The Anterior Cingulate Cortex, Risk-Taking, & Impulsivity: A closer look into Bipolar Disorder & ADHD

A Thesis Proposal

by

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Introduction

The documented presence of mental disorders has increased rapidly in the past few decades with over 51.5 million American adults diagnosed with a mental disorder in 2019 – a 1.5 million increase from 2018 (Substance, 2020). With the rise in these diagnoses, there is a greater need to understand both the neuroanatomy and symptomatology of mental illness and disorders. Attention Deficit Hyperactivity Disorder (ADHD) and Bipolar Disorder (BD) are two such disorders that have increased in prevalence and demanded more attention in the neuroscience and psychology fields with ADHD and BD affecting 4.4% and 2.8% of adults in the United States, respectively (U.S., 2021). This study sets out to investigate one of the key behavioral deficits in both disorders- an increase in impulsivity and risk taking (Johnson et al., 2012; Lombardo et al., 2012; Najt et al., 2007; Reddy et al., 2014; Groen et al., 2013, Pollak et al., 2018). Specifically, the study explores how the Anterior Cingulate Cortex (ACC), and the disorders, BD and ADHD, relate to both risk-taking and impulsivity.

The Anterior Cingulate Cortex, Risk-Taking, and Impulsivity: A closer look into Bipolar and ADHD

Previous research shows that fMRI activity and gray-matter volume of the ACC are correlated with increased potential for impulsivity (Brown & Braver, 2007; Fukanaga et al., 2012; Matsuo et al., 2009). In addition, the Balloon Analogue Risk Task (BART), a decision-making test to determine a participant's risk-taking propensity by having them inflate a balloon at the risk of gaining or losing money, notes a positive relationship between the BART and impulsivity (Lejuez et al., 2002; Lejuez et al., 2003). Although both the ACC and BART are connected with impulsivity individually, research directly comparing the BART and gray matter volume of the ACC is lacking. This gap in research offers an opportunity to further investigate the ACC's relationship with impulsivity in the context of a formal assessment of decision-making.

The research will extend beyond the healthy population by including participants with ADHD and BD. These psychiatric illnesses have been associated with smaller gray matter volumes in the ACC and increased risk-taking and impulsivity. Utilizing the traits 'impulsivity" and "risk-taking," a main objective of this study is to clarify the relationship between risky behavior, ACC volume, and psychiatric disorders. The study also explores gender differences because risk-taking and impulsivity present differently between males and females in both healthy and psychiatric populations (Reddy, 2014; Volkow, 2011). By better understanding these components, treatments could be targeted towards brain areas that impact impulsivity. As a result, these treatments would offer increased safety and decreased severity of symptoms associated with risky behavior.

Using an extensive database from the UCLA Consortium for Neuropsychiatric Phenomics (Poldrack et al., 2016), the current study analyzed MRI images using voxel-based morphometry to determine the gray matter volumes of the anterior cingulate cortex. These scores were compared in parallel to the results from the Balloon Risk Analogue Task to determine relationships, if any, between each other and the neuropsychiatric conditions. It is expected that both risk-taking and impulsivity will have a negative correlation with the gray matter volume (GMV) of the ACC, and participants with BD and ADHD will demonstrate increased risk-taking on the BART, decreased GMV in the ACC, and a stronger correlation between the two.

Literature Review

This literature review establishes baseline findings on the anterior cingulate cortex (ACC) and its relationship with psychiatric disorders and risk-taking. Likewise, the Balloon Analogue Risk Task (BART) is investigated further to determine its validity as a risk-taking task, often used for understanding psychiatric disorders (Lauriola et al., 2013). Bipolar Disorder (BD) and Attention Deficit Hyperactivity Disorder (ADHD) are specific psychiatric disorders with extensive previous research on impulsivity and risk-taking behavior. While they can present individually, both disorders share similar symptomatology, although BD reflects greater involvement in thrill-seeking, potentially dangerous activities—a critical characteristic of impulsivity and risk-taking (Klassen, Katzman & Chokka, 2010). By investigating the link between the ACC and risk-taking, there is potential to better understand whether the ACC is involved in the underlying neuropathology which results in risky decision-making and the occurrence of ADHD and BD.

Anterior Cingulate Cortex

The anterior cingulate cortex (ACC) is a brain area with connectivity to the motor cortex, prefrontal cortex, brainstem, striatum, and hypothalamus (Rogers et al, 2004). The dorsolateral portions of the ACC are heavily connected with motor areas, whereas the ventral ACC is more associated with emotional processing because of its communication with prefrontal and hypothalamic regions of the brain (Rogers et al, 2004). The left ACC is a particular area of interest because it shows greater activation during impulse control tasks (Matsuo et al., 2009) Recently, studies focus on the role that the ACC plays in decision-making, especially risky versus safe decisions. Previous studies indicate that the ACC has two primary functions related to decision-making. The ACC is first involved in the detection and appraisal of a risk, indicated by fMRI activity (Brown & Braver, 2007; Fukanaga et al., 2012). Additionally, evidence suggests that it is involved in inhibition of risky decisions (Brown & Braver, 2007; Helfinstein et al., 2014); however, other studies have contended that the ACC only introduces awareness of the risk but does not influence behavior (Fukanaga et al., 2012). This recall and potential inhibition of risk could be mediated by hippocampal input where memory of prior choices and outcomes influence risk assessment and decision-making (Wang, John & Barbas, 2021). Differences in ACC activity are reflected in studies that look at addictive behavior and impulsivity to find that abnormal dorsal anterior cingulate cortex activity is correlated with increased cigarette cravings (Wei et al., 2016). There is greater ACC activation during impulse control task for males, whereas females have greater activation in the middle temporal cortex (Liu, 2012). While these previous findings focus primarily on fMRI activity and functional connectivity studies, a connection between anterior cingulate cortex and behavior is reflected in studies looking at the gray matter volume of the ACC. One study reports that the left ACC's gray matter volume is inversely correlated with self-rated impulsivity scores using the Barratt Impulsiveness Scale (BIS) (Matsuo et al., 2009). An important consideration related to VBM is that gray matter volumes naturally decline with age and need to be properly accounted for when conducting VBM studies (Peelle et al., 2012). ACC volume also differs between gender, so males and females are investigated independently (Rogers et al, 2004).

