rare disorders with DID specifically affecting about 1% to 1.5% of the global population (Mitra & Jain, 2021). Dissociative disorders are defined by the dysfunction they cause with memory, behavior, identity, and one's sense of self (Kihlstrom et al., 1994). More specifically, those with these disorders often have gaps in memories ranging from their everyday memories to specific memories about traumatic events. Along with this, individuals experiencing a dissociative disorder often report feeling as if they are outside of their body, and feel as if they are more of an observer of themselves than the person in control of their own actions, emotions, and thoughts. These feelings of not being in control of their own senses of selves usually stem from reports of hearing multiple voices all at once, as well as their own perceived sense of control over themselves alters with their current identity state (DSM-5, 2013). In addition to these dysfunctions and symptoms, those with DID tend to display high instances of self-harm and high rates of suicide (Kluft, 1995). Overall, dissociative disorders, including DID, tend to affect women more than men at a 9 to 1 ratio (Spitzer et al., 2003).

Suicidality and Dissociative Identity Disorder

Suicidality is defined by a combination of suicidal ideation, plans of suicide, as well as suicide attempts (VandenBos, 2007). According to the World Health Association, roughly 800,000 people die per year from suicide, globally, independent of any psychological factors (Sudol & Mann, 2017). One issue with global suicide statistics is that they often do not include those experiencing psychiatric disorders, including those with DID, where the suicide rates are even more drastic.

According to the DSM-5, DID is often linked to past suicide attempts and physical self-harm (Webermann et al., 2016), noting that over 70% of those diagnosed with DID have attempted suicide at least once (Foote et al., 2008; Webermann et al., 2016). Overall, around 67% of those with DID have attempted suicide multiple times (Foote et al., 2008), and around 1 - 2% of those with DID complete their suicide attempts (Kluft, 1995, Galbraith & Neubauer, 2000). Along with this, an experiment conducted with outpatients at a psychiatric clinician Switzerland found that 23.5% of those with DID attempted suicide at least once during a 12 month observation period, while 0% of the outpatients without DID attempted even once during the same observational period (Tanner et al., 2017). In comparison to the average population, those with DID attempt suicide at least once 70 times more (Foote et al., 2008; Webermann et al., 2016). In our patient population for our study, this rate was even higher, where 77% of patients diagnosed with DID attempted suicide at least once, making our cohort attempt suicide at a rate almost 77% more than the average population.

Suicide and suicide attempts also differ between men in women. Specifically for suicidality independent of DID, research has found that in general, men commit suicide at a higher rate, but women attempt to commit suicide more (O'Rourke et al., 2021; O'Loughlin & Sherwood, 2005). Though there are no sex or gender statistics investigating suicide in DID patients, with these existing statistics we can infer that since dissociative disorders affect women more than men, most of the DID patients who attempt suicide are women.

Childhood Trauma, Dissociative Identity Disorder, and Posttraumatic Stress Disorder

In research involving DID, patients are often co-diagnosed with Post-traumatic Stress Disorder (PTSD). PTSD is a psychiatric disorder defined by intense distress and dysfunction in all aspects of life due to intrusive and involuntary symptoms following a month after exposure to traumatic event(s)(DSM-5, 2013). These symptoms include distressing memories, dreams or nightmares, dissociative reactions (such as flashbacks, depersonalization, derealization), distress due to internal or external reminders or cues, avoidance of reminders, as well as negative changes in cognitions and mood - all in association with the traumatic event(s) (DSM-5, 2013).

Most studies using populations with DID involve investigating populations with a dissociative subset of PTSD (PTSD-DS), or with both DID and PTSD (Rodewald et al., 2011). This is due to their overlapping symptomatology; specifically their primary focus on dissociative tendencies caused by traumatic events and the emphasis on a dysfunction with memories. Both those with PTSD (Bryan, 2016) and DID (Foote et al., 2008) also show high instances of suicidal behavior and self-harm. One main difference between the two is how they are affected by their own memories. Those with DID often experience gaps in memory — whether they be everyday memories or specific past memories (Mitra & Jain, 2021) while those with PTSD may experience painful flashbacks to memories of trauma, or may also showcase a gap in memories surrounding the traumatic events (DSM-5, 2013).

DID and Suicidality Considerations

In those diagnosed with DID it is difficult to investigate suicidality using normal therapeutic or existing qualitative methods, due to their reliance on patient self-report and scale-based diagnostic techniques (Rifkin et al., 1998). In patients with DID, their dissociative symptoms force them to be considered an unreliable narrator (Gillig, 2009; Krause-Utz et al., 2017), thus making self-report ineffectual. More specifically, patients may not remember their past suicidal behaviors due to common amnesia and memory symptoms, as well as the patient's current or presenting identity state may not be the identity state that is responsible for suicidal tendencies and self-harm. By investigating the neural substrates of suicidality in those with DID, it will allow for clinicians to better treat and recognize suicide risk in DID affected populations because it will not rely on the own patient's memory or current identity state. Investigating neural substrates also will provide a neuroanatomical foundation that will allow for possible better regulation of medicinal treatments by targeting specific regions and related functions. Neural substrates are ideal in those with DID for many reasons, but mainly because neural substrates are not often affected by current personality state (Tsai et al., 1999). The current personality state and every other possible personality state all share the brain of one individual, which means that each personality state should see and share identical neural substrates (Tsai et al., 1999;), even if the patient's personality state has changed. This means that even if the patient is not in the suicidal identity state, clinicians and diagnostic professionals will be able to rely on similarities in brain regions when assessing overall risk of suicide and suicide behaviors.

