Title

Anhedonia as a transdiagnostic symptom: Implications for cognition and white matter development

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Publication Date

2024

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Anhedonia as a transdiagnostic symptom:

Implications for cognition and white matter development

A dissertation submitted in partial satisfaction

of the requirements for the degree

Doctor of Philosophy in Psychology

by

Danielle Leigh Currin

2024

ABSTRACT OF THE DISSERTATION

Anhedonia as a transdiagnostic symptom:

Implications for cognition and white matter development

by

Danielle Leigh Currin

Doctor of Philosophy in Psychology

University of California, Los Angeles, 2024

Professor Katherine H. Karlsgodt, Chair

Anhedonia is a transdiagnostic symptom characterized by the loss of the experience of pleasure from typically enjoyable activities. An established body of research has explored the impact of anhedonia on functioning and long-term outcomes in psychiatric populations, and emerging research has examined the role of anhedonia in adolescents with no psychiatric diagnosis. Anhedonia has been found to impact goal-directed behavior, reward processing, and future-oriented thinking. These behaviors are associated with cognitive abilities, which include both “hot” and “cold” cognition. These two cognitive systems develop throughout adolescence and are impacted in numerous psychiatric disorders. However, existing work has not provided a clear picture of how these pieces – anhedonia, adolescent development, and cognitive systems – fit together across diagnostic categories.

The goal of this dissertation, which comprises three studies, was to bridge this gap by providing an in-depth look at anhedonia across adolescence and early adulthood using a dimensional lens and multiple modalities, including self-report, task performance, and brain imaging. In Study 1, I investigated associations between subcategories of anhedonia and aspects of risk-taking behavior in university students using hierarchical linear regression. Individuals who experienced less anticipatory pleasure (i.e., looking forward to an activity) engaged in more risk-taking behavior. In Study 2, I expanded these findings by investigating relationships among anhedonia, risk-taking behavior, risk perception, and working memory in adolescents across a wider age range using linear regression and a moderation analysis. I replicated the positive association between anhedonia and risk-taking behavior and found a positive relationship between age and working memory performance. The hypothesized moderation model was not significant. In Study 3, I examined the associations among psychosis diagnosis, anhedonia, and white matter integrity in adolescents using linear regression and a linear mixed model. I found a significant group difference in a frontrostriatal tract associated with "hot" cognition, and a significant negative relationship between anhedonia and integrity in a white matter bundle associated with "cold" cognition. I highlight the need to continue exploring relationships among anhedonia, cognition, and white matter in adolescence. The implications of this work, including further illumination of the impact of anhedonia on functioning across diagnoses, are also discussed.

The dissertation of Danielle Leigh Currin is approved.

Carrie E. Bearden

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Katherine H. Karlsgodt, Committee Chair

University of California, Los Angeles

2024

This dissertation is dedicated to those who came before me to forge this path, those who walked alongside me as I traversed it, and those who will one day look to me to guide their way.

TABLE OF CONTENTS

LIST OF FIGURES AND TABLES

TABLES

FIGURES

ACKNOWLEDGEMENTS

There are numerous people without whose support this dissertation would not have been possible. First, I extend a huge thank you to my academic advisor and dissertation chair, Dr. Katherine Karlsgodt, who has been a guiding voice, a pillar of patience, and a dedicated cheerleader throughout this process. I also thank the rest of my dissertation committee – Drs. Bearden, Lee, and Silvers – for agreeing to take this journey with me and providing incredibly helpful suggestions and feedback at every step. The Clinical and Cognitive Neuroscience lab has been invaluable as I have worked on this dissertation. I am grateful for the camaraderie I have found with the graduate students (Dr. Pooja Patel, Logan Leathem, Rachel McKinney, Haley Wang, and Mary Rshtouni), the willingness to do the "grunt work" I have appreciated in the undergraduate research assistants (Isabel Aks, Leyla Boyar, Abby Dalton, Sophie Delta, Jacob Lee, Candhra Lopez, Alondra Razon, Hannah Reiter), and the can-do attitude I have admired in the lab manager (Kristen Laulette). In addition to the friends I have made within my lab, I have been incredibly fortunate to make lifelong friends throughout my time in graduate school, including Jordan Thomas, Julia Yarrington, Lindsay Meredith, Sarit Forman, and Stephanie Yu. They have encouraged me to push myself academically and professionally while maintaining my humanity through not only their words, but also their humble modeling of excellence.