Risk-Taking and Impulsivity

The gray matter volume of the anterior cingulate cortex was analyzed alongside risky performance on the Balloon Analogue Risk Task (BART). The BART is a commonly used experimental task, looking at risky versus safe decision-making. During the task, participants inflate a balloon to increase their earnings and must decide when to stop inflating the balloon to prevent it from popping (Lejuez et al., 2002; Lejuez et al., 2003). This process of trying to maximize profit reveals differences in decision-making and includes elements of arousal, cognitive strategies, learning, and risk propensity (Li et al., 2020). The Barratt Impulsiveness Scale and Eysenck Venturesome Subscale are two self-report questionnaires that are connected with increased risk-taking behavior (Lejuez et al., 2002; Lejuez et al., 2003). In addition, certain subsets of people, such as those experiencing addiction at varying levels of intensity, reflect greater BIS scores. Impulsive choice tasks such as the Delay and Probability Discounting task (DDT), Iowa Gambling task (IGT), and BART have all been portrayed to have connections with impulsivity; however, the DDT is heavily modulated by day-to-day mood states and the IGT has lower reliability (Weafer, Baggott & Wit, 2013; Xu et al., 2013). Meanwhile, the BART has the greatest retest reliability when looking at fMRI scans (Li et al., 2020; Weafer et al., 2013).

Bipolar Disorder

Within the ACC and BART comparison, participants with Bipolar Disorder (BD) were introduced for comparison. Bipolar Disorder is a mental health condition classified in the Diagnostic and Statistical Manual of Mental Disorders that is characterized by periods of both mania and depression (Johnson et al., 2012). It is classified as either BD1 or BD2, depending on the symptomatology. Research is primarily focused on the first categorized disorder, BD1, where the periods of mania are typically longer and more pronounced (Johnson et al., 2012). People with BD1 behave more impulsively during both their depressive and manic states, and many studies examine this relationship. Research shows that self-rated impulsivity, scored by Barratt's Impulsiveness Scale, is greater among adults with BD1 (Johnson et al., 2012; Lombardo et al., 2012; Najt et al., 2007; Reddy et al., 2014). Likewise, adults with BD1 also score significantly higher than controls on the Sensation Seeking Scale (Cronin & Zuckerman, 1992). Performance on these tests is not necessarily related to real-life impulsivity for people with BD1 because riskiness presents in various ways and a single experimental task or questionnaire rarely captures all aspects of impulsivity and sensation seeking (Lauriola et al., 2013; Najt et al., 2007). During the Balloon Risk Analog Task, those with BD1 did not perform riskier than the controls (Reddy et al., 2014). Along with impulsivity, BD1 is inversely correlated with the left anterior cingulate cortex gray matter volume. This finding is consistent among multiple studies (Bora, et al. 2010; Matsuo et al., 2009; Lochead et al., 2004; Sassi et al., 2004), although one study found that the gray matter volume in the ACC was increased for BD1 (Adler et al., 2005). These variations could be due to medication, differing mood states, age, and gender--all of which impact gray matter volume (Adler et al., 2005). When dividing patients with BD1 into treatment categories, studies show that lithium increases or has no effect on the gray matter volume in the ACC (Bora et al., 2010; Sassi et al., 2004), whereas untreated BD1 results in a smaller volume (Sassi et al., 2004). The relationship between BD1, ACC volume, and riskiness on the BART has been loosely connected using impulsivity; however, the exact link between the three is not fully understood due to differences in medication history and various presentations of BD.

Attention Deficit Hyperactivity Disorder

Attention Deficit Hyperactivity Disorder (ADHD) often occurs in conjunction with BD and involves similar symptoms; therefore, this condition was also be investigated in the study. ADHD is typically diagnosed in children and is characterized by impulsivity, hyperactivity, and attentional problems (Groen et al., 2013). The symptoms typically reduce from childhood to adulthood; however, there are still behavioral and cognitive impacts later in life (Groen et al., 2013). ADHD in adults is strongly associated with riskier behavior and impulsivity, shown through increased participation in sexual activity, criminality, risky driving, and drug use (Groen et al., 2013). Additionally, people with ADHD are at greater risk for drug or gambling disorders and are more likely to favor immediate rewards even if they are smaller (Groen et al., 2013, Pollak et al., 2018). Given this symptomatology, many studies consider the relationship between ADHD and the Balloon Risk Analog Task (BART). While some find that differences in risky decision making are only prevalent in children with ADHD (Groen et al., 2013; Pollak et al., 2018), others show that adults with ADHD take more initial risks (Mantyla et al., 2012). There is controversy in literature over whether experimental tasks are an accurate representation of real-life behavior, especially in ADHD. Some studies find that the experimental findings are inconsistent with expected behaviors, meaning that participants with ADHD do not perform with increased risk during behavioral tasks, even though their real-life behavior is consistent with riskiness and impulsivity (Amico et al., 2011; Pollak et al., 2018). To account for this inconsistency, tasks that offer real rewards are more sensitive to behavioral deficits of ADHD and better reflect real-life behavior (Scheres et al., 2008). Studies also show that there is a significant decrease in left ACC volumes for ADHD adults (Amico et al., 2011; Makris et al., 2010). These findings apply to treatment-naive adults, whereas studies involving medication introduce some limitations, depending on length and type of medication treatment. Specifically, it is difficult to control for differences in medication history while maintaining an adequate sample size (Amico et al., 2011; Mantyla et al., 2012).