Neural Substrates for those with DID

In order to begin our investigation of using neural substrates as a way to combat the high suicidality risk in those with DID, we needed to understand the pre-existing neural substrates associated with DID already. Although there is a discussed comorbidity between those with DID and suicidality (Kluft, 1995; Webermann et al., 2016; Foote et al., 2008; Galbraith & Neubauer, 2000; Tanner et al., 2017) there is a need for neuroanatomical research in order to better treat and diagnose those with DID as in danger of attempting suicide. From the research that exists so far, researchers have discovered that there is significant abnormal cortical thickness involved with particular regions in patients with DID. More specifically, most research has found that these decreases are most prevalent in the insula, the anterior cingulate, the lateral occipital cortex, the temporal cortex, as well as parietal and frontal cortices, most likely due to their roles in memory, fear, and emotion (Reinders et al., 2018; Perez et al., 2018; Chalavi et al., 2015). Researchers believe these regions show abnormal cortical thickness based on exposure to intense trauma, especially childhood trauma, and the experience of specific symptoms of dissociation such as feeling outside of one's body and depersonalization (Reinders et al., 2018;Perez et al., 2018; Chalavi et al., 2015). More specifically, abnormal cortical thickness in the anterior cingulate was found to be associated with high levels of somatoform dissociation, which is a type of dissociation used to describe specific forms of dissociative symptoms experienced as somatic disturbances due to alterations in the functions of consciousness, memory or identity specifically related to stressful experiences (Perez et al., 2018; Bob et al., 2013). Those with DID are known to suffer from high levels of somatoform dissociation (Nijenhuis, 2009), and research has shown that patients with higher levels of somatoform dissociation also show higher symptoms of traumatic stress, depression, anxiety, and alexithymia (a term used to define when a person has trouble identifying, describing, and distinguishing feelings in their body and cognitions) (Bob et al., 2013; Goerlich, 2018). When compared to the neuroanatomical evidence of suicidality, DID shares abnormal cortical thickness in the hippocampus, as well as possibly some parietal and frontal structures - structures known to be associated with memory, emotions and emotional behavior, and cognition (Anand & Dhikav, 2012; Budson & Solomon, 2016; Jankovic et al., 2022; Fuster, 1999). An implication for shared abnormal cortical thickness in both suicidality and DID could be correlated with the observation that many of those diagnosed with DID have past experiences with suicide attempts and/or suicidal ideation. Another implication of the shared cortical thickness could relate to the comorbidity of depression symptoms and suicidality, given the correlation between high levels of somatoform dissociation and depression symptoms (Vandivort & Locke, 1979; Jeon, 2011; Wagner et al., 2012; Bob et al., 2013). Overall, using neural substrates to study suicidality can be difficult due to the possibility of causal relationships between neuroanatomical changes, and whether or not these changes cause suicidality symptoms or if these changes are an effect of past suicide attempts and overall heightened levels of suicidality.

Neural Substrates Associated with Suicidality in All Populations

In addition to understanding the neural substrates behind DID, we also needed to investigate the established neural substrates involved with suicidality and how they may overlap with those involved with DID. Investigating suicidality from a neurobiological standpoint provides clinicians with more specific tools to assist with the diagnosis and prevention of suicidal behavior, especially in vulnerable populations such as those with DID (Balcioglu & Kose, 2018). Research shows that suicidality is linked to abnormal cortical thickness in areas of the brain in many regions as described in Table 1, including regions associated with memory and emotional behavior such as the amygdala, the anterior cingulate cortex, the hippocampus and the orbitofrontal cortex (Balcioglu & Kose, 2018; Wagner et al., 2012). Mainly, the problem with the existing neurobiological research on suicidality is that it tends to exclude those with dissociative disorders as part of their population and instead choose to either use populations that have people with multiple disorders or illnesses (excluding dissociative disorders) - such as bipolar disorder (Lijffijt et al., 2014; Johnston et al., 2017), schizophrenia (Aguilar et al., 2008; Spoletini et al., 2011), and depression (Wagner et al., 2012; Colle et al., 2014), however none of these studies focused on finding the neural substrates specific to those with dissociative disorders or disorders with high dissociative symptomatology.

Table 1

Neural substrates, function, and associated psychological link

Brain area/neural substrate	Area function
Suicidality	
Gray matter of prefrontal cortex	Control of movement, memory, emotions
White matter of prefrontal cortex	Axonal signal transmission (myelin), cognitive function
Orbitofrontal cortex*	Taste, touch, reward/punishment behavior, emotional behavior, reversal of stimulus-reinforcement associations
Left Angular Gyrus	Word processing, semantic processing, reading comprehension, number processing
Right Cerebellum	Reflexive and planned motor coordination, emotion and cognitive processes
Nucleus Raphe	Serotonin release
Nucleus lentiformis	Motoric coordination, executive function, attention, working memory, reward
Insula*	Sensory and affective processing, high-level cognition, sensorimotor processing
Hippocampus*	Learning, memory, spatial navigation, emotional behavior
Rectal gyrus	Language, memory recall, major depression
Superior temporal gyrus	Auditory and language processing, social cognition, autism
Caudate	Successful goal-directed action, effective behavior
Corpus Callosum	Abnormalities associated with early-life trauma
DID	
Anterior Cingulate Cortex*	Affect-regulation (The ability to control and manage uncomfortable emotions)
Parietal Structures	Language perception, perception of spatial orientation, spatial function
Frontal Structures*	Skeletal and eye movement, speech and logic reasoning,
Amygdala	Emotional learning, memory

Note. Areas that are associated with both DID and suicidality are marked by *. Gray matter information taken from (Mercadante, 2020). White matter information taken from (Filley & Fields, 2016; Bolandzadeh et al., 2012). Orbitofrontal cortex information taken from (Rolls, 2004). Left angular gyrus information taken from (Seghir, 2013). Right cerebellum information taken from (Witter & De Zeeuw, 2015). Nucleus raphe information taken from (Hornung, 2003). Nucleus lentiformis information taken from (Li et al., 2021). Insula information taken from (Uddin et al., 2017). Hippocampus information taken from (Anand & Dhikav, 2012). Rectal gyrus information taken from (Joo et al., 2016; Bremner et al., 2002). Superior temporal gyrus (Bigler et al., 2007). Caudate information taken from (Grahn et al., 2008). Corpus Callosum information taken from (Harker, 2018). Anterior Cingulate Cortex taken from (Stevens et al., 2011). Parietal structures taken from (Budson & Solomon, 2016; Jankovic et al., 2022). Frontal structures taken from (Fuster, 1999). Amygdala information taken from (Balleine & Killcross, 2006).

Findings Using the Same Patient Cohort

A previous study in preparation to be published, using a part of the same population cohort and the same methods for analysis as the study we conducted, used Artificial Intelligence (AI) and Machine Learning (ML) to identify dissociative patients and to predict and prevent suicide (Srinivasan et al., 2022). Their population involved more than just those with DID as well as they did not incorporate neuroanatomical methods such as structural MRI. They found one of the AI/ML algorithms (the unsupervised machine learning algorithm) identified patients along a spectrum of dissociation. They also found that the supervised machine learning algorithm accurately predicted a history of suicide attempts with an accuracy of 83% — overall they found that those with DID had the highest risk of suicide attempts, and distinct symptoms of dissociation, such as hearing voices and a lack of control over thoughts and actions, predicted suicide attempts in PTSD and DID (Srinivasan et al., 2022). They also found that when comparing the DID and PTSD/PTSD-DS groups, the odds of a patient attempting suicide was 140% higher in patients with DID and those with a DID diagnosis had a 40% increased risk of attempting suicide (Srinivasan et al., 2022). To go a step further, in addition to using this same AI method for suicide prediction, this study focused our patient group on those now defined as most at risk, (i.e., those with a primary diagnosis of DID, compared with controls), and wanted to use a neuroanatomical measure, structural MRI data, to predict suicidality. This is due to an issue using purely clinical characteristics such as qualitative assessments, for example the Beck Depression Inventory-II (BDI-II). The BDI-II has an item to predict suicide and is often relied on in studies investigating suicidality, but was found to be very poor at accurately predicting suicide in patients (Srinivasan et al., 2022). To combat this, we introduced the potential for using structural MRI as a way to predict suicidality and thus improve targeting of suicide risk and better assist suicide prevention. Structural MRI will also allow us to establish a foundation in DID research to understand the neural substrates involved with suicidality in this population, not currently available in research today.