I am indebted to the teams who collected the data used in this dissertation, including Dr. Karlsgodt's team at Zucker Hillside Hospital (Melanie Blair-Thies, Ashley Moyett, Dr. Pamela DeRosse), as well as the Clinical and Cognitive Neuroscience Lab. Their dedication to science has fueled my own. In addition, I extend my humblest thanks to the participants in all of the studies I have included in my dissertation; that they chose to volunteer their time to assist in the advancement of science (for some, in the midst of incredibly stressful mental health challenges)

is one of the greatest gifts a budding researcher can receive. I am grateful for the opportunities I had to build community in Los Angeles through work and volunteer opportunities (Nya, Jeff, Allie, Mel, Mariel, Pam), as well as to reconnect with family I had not seen since I was too young to remember (Michael, Kirsten, Christopher). My community has also extended to virtual spaces, as I have weathered the storms of early adulthood with friends I picked up along the way (Tyler Blackmon, Shannon Grogans, Catherine Jameson, Franchesca Kuhney, Isabel McCullough, Angela Pollard, Dr. Alan Zhang). Thank you to all of you for enduring my unprompted explanations of how the "dissertation research thing" works. I also must express my undying gratitude for my family, who cheered me on from afar and from close by: my sister, Kellsie, who has mastered the art of balancing the urge to brag about her little sister with the need to keep my head from getting too big; my parents, John and Joyce, who told me from the beginning that I was going to accomplish great things; and my grandmother, aunts, uncles, and cousins (Mary, Beth, Richard, Cavin, Austin, Nina), who started calling me "doctor" as soon as I began graduate school. Finally, I give a special thank you to my dog Rose, who, even though she had no idea what I was doing, was there with me through all the ups and downs. To all mentioned here and countless others who remain unnamed, words cannot express my gratitude for your insight, support, and faith. From the bottom of my heart, thank you.

This research was supported by the following: NIMH 1R01MH101506 Multimodal Imaging of Executive and Reward Networks across the Psychosis Spectrum (PI: Karlsgodt) and NICHD 1T32HD091059 Brain and Behavioral Development during Adolescence (PIs: Fuligni, Galvan, Dapretto). Study 1 of this dissertation was previously published as Currin, D., Hart, K., Gupta, M., Patel, P., Leathem, L., & Karlsgodt, K. (2022). The role of anhedonia in predicting risk-taking behavior in university students. Journal of Psychiatric Research, 155, 451-457.

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SELECTED PRESENTATIONS

Currin, D., Kaslow, N. *Caring Contacts: A Simple Yet Effective Tool for Suicide Prevention.* Presentation given at Bite-Sized Teaching conference, Emory University School of Medicine, Atlanta, GA, September 2023.

Currin, D., Laulette, K., & Karlsgodt, K. *Adolescent anhedonia and risk-taking in an online community sample.* Poster presented at Society of Biological Psychiatry, San Diego, CA, April 2023.

Currin, D., Leathem, L., Madrid, M., Arkin, S., Kim, L., McCarthy, K., & Karlsgodt, K. *The distress of negative symptoms: Contributions of perspective-taking skills and attributional biases.* Presentation given at Society for Research in Psychopathology, Virtual Conference September 2021.

Currin, D., Hart, K., Gupta, M., Patel, P., Leathem, L., & Karlsgodt, K. *The role of anhedonia in predicting risk-taking behavior in university students.* Poster presented at Society of Biological Psychiatry, Virtual Conference April 2021.

Currin, D., Hegarty, C., Leathem, L., Galván, A., & Karlsgodt, K. *White matter integrity, inhibition, and subclinical psychosis in early adults.* Poster accepted at Society of Biological Psychiatry, New York, NY, May 2020 (conference cancelled).