Summary

This review introduces the anterior cingulate cortex (ACC) and its functional correlations with impulse inhibition and risk-taking. The relationship between gray matter volume of the ACC and these behaviors lacks previous research, especially in the context of neuropsychiatric conditions such Bipolar Disorder or Attention Deficit Hyperactivity Disorder. This review of extensive previous research sets the foundations to investigate how the ACC is involved in risky performance on the BART, specifically for people with disorders that affect impulsive behavior. With this knowledge, there is potential to better understand the neuropathology of both disorders, especially pertaining to their similar symptomology and connectivity as they relate to risk-taking and the anterior cingulate cortex. These findings may contribute to the development of treatments targeting risky behavior and impulsivity, especially for people with psychiatric disorders.

Methods

Data acquisition

Data for this study was acquired through a dataset from the UCLA Consortium for Neuropsychiatric Phenomics (Poldrack, 2016). The MRI data was obtained via two 3T Siemens Trio scanners, one located at the Ahmanson-Lovelace Brain Mapping Center (Siemens version syngo MR B15) and on at the Staglin Center for Cognitive Neuroscience at UCLA (Siemens version syngo MR B17).

Participants

The participants in this study were recruited from the Los Angeles area to include healthy adults as well as adults with ADHD, Bipolar Disorder, and Schizophrenia. For the purpose of this study, the schizophrenia condition was excluded from research. Informed consent was received using procedures approved by the Los Angeles County Department of Mental Health and the Institutional Review Boards at UCLA. For both healthy and patient groups combined, there were 203 participants (97 F; 106 M) with ages ranging from 21 to 50 years old. All participants were required to have a negative urinalysis for commonly abused drugs (Cocaine; Methamphetamine; Morphine; THC; and Benzodiazepines). The healthy group of participants were excluded if they had a lifetime diagnosis of the following mental disorders: Schizophrenia or other psychotic disorders, Bipolar I or II disorder, or Substance Abuse or Dependence disorder. They were also excluded if they had a diagnosis Major Depressive Disorder, suicidality, Anxiety Disorder, or Attention Deficit Hyperactivity Disorder currently or within the last 12 months.

All participants were assessed using the Adult ADHD interview (Kaufman, 2000). For the healthy group, adults were required to have no more than four ADHD symptoms in either childhood or adulthood, nor could they have taken ADHD medication within the last year. Diagnosis for Bipolar Disorder, ADHD, and Schizophrenia were outlined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (American, 2000) and were based on the Structured Clinical Interview from the DSM-IV (First, 2002). All interviewers and raters were trained in the criteria and underwent annual quality assurance checks during the course of the study to ensure proper placement of the conditions. Additional information on the recruitment process can be found at the dataset from the UCLA Consortium for Neuropsychiatric Phenomics (Poldrack, 2016). The final dataset includes 119 healthy individuals (57 F; 62 M), 46 individuals diagnosed with Bipolar Disorder (20 F; 26 M), and 38 individuals diagnosed with ADHD (20 F; 18 M).

Balloon Analogue Risk Task

The Balloon Analogue Risk Task (BART) acts as a laboratory measure to determine risk taking propensity in both self-rated questionnaires and based on real life behavior (Lejuez, 2002). In this task, participants completed the task with the goal of earning points. Participants saw forty balloons of both red and blue color. For each trial, the participant decided between pumping the balloon or cashing out for points. If the balloon was pumped successfully, the participant earned five points, a larger balloon appeared, and the decision to pump or cash out was asked again. After each successfully unpopped balloon, the earnings were displayed, and the round continued with another balloon. If the balloon exploded as a result of a pump, the participants lost their points for that round.

Balloons exploded in a random uniform distribution over the number of pumps, meaning that the likelihood of loss increased with each trial. The participants were not informed of the probability of explosion or that the maximum number of pumps was twelve. After an outcome trial where the participant successfully cashed out or the balloon exploded, the reward was displayed for two seconds. Each trial was preceded by a blank screen that lasted between 1-2 seconds and each round lasted between 1-12 seconds. This task offers a variety of measures that can be used to measure risk taking. One measure of particular interest is the total adjusted number of pumps, which accounts for the average number of pumps on trials in which the balloon did not explode. This could also be understood as trials in which the person stopped pumping voluntarily. The general understanding for the BART is that a higher number of adjusted pumps indicates greater risk taking. However, this measure does not account for trials where the balloon exploded, discounting instances where a particularly risky participant pumped until explosion on the majority of trials.

Barratt’s Impulsiveness Scale

The Barratt’s Impulsiveness Scale is used as a measure of impulsivity. The participants in this study took the BIS-11, which is composed of 30 questions to outline different aspects of impulsivity. The scores from the questionnaire are reported on a 4-point scale with the options including: “Rarely/Never,” “Occasionally,” “Often,” and “Almost Always/Always.” The BIS is composed of three subfactors: Attentional, Motor, and Non Planning. Each question on the BIS is placed in a corresponding subfactor and the three sections are added to obtain a total BIS score.

Voxel-based Morphometry

The gray matter volume of the left anterior cingulate cortex (ACC) was analyzed using standard voxel-based morphometry methods in SPM12 (Wellcome Department of Cognitive Neurology, London, UK). The structural MRI images were segmented using the New Segment option, which identifies the tissue types and segments them into gray matter, white matter, and CSF images. The gray matter images were then spatially normalized into standard Montreal Neurological Institute space (MNI space) to increase the inter-subject alignment. This process took place using the Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra (DARTEL) (Ashburner, 2007). Normalization (1.5 mm3 isotropic voxels) was run with smoothing to generate spatially normalized images using an 8 mm full-width at half-maximum of the Gaussian smoothing kernel (Mechelli, 2005). The VBM analyses were conducted utilizing the modulated, smoothed gray matter images to provide a measure of regional, relative gray matter volume across participants in the left ACC. The left ACC was chosen as the primary target since greater activity has been previously correlated with impulse control (Matsuo et al., 2009).

VBM statistical analysis

To retrieve raw relative volume values from the MRI data, an analysis was conducted within a region of interest to limit the multiple-comparisons problem. In this case, the region of interest, the left anterior cingulate cortex, was created using the Wake Forest University PickAtlas for SPM (Maljian et. al, 2003, 2004). Once the mask was generated, the Volumes Toolbox was used to extract data located within the left ACC mask. The raw scores and their standard deviation were output to MATLAB (R2021a).