Method

Participants

This study included 97 female participants (73 patients with DID, 24 individuals without DID) who were recruited at a psychiatric hospital in the Northeastern United States. The participants were mainly White (89.7%) and ranged between 18 to 62 years in age ($M = 34.6$), see Table 2 for a summary of the participants demographic and clinical characteristics. Participants were mainly right-handed (76%), while 7% were left-handed, 2% were ambidextrous, and 14% did not report hand dominance. During the study, the 73 patients diagnosed with DID received varied levels of care including inpatient, residential, and outpatient care, depending on the individual’s severity of symptoms. All 73 patients were diagnosed with PTSD and various levels of dissociation, including some with the dissociative subtype of PTSD (PTSD-DS), and some with dissociative identity disorder (DID) or a dissociative disorder not otherwise specified (DDNOS). Patients were excluded if they had a current alcohol or substance use disorder within the past month or a history of or current psychotic spectrum disorder through self-report methods provided by the psychiatric hospital. Control participants had no psychiatric diagnoses. The study was approved by the appropriate ethical institutional review boards. Informed consent was obtained from all research participants.

Materials

The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)

The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) is a 30-item structured diagnostic interview that assesses the diagnostic and symptom severity of PTSD (Weathers et al., 2018). The standardized questions assessed 20 defined PTSD symptoms according to the DSM-5, some examples include: “In the past month, have you had any unwanted memories of (insert the event) while you were awake, so not counting dreams?”, “How much do these memories bother you?”, ”How often have you had these memories in the past month?”, etc (Hamblen & Barnett, 2018). These are rated on a 5-point Likert-type scale from 0 to 4 by the clinicians themselves, and are completely up to their judgment. This might look like, a clinician rating a patient as “0” or “absent” for a certain PTSD criterion; or “3” for “severe/markedly elevated” meaning that a patient struggles with this PTSD criterion about 2x a week but it isn’t completely debilitating (Weathers et al., 2018).

The Childhood Trauma Questionnaire (CTQ)

The Childhood Trauma Questionnaire (CTQ) is a 70-item self-report measure that uses a 5-point Likert-type scale (1 being “ never true” and 5 being “very often true”) in order to assess experiences of abuse in childhood as well as childhood environment. Questions are organized based on four types of abuse: physical and emotional abuse, emotional neglect, sexual abuse, and physical neglect (Bernstein et al., 1998).

The Multidimensional Inventory of Dissociation (MID)

The Multidimensional Inventory of Dissociation (MID) is a 218-item self-report measure that uses a 11-point Likert-type scale (0 being “Never” and 10 being “Always”). One hundred and sixty eight items are used to assess dissociation (i.e., self-confusion, amnesia, angry intrusions, etc.) and the remaining 50 items are used as validity checks to assess things like defensiveness, emotional suffering, rare symptoms, attention-seeking behavior, factitious behavior, and a severe borderline personality disorder index. Some examples of the questions asked in this questionnaire include rating how often: “Things around you suddenly seem strange.” and “Feeling as if your body (or certain parts of it) are unreal” (Chu, 2011; Dell, 2006; Dell et al., 2017).

The Beck-Depression Inventory-II (BDI-II)

The Beck-Depression Inventory-II (BDI-II), is a 21-item self-report measure that uses a 4-point Likert-type scale (0 to 3), to assess the presence and severity of depressive symptoms. This is done through given items such as work inhibition or suicidal ideas. An example of the suicidal ideas item would be: 0 being “ don’t have any thoughts of killing myself”, 1 being “I have thoughts of killing myself but I would not carry them out”, 2 being “I would like to kill myself”, and 3 being “I would kill myself if I had the chance” (Lee et al., 2017).

Magnetic Resonance Imaging (MRI)

Patients were placed for no longer than ten minutes into a magnetic resonance imaging machine (MRI) to obtain an structural image of the patient's brains. This is done using a combination of a stagnant magnetic field, computer-generated radio waves through radiofrequency coils, and gradient coils. These all work together to stimulate the protons in our body, and realign our protons to obtain an image (National Institutes of Health, 2019).

MRI Image Preprocessing

MRI data often needs to be preprocessed and cleaned of noise before being properly analyzed in a study (Esteban et al., 2019). We used fMRIprep to correct for head movement, susceptibility distortion (corrects whether or not there were any distortions of the images due to local signal change of the local magnetic field), and spatial normalization (normalize a brain's shape, size, and weight) (Esteban et al., 2019). This allows us to map locations as approximately the same in all brains. Finally, we also used fMRIprep to strip the skull to ensure patient anonymity by removing any recognizable aspect of their faces. After correcting for noise, we corrected for intensity nonuniformity (Belaroussi et al., 2006) then reconstructed the brain image in FreeSurfer using the morphometric features of the Desikan-Killiany Atlas. This allows us to have a brain image with uniform intensity, essentially so we can see each region equally clearly. Then we were able to complete our analysis via our AI and ML approach.

Procedure

After obtaining informed consent from each patient, patients were then placed into an MRI machine in order to acquire structural images of each patient's brain (ie., patients were not given any task during the MRI process).