Currin, D. *Inhibition and white matter integrity in early adults with subclinical psychosis symptoms*. Presentation given at the UCLA Department of Psychology Clinical Area Program Meeting, University of California, Los Angeles, CA, January 2020.

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Currin, D., Kohn, P., Kippenhan, J., Rubinstein, D., Hegarty, C., Czarapata, J., Eisenberg, D., & Berman, K. *Altered prefrontal activity during naturalistic receptive language processing in medication-free patients with primary psychosis*. Poster presented at Society of Biological Psychiatry, San Diego, CA, May 2017.

Currin, D. *The relationship between risk perception and risk-taking behaviors*. Presentation given at the Paskus Mellon Forum at Yale University, New Haven, CT, February 2016.

CHAPTER 1 | BACKGROUND

Anhedonia is typically defined as a loss in the experience of pleasure from previously enjoyed activities (Der-Avakian & Markou, 2012). It is typically considered a symptom of underlying psychopathology, with a wide body of research investigating its presence in psychosis spectrum disorders (e.g., (Marder & Galderisi, 2017)) and depression (e.g., (Pizzagalli, 2014)). In recent years, its appearance has been noted in a variety of psychiatric populations, including ADHD (Babinski et al., 2019), substance use (Stull et al., 2022), and eating disorders (Murray et al., 2022). Additionally, anhedonia is found at varying levels of severity in the general population (Barkus & Badcock, 2019). The ubiquity of this transdiagnostic symptom highlights its importance as a widely-occurring facet of the human experience, and one worthy of more in-depth exploration.

Beyond serving as a diagnostic criterion, anhedonia can significantly influence an individual's functioning above and beyond any official diagnosis they may or may not have received. For instance, individuals with psychosis or depression who are experiencing anhedonia typically experience a decrease in goal-directed behavior (Gard et al., 2007), and increased anhedonia is a significant predictor of poorer functioning and longer time to remission of symptoms in these populations (Kiwanuka et al., 2014; McMakin et al., 2012). Anhedonia is a broad term encompassing different aspects of the experience of pleasure; as such, it may have the same name but different presentation in individuals with different diagnoses. For instance, it may appear as disorganized reward processing (akin to consummatory pleasure) in schizophrenia but a deficiency in associating actions with rewards (akin to anticipatory pleasure) in depression (Lambert et al., 2018). These distinctions further highlight the need to investigate different types of anhedonia and how they may impact functioning and response to treatment. Even in

individuals who do not carry a psychiatric diagnosis, those who self-report anhedonia typically have poorer social functioning, less willingness to engage in social interactions, and disrupted future-oriented thinking (Barkus & Badcock, 2019; Lempert & Pizzagalli, 2010). All told, the importance of understanding this transdiagnostic symptom cannot be understated.

Individuals with many of the psychiatric diagnoses mentioned here often experience cognitive deficits as well as anhedonia. Cognitive deficits have been extensively studied in individual with psychosis spectrum disorders (Bora et al., 2024; Dickinson et al., 2004; Sheffield et al., 2018) and, though not officially a diagnostic symptom of psychosis, have long been considered core to the experience of psychosis. Cognitive deficits have been studied in other disorders, including depression (Chakrabarty et al., 2016), alcohol use disorders (Stavro et al., 2013), and ADHD (Kofler et al., 2019). While these disorders similarly do not count cognitive deficits among their symptoms, the presence of these deficits may impact an individual's experience of other symptoms as well as treatment response (Czerwinska & Pawlowski, 2020; McCleery & Nuechterlein, 2019).

Typically, cognitive research in clinical populations focuses on domains of cognition that fall into the umbrella category of non-affective, or "cold", cognition. This includes abilities like working memory and verbal learning, and has been an essential and productive area of study over many decades. Another area of cognition that has been studied in clinical and subclinical populations is affective, or "hot", cognition. While in the literature, hot cognition is not often categorized together with cold cognition functions, the mechanisms behind hot cognitive tasks like decision-making and risk-taking include cold cognition aspects, such as working memory (to recall consequences of prior actions) and learning (to apply knowledge to future actions) in addition to the affective or emotionally driven aspect of the behavior. These hot cognitive

abilities are also affected in individuals experiencing psychiatric illness, whether a diagnosed disorder or a subclinical experience of anhedonia (Ashenhurst et al., 2014; Cheng et al., 2012; Lewandowski et al., 2016; Whitton et al., 2015; Zhou et al., 2019).