Analysis

The data used for analysis was computed and stored via Microsoft Excel. Values such as BIS total and mean adjusted pumps were already calculated in the downloaded data, and raw scores were not included for the BART. Since each task was stored as a '.tsv', the Python programming language (3.9.4) was the primary method for retrieving the data. The code was created to exclude participants who either did not fully complete the tasks or meet this study's criteria.

For Barratt's Impulsiveness Scale, the sum of the BIS scores were utilized. For the BART, the mean adjusted pump value was determined by the average number of pumps on trials where the balloon did not pop. These are the standard measures for determining risk or impulsivity. The left ACC volume scores were obtained in MATLAB (R2021A) and transferred into the Microsoft Excel spreadsheet. The statistical analysis then took place in JASP (0.16.1), which utilizes the R programming language. The variables evaluated include gender, patient group (HC, BD, ADHD), BIS total scores, mean adjusted pumps, and left ACC volumes, and they were analyzed using independent sample t-tests, single factor ANOVAs, and classical correlations.

Results

Left ACC vs Risk-Taking

This study considers how risk-taking relates to impulsivity, psychiatric disorders, and ACC volume. A major objective was to investigate the relationship between left ACC volume and the BART. To elucidate the relationship without additional variables, the healthy control group was the primary focus. A classical correlation was run, and the ACC data was conditioned on gender to compensate for differences in ACC volume between males and females (Peelle et al., 2012). When considering the adjusted number of pumps and the left ACC volume, the statistical analysis found no correlation for females, shown by r(55)=-0.020, p=0.884, but a significant correlation for males, shown by r(60)=-0.298, p=0.021(Fig. 1). The specific result indicates a negative relationship where mean number of pumps on the BART decreases as left ACC volume increases in males.

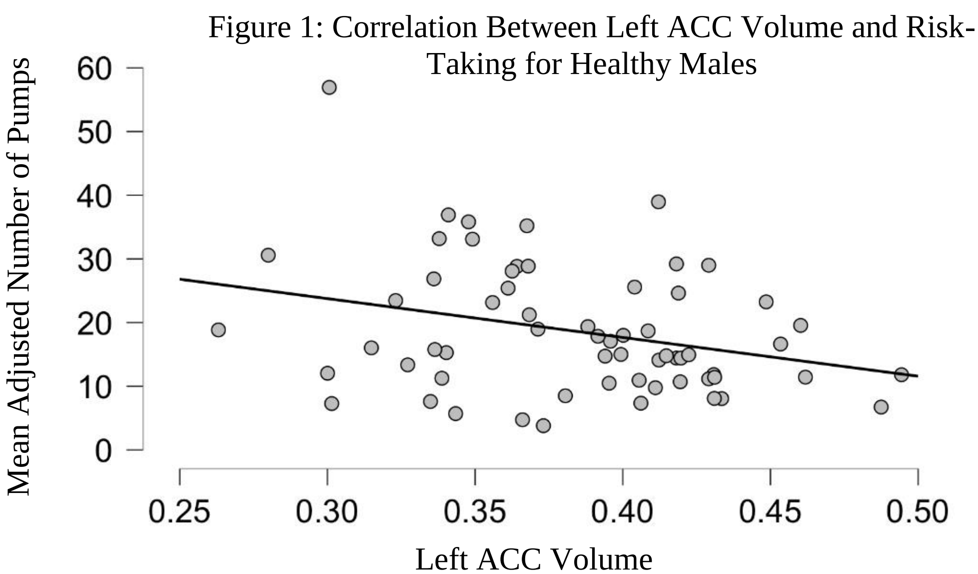

Figure 1: This figure reflects the correlation between the left ACC volume and mean adjusted number of pumps on the "Balloon Analogue Risk Task." The y-axis represents the mean adjusted number of pumps and the x-axis represents the left ACC volume. The analysis was conducted on males in the healthy control condition only and the correlation found r(60)=-0.298, p=0.021.

Because the healthy males portrayed a correlation (Fig. 1), additional analyses were run on the male subjects within psychiatric conditions. When considering the psychiatric conditions separately, the men in the ADHD condition portrayed a trend between left ACC volume and risk-taking on the BART that was opposite and weaker than the trend of the HCs, indicated by r(16)=0.439, p=0.089 (Fig. 2). Specifically, men with ADHD had more adjusted pumps with larger ACC volumes. The men with BD did not portray any significant correlations, indicated by r(24)=0.055, p=0.797. An analysis was also run on females within the psychiatric conditions. Females with neither ADHD nor BD portrayed any significant findings with p-values of r(18)=-0.88, p=0.729 and r(18)=0.-151, p=0.548, respectively.