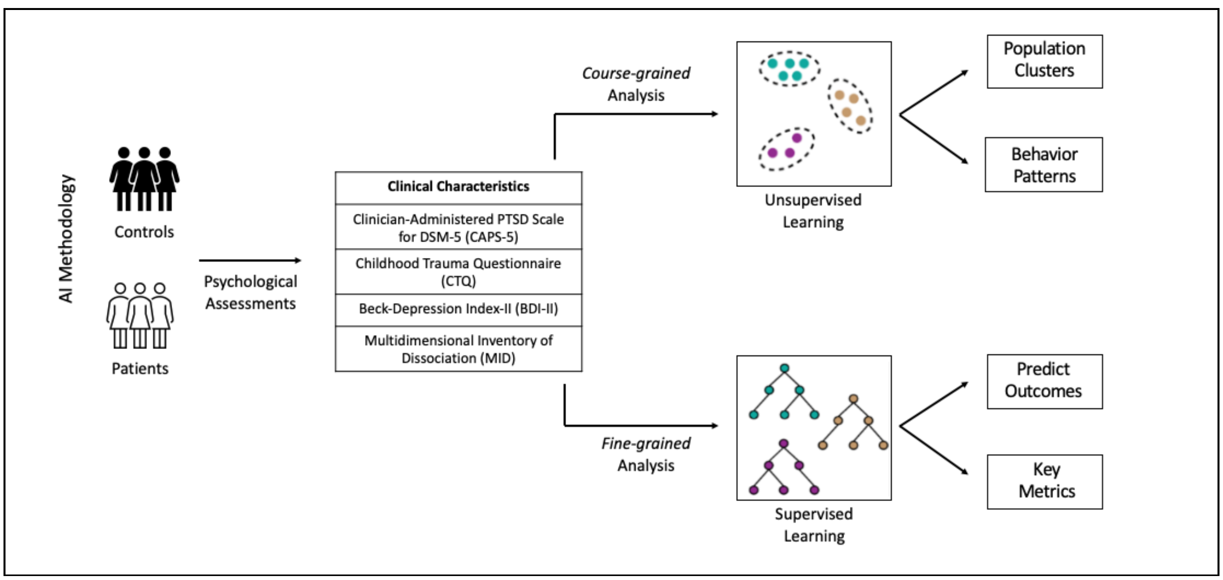
Results

Artificial Intelligence and Machine Learning Algorithms

We implemented a developed integrated AI approach (Figure 1) and applied it to our clinical dataset of participants enrolled at a psychiatric hospital in the northeastern United States, where each patient's data is represented as a numeric feature (variable) vector consisting of self-report and clinical interview characteristics. We then apply two AI algorithms in order to apply this data to cortical thickness data found from our patient's structural MRI images. The two algorithms were the unsupervised and supervised AI algorithm, which were utilized to study patterns, categorize the high-dimensional data, and to identify clinical characteristic signatures in the patient sample (e.g., the scores from the qualitative assessments). More specifically some of the signatures were based on the clinical assessments and included things such as history of suicide attempts and dissociative symptoms. We then took this data and applied it to cortical thickness in our patient's structural MRI images.

Figure 1

AI Methodology



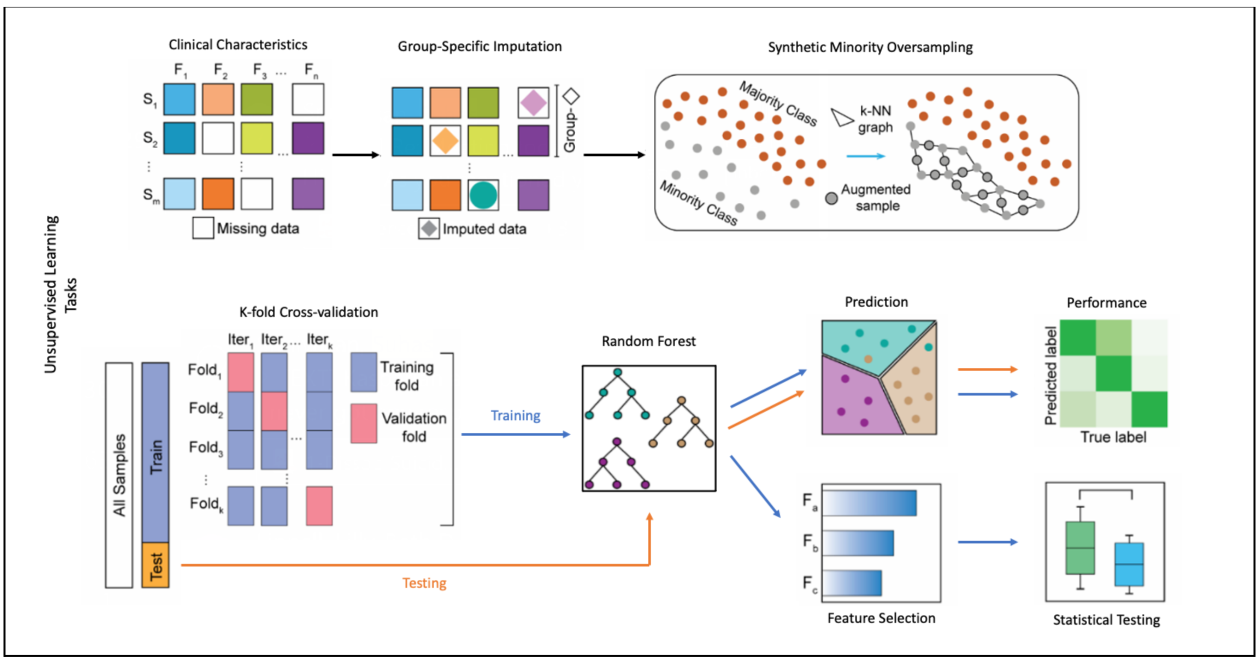
Machine Learning - Unsupervised Learning

Unsupervised learning algorithms allow for the identification of patterns in the data at a low, coarse-grained, resolution. Our unsupervised learning algorithm (Koutroumbas &

Theodoridis, 2008) was used to mine for the presence of a complex intrinsic structure in the dataset that was not discovered via a traditional statistical analysis of the patient clinical characteristics, thus expanding the basic delineation by diagnostic groups and obtaining a coarse-grained knowledge of the entire cohort (Figure 2). For this approach, only the numeric features were used (such as Likert-type scale numbers taken from the clinical assessments): the goal was to identify clusters of data points sharing common patterns and then describe the relationships among the clusters to assess clinical behaviors and categories of interest, in our case previous suicide attempts.

Figure 2

AI Methodology, Unsupervised Learning Task Organization



To discern these patterns, we employed clustering (Jain et al., 1999) and dimensionality reduction techniques, to map and visualize high-dimensional data into two-dimensional (2D) spaces while preserving the similarity between the data points. Specifically, we applied t-distributed stochastic neighbor embedding (t-SNE; Van der Maaten & Hinton, 2008), a technique commonly used to analyze biological data (Klein et al., 2015). We chose this technique because it is efficient in capturing critical parts of the local structure of high-dimensional data and mapping it into 2D space, as well as it can determine clusters without prior knowledge of cluster number or sizes. The 2D points were then annotated according to the categories of interest (e.g., categories that were initially excluded), revealing the pattern of correlation between data structures and clinical labels. Next, we used a more generalizable dimensionality reduction method with deep learning architecture, Denoising Autoencoder with Neuronal Approximator (DAWN; Srinivasan et al. 2020), to uncover additional high-dimensional relationships in the patient sample.