An emerging area of research considers differences in the trajectories of the development of cold cognitive (non-affective) and socioemotional (affective) systems in adolescence (Shulman et al., 2016). Cognitive deficits in individuals experiencing various types of psychopathology are well established, but this distinction between cognition that does and does not involve affective processes, as well as how the two work either in concert with or against one another, remains relatively novel in psychological research. Therefore, a key aim of this dissertation is to better define the relationship between anhedonia and the different categories of cognition (hot and cold) in adolescents and early adults across a wide spectrum of psychopathology.

The development of hot and cold cognition in adolescence and early adulthood, as well as increased experiences of anhedonia contribute vulnerability during this period. It is a critical window in which natural changes in mood and behavior may evolve into impactful challenges for the individual (Dalsgaard et al., 2019; Immonen et al., 2017; Mitchell et al., 2008). From a neurological perspective, adolescents and young adults are also undergoing continued brain development, including some remodeling of the white matter, which structurally connects different brain regions (Bava et al., 2010; Herting et al., 2017; Lebel & Deoni, 2018). White matter is known to be impacted in mood and psychosis spectrum disorders such as schizophrenia, bipolar disorder, and depression (Abraham et al., 2022; Brown et al., 2021; Vanes et al., 2020). In particular, white matter tracts associated with the hot (accumbofrontal tract) and cold (superior longitudinal fasciculus) cognitive processes described above are still developing

during adolescence and are known to be impacted in individuals with schizophrenia (Diaz et al., 2021; Karlsgodt et al., 2015; Peters et al., 2014). The co-occurrence of these biological and behavioral changes characterizes a period of life that is dynamic in many meaningful ways, leading to a number of fascinating and important questions about how these pieces fit together in the overarching experience of adolescent development.

In this dissertation, I hope to fit the pieces of development together in a way that can help us better understand the broad spectrum of the adolescent experience. With anhedonia as the common thread, I have investigated relationships among the experience of anhedonia, white matter development, and hot and cold cognition in varying samples of adolescents and early adults who lie along a wide spectrum of mental illness. A visual representation of this is seen in Figure 1.

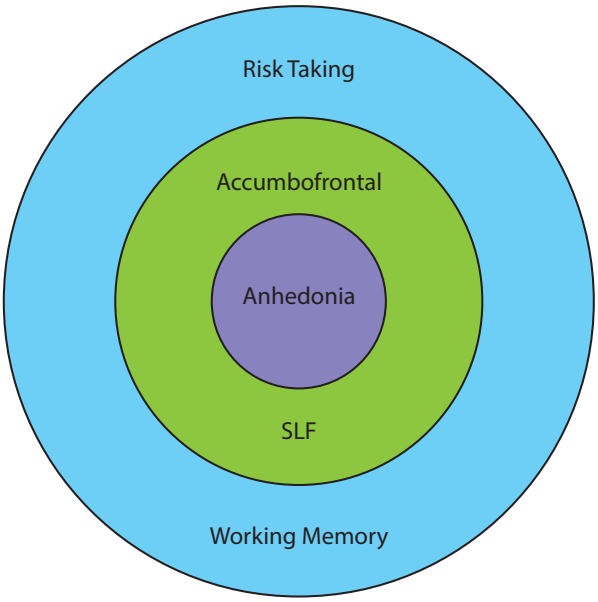


Figure 1. Representation of areas of interest in the current dissertation.

This goal has been addressed through the use of three distinct yet related studies. In Study 1, I have focused on the relationship between anhedonia and risk-taking (a type of hot cognition)

in late adolescence and early adulthood using a university sample from the University of California, Los Angeles (UCLA). In Study 2, I have used on-line sampling to remotely collect data on anhedonia, hot cognition (risk-taking), and cold cognition (working memory abilities) in adolescents as young as 12 from across the United States. Finally, in Study 3, I have focused on the relationship between anhedonia and white matter development in tracts associated with hot (accumbofrontal tract) and cold (superior longitudinal fasciculus) cognition, using longitudinal data collected in adolescents with and without a diagnosis of a psychosis spectrum disorder. By investigating these relationships, I hope to shed light on psychological, behavioral, and neurological changes occurring in adolescence and provide a new perspective on the impact of anhedonia on the adolescent experience.