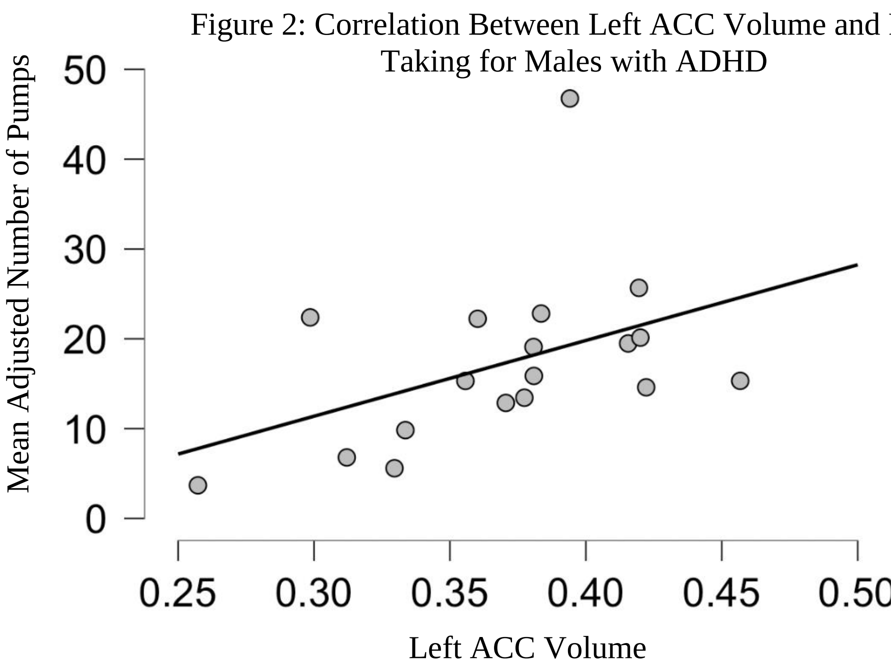

Figure 2: This figure reflects the correlation between the left ACC volume and mean adjusted number of pumps on the "Balloon Analogue Risk Task." The y-axis represents the mean adjusted number of pumps and the x-axis represents the left ACC volume. The analysis was conducted on males in the ADHD psychiatric condition only and a positive trend was found r(16)=0.439, p=0.089.

Left ACC vs Impulsivity

The volume of the left ACC was then compared with the total score on Barratt's Impulsiveness Scale. The healthy controls and both psychiatric conditions were conditioned on gender. The analysis found no correlations in either gender when the BIS and left ACC volume were compared for healthy adults, shown by r(60)=-0.147, p=0.261 for males and r(55)=-0.025, p=0.853 for females. Likewise, when looking at the analyses within both psychiatric conditions, no correlations were found. Males with ADHD and BD reflected r(16)=-0.291, p=274 and r(24)=-0.140, p=0.513. Females with ADHD and BD were also considered, and the analyses found no correlation (f(18)=-0.023,p=0.929; f(18)=-0.308, p=0.214).

Psychiatric Conditions vs Traits

In this section, Bipolar Disorder and ADHD are considered in relation to both impulsivity and risk-taking. Scores of the BIS were compared between healthy controls and participants with BD and ADHD to determine impulsivity. Based on the independent sample t-test, people with BD and ADHD scored significantly higher than the controls, shown by t(163)=8.388, p=<0.001 (Fig. 3) and t(155)=11.828, p=<0.001 (Fig. 4), respectively.

Figure 3: How Impulsivity Corresponds to Healthy Controls Versus Participants with BD

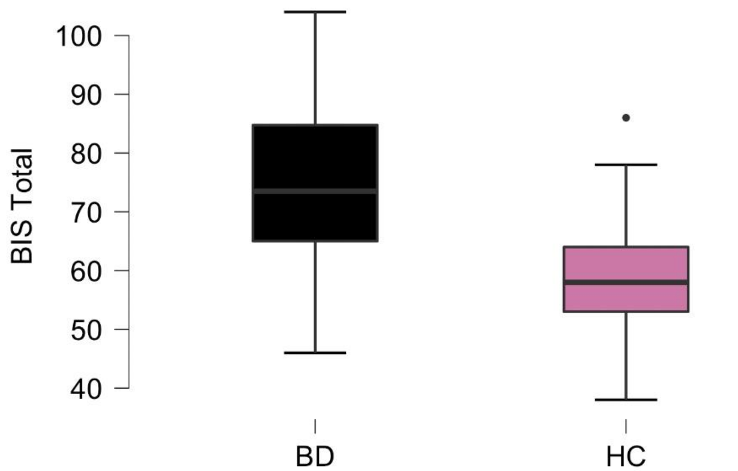

Figure 3: This figure looks at the relationship between the "Barratt's Impulsiveness Scale" ('BIS Total') and Bipolar Disorder. The left box plot represents participants with Bipolar Disorder ('BD') and the right box plot represents Healthy Controls ('HC'). The graph was created based on the independent sample t-test and the results found t(163)=8.388, p=<0.001.

Figure 4: How Impulsivity Corresponds to Healthy Controls Versus Participants with BD

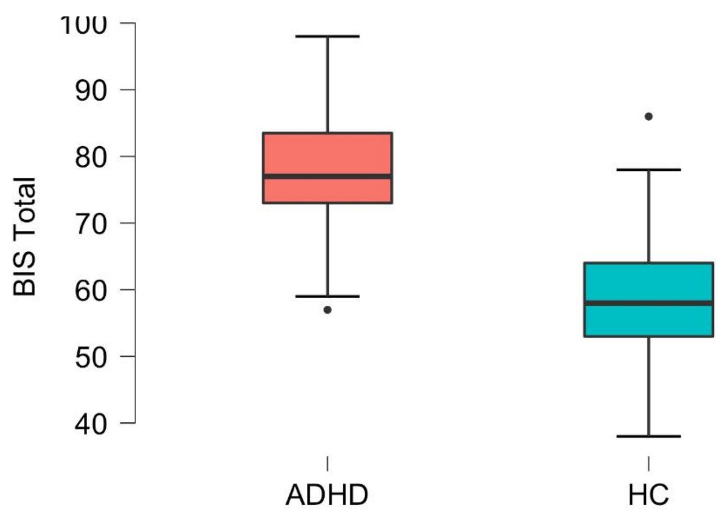

Figure 4: This figure looks at the relationship between the "Barratt's Impulsiveness Scale" and Attention Deficit Hyperactivity Disorder. The left box plot represents participants with ADHD and the right box plot represents Healthy Controls ('HC'). The graph was created based on the independent sample t-test and the results found t(155)=11.828, p=<0.001.

To determine riskiness, the psychiatric conditions were compared to the mean adjusted number of pumps on the BART using an independent sample t-test. Participants with BD and ADHD did not score significantly differently on the BART compared to healthy controls with findings of $t(163)=0.743$, $p=0.458$ and $t(155)=6.9e\text{-}4$, $p=0.999$, respectively. To reflect the lack of differences on the BART, a single factor ANOVA was run ($F(1,200)=0.290$, $p=0.749$) and the plot is displayed below (Fig. 5).