Machine Learning - Supervised Learning

For the higher resolution analysis, a different class of algorithms— supervised learning (Kotsiantis et al., 2007)—was required, where the distinction between the groups could be enhanced with the identification of important metrics. The algorithm first undergoes training on the paired input-output data, where the input corresponds to clinical characteristics and output corresponds to categories of interest, e.g., PTSD status, final diagnosis, risk of attempting suicide, etc.

We designed two types of classification tasks, but only used the second task in our study. The first type, models categorized individuals between the controls and entire patient sample, or between the controls and patient diagnostic groups. For the second type of classification task, the patient inter-group categorization, we developed models to identify inter-group predictors and attempted to model the risk of attempting suicide based on our predicted history of suicide attempt per patient.

A hybrid technique was developed for the supervised learning tasks to overcome challenges inherent in the study design and to obtain robust models with consistent predictions and predictors. The primary issue with using the original data was the class imbalance problem (Jankovic, 2022), where sample sizes of the control group and patient sub-groups were highly uneven, which could introduce classification bias in the supervised learning models. We used a data augmentation technique to add samples, known as synthetic minority over-sampling technique (SMOTE) (Chawla et al., 2002). Samples were added geometrically by creating intermediate points in the existing feature space of the k-nearest neighbors (i.e., k-NN graph, Figure 2) (Fukunaga & Narendra, 1975) of each control sample. These augmented and balanced data were used for all further steps.

Next, an ensemble supervised learning algorithm was implemented, the multi-class Random Forest (RF; Liaw & Wiener, 2002). This works by building many decision trees and avoids overfitting by randomly sampling the features. The final prediction is the consensus of the decision trees. Because the number of features were much greater than the overall sample size, a train/test split strategy was used to further avoid overfitting and rigorously evaluate the created model (Vabalas et al., 2019). Stratified random sampling was used to partition 80% of the samples for training and 20% for testing (Acharya et al., 2013). Since the augmented data could make the model evaluation seem unrealistic or optimistic, the 20% test data contained only the original samples, and the augmented data were included only in the training set. Additionally, the 80% training data was used with a 10-fold cross-validation protocol (Kohavi, 1995) for the RF algorithm to reduce bias and variance in predictions. Cross-validation is a resampling procedure that randomly splits the data into k-folds, $k = 10$, where 10 iterations were created to cover the entire training data, each with a complementary split of the data with 9-training folds and

1-validation fold. During the 10-fold cross-validation procedure, the prediction of each iteration is measured for accuracy, represented by F_1 score.

$$F_1 \text{ score} = \frac{TP}{TP + \frac{1}{2}(FP + FN)}$$

where FP is the number of false positives, FN is the number of false negatives, and TP is the number of true positives. Each iteration in the 10-fold cross-validation produces a F_1 score, which is averaged across the 10 iterations and reported with a standard deviation.

Furthermore, during the 10-fold cross-validation process, we implemented recursive feature elimination (RFE; Darst et al., 2018) to sequentially remove non-beneficial and highly correlated features. The combined 10-fold cross-validation and recursive feature elimination can lead to highly complex models with many features. Therefore, at the end of the cross-validation process, we analyzed changes in the F_1 score due to the consecutive reduction of the feature set, selecting a minimal number of features while preserving a high F_1 score. In addition to the feature selection, the RF model also provided a ranking of the features (Saeys et al., 2008).

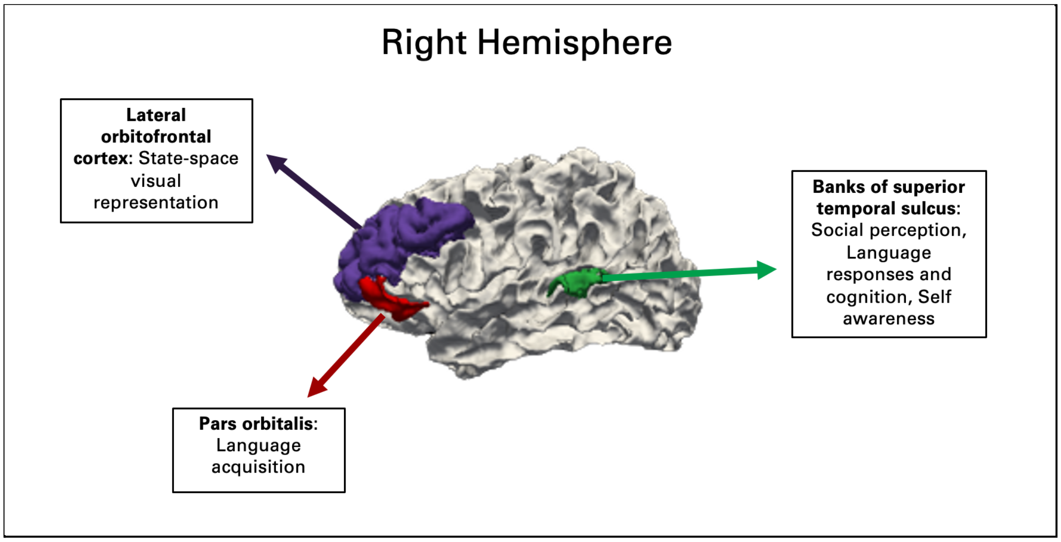
To verify the fitness and generalizability of the selected features, a new model was retrained on the 80% training data using 10-fold cross-validation. This retrained model was then applied to the withheld test data to generate the final predictions. For predicting suicide attempt in the patients, we used the patient responses for the question “Have you ever attempted suicide?” with yes/no answers as the output labels, that would be predicted by our supervised learning model. The unsupervised learning and supervised learning methods were implemented using scikitlearn (Pedregosa et al., 2011). Since the group with a dissociative disorder not otherwise specified (DDNOS group) contained only three patients, the low sample size prohibited accurate application of a supervised learning algorithm and was excluded from this analysis.

Neuroanatomical Results

Overall, we found nine features of interest in terms of changes of cortical thickness. The initial accuracy of the predictive model was 77% (F-score of 0.768), meaning that each of the nine features initially accurately predicted history of suicide attempts 76.8% of the time. Then we used a ten-fold cross validation, where the predictive model fit is tested 10 times with 90% of the data (selected at random) being used to train the model and 10% of the data is used for validation. This indicated a model accuracy of 85.3% with a coefficient of variation of 11.2% (F-score of 0.853 (0.112)), meaning our model actually accurately predicted past suicide attempt 85.3% of the time. Those nine features were split with five features belonging to the left hemisphere (55.6%)(Figure 3) and four features belonging to the right hemisphere (44.4%)(Figure 4). The features of the left hemisphere were the isthmus cingulate, rostral middle frontal gyrus, banks of superior temporal sulcus, posterior cingulate, and pars orbitalis. The features of the right hemisphere were the lateral occipital cortex, lateral orbitofrontal cortex, inferior temporal cortex, and the entorhinal cortex (See Appendix A for more representative figures).