Figure 5: How Risk-Taking Corresponds to Patient Groups

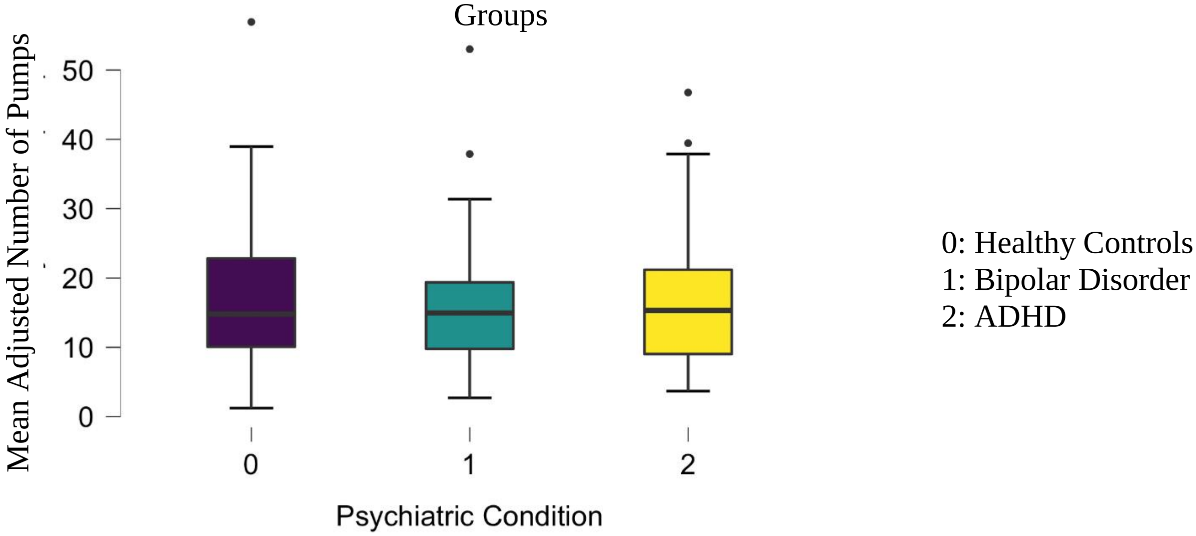

Figure 5: This figure looks at the relationship between the "Balloon Analogue Risk Task" and the psychiatric conditions, Bipolar Disorder and Attention Deficit Hyperactivity Disorder. The '0' represents HC, the '1' represents participants with BD, and the '2' represents participants with ADHD. The graph was created based on a single factor ANOVA and the results found F(1,200)=0.290, p=0.749.

Impulsivity (BIS) vs Risk Taking (BART)

The tasks, Barratt's Impulsiveness Scale and the Balloon Analogue Risk Task, were then compared to determine the relationship between impulsivity and risk taking. Healthy controls were measured as a baseline and a positive correlation was found between the BART and BIS for both genders. Specifically, the classical correlation found that as BIS scores increased, the mean adjusted number of pumps increased as well, shown by $r(118)=0.263$, $p=0.004$ (Fig. 6). The BIS and BART scores of participants with BD were then correlated and no relationship was determined $r(45)=-0.029$, $p=0.849$ (Fig. 7). No correlation was displayed for participants with ADHD either ($r(37)=0.009$, $p=0.959$) (Fig. 8).

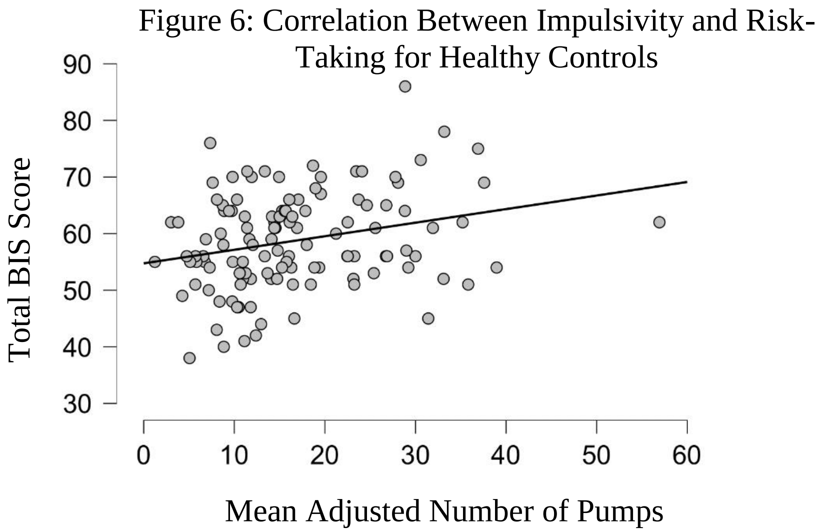

Figure 6: This figure looks at the relationship between the "Balloon Analogue Risk Task" and the "Barratt's Impulsiveness Scale" for healthy controls. The y-axis represents the total BIS score, and the x-axis represents the mean adjusted number of pumps on the BART. The analysis was conducted on all genders within the Healthy Control condition and a positive correlation was shown by r(118)=0.263, p=0.004.

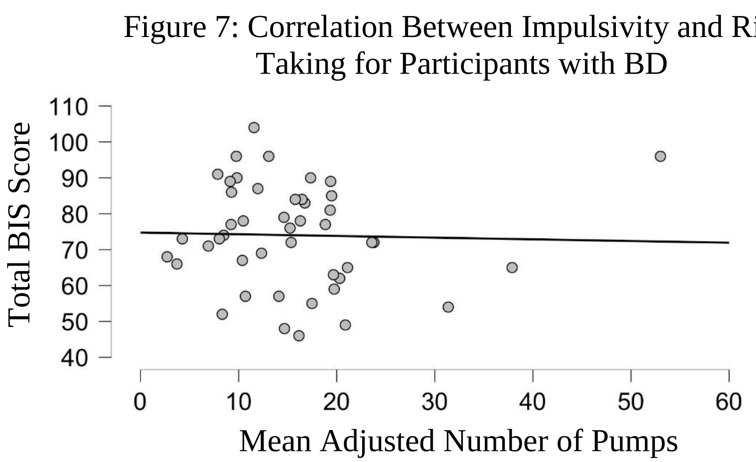

Figure 7: This figure investigates the relationship between the "Balloon Analogue Risk Task" and the "Barratt's Impulsiveness Scale" for participants with Bipolar Disorder. The y-axis represents the total BIS score, and the x-axis represents the mean adjusted number of pumps on the BART. The analysis was conducted on all genders within the BD psychiatric condition and no correlation were shown by r(45)=-0.029, p=0.849.