Figure 3

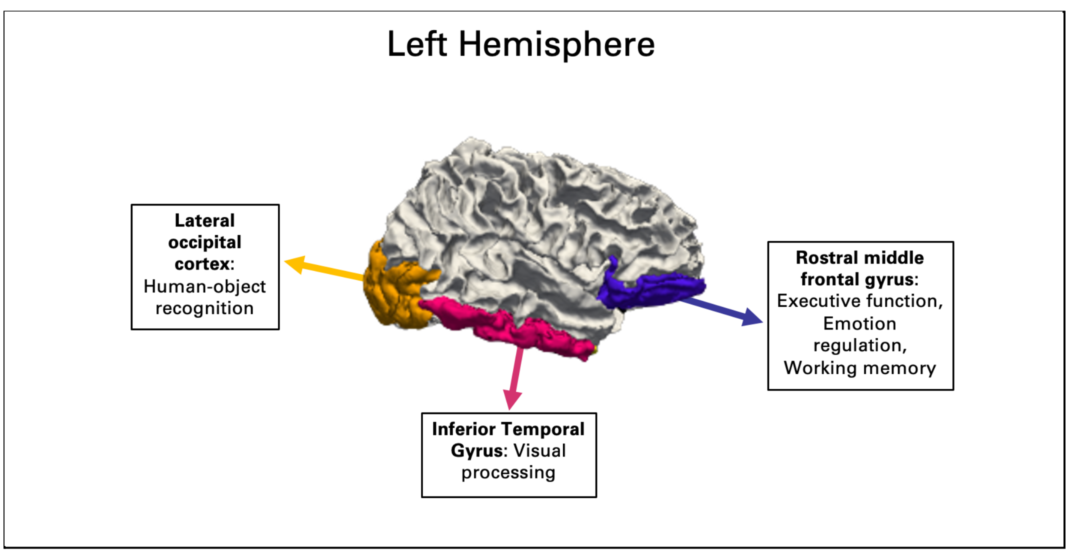
Sagittal view of the right hemisphere of the brain.



Note. View shown with representative coloration and function description of regions that showed abnormal cortical thickness in those with DID.

Figure 4

Sagittal view of the left hemisphere of the brain.



Note. View shown with representative coloration and function description of regions that showed abnormal cortical thickness in those with DID.

Left Hemisphere Results

Isthmus Cingulate Cortex. The Isthmus cingulate (ICC) is mainly known to be associated with emotion regulation, sensing, and acting or reacting in response to emotional stimuli (Luu et al., 2003). Stressful and traumatic life events are associated with reduced ICC volume (Calati et al., 2018), which is supported by the development of DID being highly correlated with severe childhood trauma (Ellason et al., 1996). This could also support our finding of abnormal cortical thickness in the ICC given increased stress and overall less life security in those with DID due to the nature of having several personality or identity states and lapses in memory. Prior research also found that higher scores on a depressive mood sub scale is also associated with decreased ICC (McLaren et al., 2016) which could imply that the variability we discovered in ICC cortical thickness could be related to the increased depressive mood of those with DID.

Rostral Middle Frontal Gyrus (RMFG). The RMFG is known for its role in executive function, emotion regulation, and working memory (Michalski, 2016). Past research has found that left RMFG cortical thickness was significantly positively associated with depressive symptoms and linked to subjective perception of stress (Michalski, 2016). This could support our findings due to the often comorbid presence of depressive symptoms in those with high rates of suicidality such as those with DID. Those with DID also tend to experience high instances of stress, most likely increasing with thoughts of suicide, self harm, and even with unsuccessful suicide attempts.

Banks of the Superior Temporal Sulcus. The left banks of the superior temporal sulcus are known to play a role in social perception, language responses, cognition, and self awareness (Deen et al., 2015). Reduced cortical thickness in the banks of the superior temporal sulcus is found in those with an antisocial personality disorder (Jiang et al., 2016) which could relate to the social struggles of those with DID due to the fluctuations in their personality states. The abnormal cortical thickness found in the banks of the superior temporal sulcus could also be a result of an extreme lack of self awareness in those with DID, given their inability to ever feel like themselves as well as often feeling as though they do not control their bodies and float outside themselves (DSM-5, 2013).

Posterior Cingulate Cortex. The left posterior cingulate is known for its role in cognition, arousal state, attention, and conscious awareness (Leech & Sharp, 2013). Abnormal cortical thickness in this region is associated with many psychological disorders and neurological diseases including bipolar disorder, schizophrenia, major depressive disorder, Alzheimer's, dementia, and Parkinson's disease (Hanford et al., 2016; Narr et al., 2005; Schultz et al., 2010; Li et al., 2016; Truong et al., 2013; Lan et al., 2014; Suh et al., 2019; van Eijndhoven et al., 2013; Lehmann et al., 2010; Zarei et al., 2013). The comorbidity and overlapping symptomology between some of these disorders with DID and suicidality may offer an explanation to the variance in cortical thickness that we found in the left posterior cingulate in our analysis. For example, as previously mentioned suicidality and major depressive disorder are often comorbid (Vandivort & Locke, 1979; Jeon, 2011; Wagner et al., 2012), meaning those with high levels of suicidality may also be diagnosed with major depressive disorder or have high depressive symptoms. Past research also shows that those with DID have high somatoform dissociation which can lead to high levels of depressive symptoms (Bob et al., 2013). This comorbidity combined with those with DID often suffering from symptoms of depression could be an indication as to why we may see abnormal cortical thickness in this region. The left posterior cingulate is also known to be associated with consciousness awareness (Leech & Sharp, 2013), which most of those with DID report losing when experiencing pronounced dissociation. For example describing feeling that they are outside of their own body and not in control of their own actions, thoughts, and emotions, as well as being unable to recall behaviors during a personality or identity shift (DSM-5, 2013). A personality or identity shift in DID is often associated with trauma and is often triggered or brought on by a type of external or internal trigger reminding them of a severe trauma (Ross et al., 2022). This could lead to a heightened and overactive state of arousal which could also begin to explain the abnormal cortical thickness we found in this region.