Figure 8: Correlation Between Impulsivity and Risk-Taking for Participants with ADHD

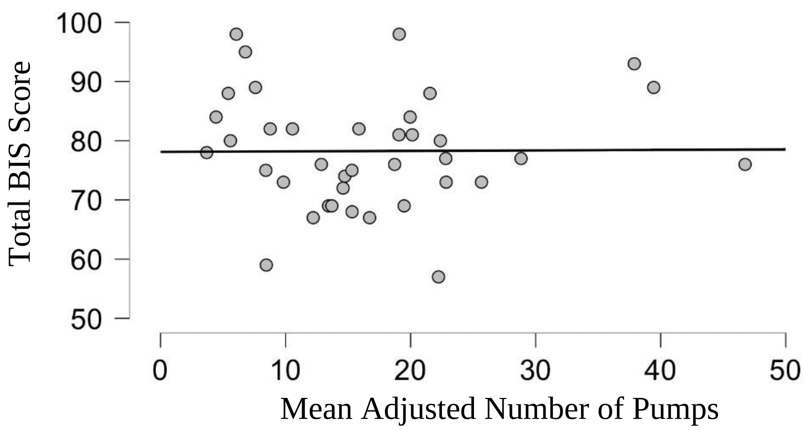

Figure 8: This figure investigates the relationship between the "Balloon Analogue Risk Task" and the "Barratt's Impulsiveness Scale" for participants with ADHD. The y-axis represents the total BIS score, and the x-axis represents the mean adjusted number of pumps on the BART. The analysis was conducted on all genders within the ADHD psychiatric condition and no correlation was found r(37)=0.009, p=0.959.

Discussion

Primary Findings

This study set out to address various questions regarding risk-taking, impulsivity, and the anterior cingulate cortex (ACC). The established literature suggests that the anterior cingulate cortex is heavily correlated with impulse inhibition, meaning that a smaller ACC volume correlates with greater impulsivity (Brown & Braver, 2007; Fukanaga et al., 2012). While this concept has been supported by comparing the left ACC with self-rated scores on Barratt's Impulsiveness Scale (BIS) (Matsuo et al., 2009), little research has been conducted on whether risk-taking measures such as the Balloon Analogue Risk Task (BART) are modulated by the ACC volume. Therefore, the first aim of this study focuses on how the gray matter volume of the ACC relates to risk-taking on the BART and impulsivity on the BIS.

Based on the correlation in Figure 1, a negative correlation exists between mean adjusted number of pumps on the BART and left ACC volume for male healthy controls (HC). These findings are consistent with previous data which suggests that a smaller ACC volume is associated with greater risk-taking behavior (Lejuez et al., 2002; Lejuez et al., 2003) These conclusions are based solely on healthy males while healthy females portrayed no correlation between ACC volume and the BART. When considering left ACC volume and impulsivity, no correlations exist for healthy controls of either gender.

The psychiatric conditions, Bipolar Disorder (BD) and Attention Deficit Hyperactivity Disorder, are incorporated to see if the same relationships apply. When considering Bipolar Disorder compared to impulsivity, risk-taking, and ACC volume, no significant relationships exist even when controlling for gender. Specifically, the BD condition does not demonstrate a relationship between the volume of the left ACC and performance on the BART or BIS for either gender. Attention Deficit Hyperactivity Disorder is compared with impulsivity, risk-taking, and ACC volume for both genders. Although there are no significant correlations found between the ACC volume and performance on the BART and BIS, the BART displays a trend of p-value=0.089 (Fig. 2). In this case, for males with ADHD, smaller anterior cingulate volumes are associated with less riskiness on the BART, which is opposite to the trend of the healthy controls. This result is inconsistent with previous findings that the anterior cingulate cortex contributes to impulse inhibition (Brown & Braver, 2007; Helfinstein et al., 2014).

Based on current literature, both ADHD and BD are characterized by structural, behavioral and neuroanatomical differences, contributing to increased impulsivity and risk-taking behavior. For adults, engagement in unsafe sexual activity, risky driving, and drug use indicate this impulsive and risk-taking behavior (Groen et al., 2013; Johnson et al., 2012). When looking at the ACC as a modulating factor of these behaviors, there are inconsistencies in research (Reddy et al., 2014., Pollak et al., 2018, Sassi et al., 2004, Makris et al., 2010). Because only healthy males reflect increased risk-taking with smaller ACC volumes, there may be a different brain area overriding the influence of the ACC on risk-taking behavior only. Some research indicates that the nucleus accumbens (NAc) is heavily activated for people with ADHD and BD (Reddy, 2014; Volkow, 2011); consequently, this activity could weaken the input provided by the ACC. These results suggest that there are structural and functional differences for males with ADHD and BD that modulate the relationship of risk with ACC volume.

While these observations are relevant for males, there was no relationship established for risk taking or impulsivity and ACC volume for females, regardless of condition. It is unclear whether the ACC or NAc plays a role in risk taking and impulsive behavior; however, there appears to be another brain area involved in risky decisions for females. This observation is consistent with literature that found males experience increased activity in the ACC while females experience increased activity in the middle temporal cortex during impulse control tasks (Liu, 2012). More research is required to establish whether the middle temporal cortex correlates with activity in only healthy females or if it also accounts for impulsivity and risk taking for females with psychiatric disorders.

The findings also suggest that impulsivity and risk taking are two distinct measures. For healthy adults of both genders, increased risk-taking is significantly correlated with increased impulsivity (Fig. 6). However, risk-taking and impulsivity for participants with ADHD and BD is not significantly correlated (Fig. 7; Fig. 8). Given there is also no correlation between the BIS and ACC volume, impulsivity is likely influenced by a different brain area entirely for participants where these traits are heightened (Johnson et al., 2012).

Since risk-taking and impulsivity appear separate in psychiatric disorders, the study then investigated which trait is more representative of ADHD and BD. Impulsivity was significantly greater for adults with ADHD (Fig. 3) and BD (Fig. 4) compared to healthy controls. During the BART, risk taking was not significantly different than the healthy controls (Fig. 5). With this knowledge, it appears that impulsive behaviors are more representative of ADHD and BD compared to risk-taking behaviors. Perhaps, the BART is an inaccurate measure of real life behavior and risk-taking when these behaviors are more “extreme” (Lauriola et al., 2013; Najt et al., 200 Amico et al., 2011; Pollak et al., 2018). Given the current findings, impulsivity in the BIS is a better representation of ADHD and BD behaviors. However, more research is required to determine the validity of the BART in representing risk-taking for psychiatric populations and to evaluate these disorders with greater accuracy.

Limitations

The findings in this study may have been impacted by a variety of factors given the clinical and realistic design. Based on the data collection alone, differences could be a result of methods in data collection, such as the use of two different MRI scanners (Poldrack, 2016). Because we are unable to validate the data collection and participant diagnoses, this study relies on the validity of the dataset from UCLA Consortium for Neuropsychiatric Phenomics. Another important consideration with the database and naturalistic design is based on the participant demographic and the limitations involved with using psychiatric patients. One such limitation relates to the patient demographics, medical history, and current medical status. For instance, subjects within the psychiatric condition groups remained on their current medication throughout the course of the study. This factor could have impacted the results because current literature demonstrates that lithium, a common medication used in Bipolar Disorder, causes an increase in or no effect on the gray matter volume of the ACC (Amico et al., 2011; Mantyla et al., 2012; Matsuo et al., 2009). These medications are also shown to impact behavior, potentially affecting both the BART and BIS (Amico et al., 2011). Because many psychiatric disorders are comorbid with other disorders, it is unclear whether the findings are indicative of the psychiatric condition alone. For instance, fifty participants in this dataset were also diagnosed with substance use disorder; this finding is notable, given that substance use disorder is also connected with both risk-taking and a smaller anterior cingulate cortex volume (Spindler, 2021; Holmes, 2009).

Within this study, there are also limitations with the method utilized, referring to the BART, BIS, and VBM analysis. The BART, for example, is not necessarily correlated with real life behavior, even in situations where self-rated impulsivity scores are high (Lauriola et al., 2013; Najt et al., 200 Amico et al., 2011; Pollak et al., 2018). The BIS may also inaccurately report real-life behavior. This phenomenon of increased scores in self-rated questionnaires could be related to illness perception in subjects who know their psychiatric disorder and its symptoms (Subramaniam, 2018). The use of voxel-based morphometry introduces some limitations. Variations in brain size, which are not completely accounted for in the VBM analysis, can be caused by age, gender, medication use, and mood states (Adler et al., 2005). Overall, the naturalistic design of the study and some of the measures used introduce limitations to the study that may impact the findings.

Future Directions

By changing methods and participant recruitment, future studies may address some of the limitations described above. If the subjects were divided into more narrow conditions and the sample size was increased, factors such as medication use could be controlled. Additionally, looking at substance use disorder (SUD) and expanding the study to include participants with BD, ADHD, or SUD separately and comorbidly could potentially elucidate the relationship between mental illness and risk-taking or impulsivity.

Other studies could examine different risk-taking tasks or track real life risk-taking behavior. These correlations may offer a clearer connection between ACC volume, psychiatric disorder, and risk-taking. While this study begins to clarify the relationship between impulsivity and risk-taking, a closer investigation of these behaviors, especially in ADHD and BD would be useful. A final area of interest would investigate the impacts of gender and brain areas on risk-taking and impulsivity. This study sets the foundation for potential relationships between ACC volume and risk taking for healthy males. Evaluating the relationship of the NAc with risk-taking and impulsivity may further elucidate anatomical differences in adults with ADHD and BD. Since there were no findings for females, investigating areas such as the middle temporal cortex may offer more information.

Implications

Attention Deficit Hyperactivity Disorder (ADHD) and Bipolar Disorder (BD) affects 4.4% and 2.8% of adults in the United States, respectively (U.S., 2021). This substantial portion of the population may face difficulties in situations that require impulse control and risk avoidance. This study first offers useful information pertaining to the role that the ACC plays in risk taking and impulsivity. By understanding gender differences and brain areas involved in risk-taking and impulsivity, more individualized and focused treatments could be utilized to target specific brain regions. Secondly, this study provides useful input on characterizing psychiatric disorders and elucidating the relationship between risk and impulsivity in mental illness. Historically, these traits have been correlated closely; however, this study suggests these traits may be quite distinct, especially for people with BD and ADHD. Utilizing this finding, offers potentially more accurate diagnostic criteria for psychological evaluations and measures.

With improved accuracy in diagnosis and clarity in brain areas involved, new treatments could be developed to offer increased safety and decreased severity of symptoms for risky behavior and impulsivity in populations most affected by these traits.

Conclusion

This thesis sets out to integrate and explain risk-taking and impulsivity as they relate to the gray matter volume of the anterior cingulate cortex. Given that Attention Deficit Hyperactivity Disorder and Bipolar Disorder are often characterized by impulsive and risk-taking behavior, this study utilizes those groups to go beyond healthy controls. With increased knowledge on the distinction between these traits and their connection to the ACC, the behavior of humans from both a psychological and neuroscientific perspective could be better understood. Moreover, detecting brain areas and gender differences related to risk and impulsivity can help researchers target treatments for these behaviors. Perhaps with more knowledge and new treatments, notable and often negative symptoms associated with psychiatric disorders can be alleviated.

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