Pars Orbitalis. The pars orbitalis is known for its role in language processing, with the left hemisphere of this region being commonly referred to as Broca's area (Guenther, Tourville, and Bohland, 2015). Broca's area is responsible for the language processing of the production and comprehension of language (Novick, Trueswell, and Thompson-Schill, 2010) and that left hemisphere dysfunction is associated with apraxia of speech, or the inability to form the motor programs to form syllables (Guenther, Tourville, and Bohland, 2015). Abnormal cortical thickness of this region is associated with clinical psychotic symptoms and major depressive disorder (Van Lutterveld et al., 2014; Colloby et al., 2011). Psychotic symptoms are based on the DSM-5's definition on what behaviors make someone at risk for a psychotic disorder. These include delusions, hallucinations, disorganized speech, disorganized or abnormal motor behavior, and negative symptoms (DSM-5, 2013). Those with DID can often suffer from psychotic symptoms (Dorahy et al., 2014), but may not have the memory or recollection in doing so and are often perceived as strange or unusual to others based on their current personality or identity state. This could potentially suggest why we may find a similar variance in cortical thickness in those with psychotic symptoms as those with DID. Along with this, the comorbidity of major depressive disorder could begin to suggest a relationship between the abnormal cortical thickness of the left pars orbitalis in our DID patients, but there is little previous research.

Right Hemisphere Results

Lateral Occipital Cortex (LOC). The LOC's main function is in human object recognition, more specifically in the recognition of shapes independent of texture and color (Grill-Spector et al., 2001). The LOC's variance in cortical thickness found in this study could be due to the overall lack of self awareness and consciousness of themselves and others in those with DID. This could also be due to the prolonged social isolation that often coincides with suicidality and depression (Calati et al., 2019; Taylor et al., 2018). This could also be related to the lapses in working memory that tend to occur at the switch of identity state (Dorahy, 2001). More specifically, when interacting with humans or certain objects in one identity state, if the individual switches from that identity state, they may not recognize the human or object. This is especially prominent when learning to identify new objects/shapes, and meeting new people. Oftentimes, the information learned or any new information taken in, such as meeting a new person, is forgotten in the switch of personality states (Dorahy, 2001). By forgetting newly learned objects/shapes, and even forgetting newly met people, this could begin to explain the abnormal cortical thickness seen in the LOC due to the individual's overall lack of ability to recognize new shapes, objects, and people.

Lateral Orbitofrontal Cortex (Lateral OFC). Though there is limited research specifying hemisphere, the lateral OFC plays a role in domains of sadness, tracking potential punishments, failed receipt of expected rewards, depression, the sight of objects, as well as a potential role in the appraisal and categorization of stimuli as sexual (Bancroft, 2009; Sturm et al., 2016; Nadeau, 2021; Rolls, 1996). The lateral OFC's role in depression and domains of sadness (meaning cognitions and body response to sadness) can relate to suicidality in those with DID since depressive symptoms can increase risk of suicidality, and those with DID often suffer from depressive symptoms with their somatoform dissociation (Bob et al., 2013). The lateral OFC also plays a role in expecting punishments, which may relate to the severe past trauma in those with DID including childhood abuse and sexual assault (Ellason et al., 1996), abnormal cortical thickness in this region could be due to those with DID expecting punishment or abuse based on past experiences.

Inferior Temporal Cortex (IT). The IT plays a major role in visual processing, more specifically in the visual recognition of objects (Kobayashi, 2009). There is no research on specifically the right inferior IT, however there is some research that states that patients with right temporal lobe lesions show impaired memory for complex visual patterns, including faces (Fukushima, 2008). This follows the same logic as other regions that play a role in visual processing, and the issue with memory in those with DID. As explained previously, those with DID often suffer from memory-loss at identity switch, meaning they will forget everything they experienced as that previous identity (Dorahy, 2001). This includes forgetting the faces of people they may have met while in a previous identity state, the abnormal cortical thickness could mimic the findings of past research when it comes to those with DID having trouble remembering and recognizing faces.

Entorhinal Cortex (EC). The EC plays a pivotal role in how people navigate in an environment and memory. Past research shows that the EC is affected in mild cognitive impairment and that lower cortical thickness is related to worsened performance on a three-factor memory test (logical memory delayed recall, visual reproduction delayed recall, and auditory verbal learning test delayed recall)(Schultz et al., 2015; Knopman et al., 2019). The abnormal cortical thickness found in this region is most likely due to the common DID symptoms such as memory loss and overall lack of cognitive control (Dorahy, 2001; DSM-5, 2013). This plays an important potential role in suicidality in those with DID because with the abnormal cortical thickness in those with DID possibly effecting their memories, this can include effecting their memories of any self-harm or suicide related behaviors.

Discussion

Overall, there were several main functions that may be affected by the abnormal cortical thickness; all of which not only associate with DID symptomatology but also with aspects of suicide and depression. The main functions throughout all regions were: memory, visual processing (navigation and object recognition), emotion regulation, language processing, social perception and cognition, and self-awareness.

Those with higher rates of suiciality tend to socially isolate or lack a social support system (Calati et al., 2019; Hollingsworth et al., 2018), same with those with DID, mostly due to the difficulty of social interaction while having multiple identity states.

Working memory is impaired in suicide attempters as well as their long-term memories of traumas may heighten the risk of suicide (Richard-Devantoy et al., 2015). Those with DID often have experienced severe trauma and may also have a heightened risk of suicide due to their long-term memories of trauma (Ellason et al., 1996).

In terms of suicidality in visual processing such as object recognition and navigation, there is little to no research. But, we could infer that similar to those with DID who often struggle with facial recognition, maybe increased social isolation and staying inside a home would lead to dysfunction in an individual's object recognition. Along with this, perhaps negative feelings of self-worth and overall negative self-esteem can lead to less confidence in their abilities to navigate the world.

Past research shows an association between perceived limited emotional regulation strategies and suicidal thoughts (Hatkevich et al., 2019). More specifically those with an increased risk of suicide showed trouble in the downregulation of negative emotional experiences and the upregulation of positive emotional experiences (Ward-Ciesielski et al., 2018). This relates with those with DID and those with high risk of suicide in terms of the failure to downregulate the negative emotions brought up by memories of past trauma and how those memories lead to often comorbid PTSD or worsened suicidality.

Past research shows that high risk for suicide may manifest itself in how individual uses language (Low et al., 2020), but there is limited research about whether or not individuals that suffer from high rates of suicidality struggle with language processing.

Those with high risk of suicide display low self-esteem and low self-worth as well as tend to hyper-fixate on themselves and their perceived negative qualities (Pyszczynski & Greenberg, 1987). Past research shows that those with major depressive disorder (and thus may be at risk for suicide), showed abnormal self-referential processing, including abnormal processes and/or representations involved in being aware of the self, abnormal knowledge about the self, and/or abnormal judgments about the self (Lou et al., 2019).

Our provided regions can now act as a foundation for suicidality in those with DID for future research to build upon and investigate further. These regions could help inform treatment in the form of medications, as well as diagnostic treatments, and can begin to help improve the rate of suicide in those with DID by providing health care professionals with unique ways to infer suicidality based on structural data, and not dependant on patient self-report.

Limitations and Future Research

There were some limitations to this study that could be corrected in future research. Our population used only women, although this could be argued to be a positive due to the 9 to 1 ratio of women to men being diagnosed with DID (Spitzer et al., 2003), men tend to have a higher suicide rate (O'Rourke et al., 2021) and it may be interesting to have future research include both men and women. Though, finding a 77% past suicide attempt rate in our population of just women may suggest that even in a population including men, the suicide rate is high enough to cause alarm and need attention.

The next limitation is purely based on a lack of past research. The brain regions we found with abnormal cortical thickness are not well-researched in general or in association with DID and suicidality. There is some past research that specifies different functions per separate region and separate hemisphere, meaning a region will have different functions depending on whether or not it lies on the right or left side of the brain. Future research is needed to increase understanding of the functional differences of brain regions in the left or right hemisphere in order to fully comprehend the implications of abnormal cortical thickness in our found regions.

The next limitation involves a lack of longitudinal data, or several images taken over a set amount of time. Those with DID are known to shift personality states, and there is only inconclusive research about whether this change will influence the brain drastically. A long term prospective study may be more likely to identify cause and effect relationships and go beyond what was possible with the data found in this study by integrating the potential of identity switches and imaging every possible identity state.

Future research may want to incorporate functional magnetic resonance imaging (fMRI) to see how the brain activity of those with DID (blood-oxygen-level-dependent (BOLD) signal). This is based on past research where researchers used a machine learning pipeline and introduced death and life related concepts ("death", "cruelty", "carefree", "praise", etc) to predict those who struggle with suicidal ideation at a 91% accuracy rate (Just et al., 2017). It would be interesting for future research to perform a longitudinal study (with the hopes that overtime, the identity that suffers from suicidality will be present during a scan) with those with DID and recreate this same study to see if they achieve the same high predictive results. Our study alone will not be affected by this since we are predicting past suicide attempts, rather than current suicidal ideation.

Lastly, neuroscience research as a whole needs to integrate more multi-modal imaging data, typically, much of the research in the neuroscience field that uses imaging data only presents one type of data and it can limit the potential of the field as a whole.

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Appendix A

Additional Views of the Brain Regions of Interest

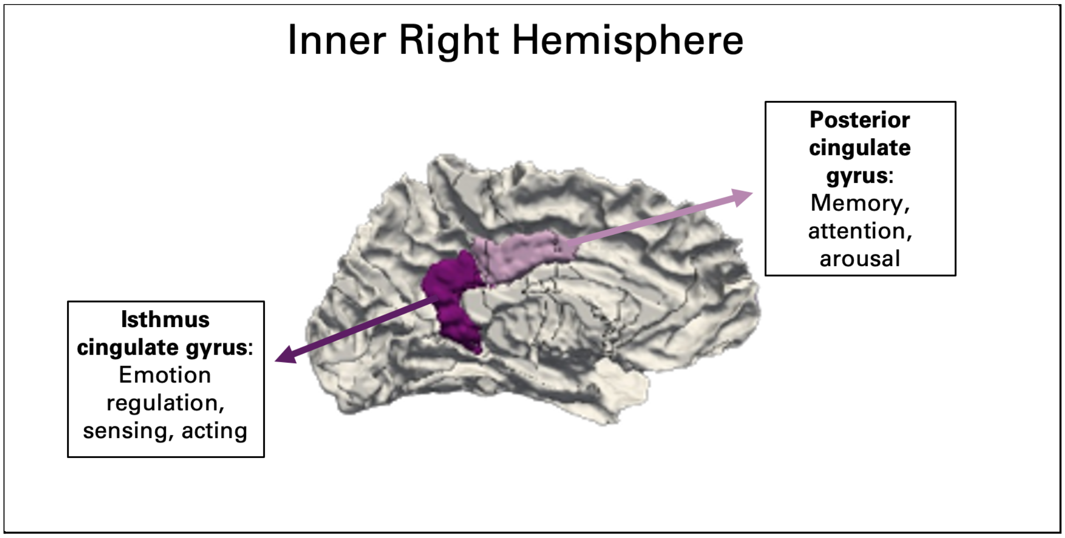

Figure A1. A sagittal view of the inner right hemisphere with representative coloration and function descriptions of regions that showed abnormal cortical thickness in those with DID.

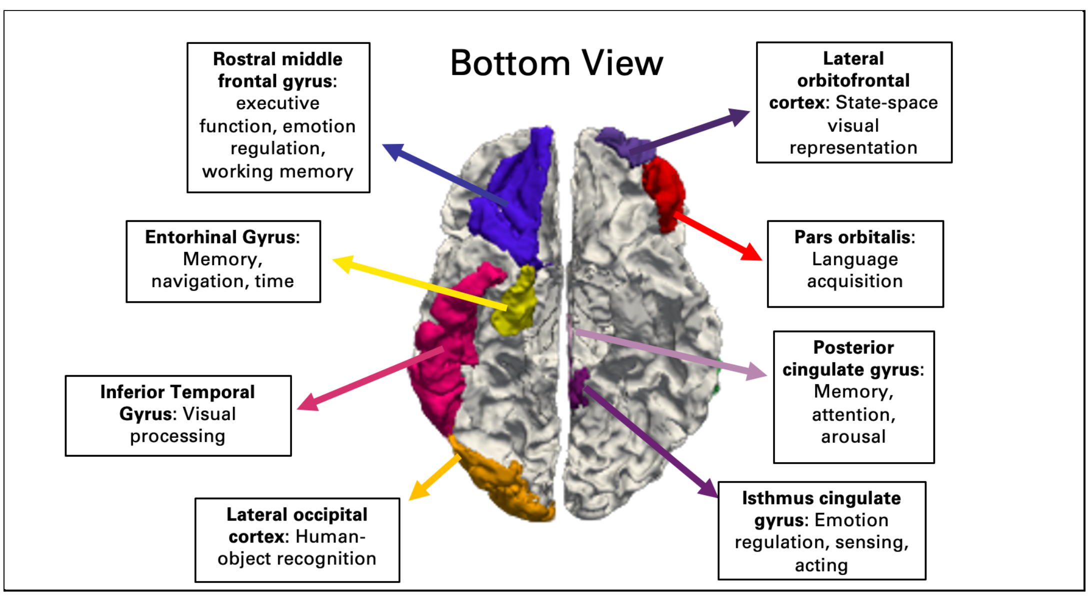

Figure A2. A bottom view of the brain with representative coloration and function descriptions of regions that showed abnormal cortical thickness in those with DID.