CHAPTER 2 | STUDY 1: The role of anhedonia in predicting risk-taking behaviors in university students

INTRODUCTION

In recent years, initiatives such as the NIMH Research Domain Criteria (RDoC) have encouraged a growing focus on symptoms of psychological distress as transdiagnostic entities (Cuthbert and Insel, 2013; Lambert et al., 2018). One such transdiagnostic symptom is anhedonia, a decrease in the experience of pleasure in response to a previously rewarding stimulus (Lambert et al., 2018). Anhedonia has been well-studied as a feature of multiple psychological disorders (Pizzagalli, 2014; Kasanova et al., 2018; Strauss and Gold, 2012), and is known to vary in a trait-like way across the general population (Barkus and Badcock, 2019). Individual differences in anhedonia can affect a number of functional outcomes (Kiwanuka et al., 2014), including social functioning and interactions (Barkus and Badcock, 2019), future-oriented thinking (Lempert and Pizzagalli, 2010), and willingness to expend effort for a reward (Barch et al., 2014; Geaney et al., 2015). While an emerging body of literature points to a broad spectrum of variability in anhedonia and its correlates across the general population, we lack a well-defined understanding of the relationship between anhedonia and risk-taking in non-clinical samples; that is, community samples not selected specifically for their experience of anhedonia or the presence of any particular psychiatric diagnosis.

Anhedonia is associated with decreases in two components of the experience of pleasure: anticipatory and consummatory pleasure. Anticipatory pleasure, or 'wanting', is the experience of pleasure related to future activities, while consummatory pleasure, or 'liking', is the experience of pleasure while engaging in an enjoyable activity (Gard et al., 2006). These components have most extensively been studied in individuals with schizophrenia, with many studies finding a deficit in anticipatory but not consummatory pleasure (Frost and Strauss,

2016; Gard et al., 2007; Kring and Barch, 2014). In addition, two dimensions of anhedonia are typically studied: social and physical anhedonia (Blanchard et al., 1994; Kerns et al., 2008). While some research has pointed to the importance of physical anhedonia (e.g., Blanchard et al., 1994) alongside social anhedonia, anhedonia has typically been considered a single entity.

Risk-taking behavior is similarly not a unitary construct. Choosing to take a risk involves the intersection of several processes, including reward learning and cognitive control (Blakemore and Robbins, 2012; Luk et al., 2019; Nusslock and Alloy, 2017). For instance, reward valuation, or the evaluation of rewarding and punishing aspects of a choice, encompasses these and other higher cognitive processes and can vary across individuals. Evidence suggests that individual differences in personality, symptomatology, and developmental stage contribute to differences in engagement with risk and which factors are weighted most heavily (Bornovalova et al., 2009). Late adolescence and early adulthood in particular are associated with a complex and continually developing relationship with risk. Evidence indicates that adolescents tend to base current behaviors on the consequences of their most recent action (Mitchell et al., 2008). This pattern highlights a potential mechanism for the observation that adolescents have a heightened proclivity to engage in risk, a proclivity that may extend into early adulthood.

Late adolescence and early adulthood also represent a window of vulnerability for the onset of disorders characterized by anhedonia (Dalsgaard et al., 2020; Immonen et al., 2017). However, the complexities of the co-occurrence of heightened anhedonia and altered risk-taking behavior in early adulthood are still understudied (Rzepa and McCabe, 2019). The current study aimed to further elucidate the relationship between anhedonia and risk-taking in a university-based community sample of late adolescents and early adults using their self-reported experience of pleasure and anhedonia and performance on a risk-taking task. The distinct components of

anhedonia outlined here (anticipatory, consummatory, social, and physical) could have different behavioral implications both in terms of functional outcomes and treatment focus, and as such, it is worthwhile to develop a deeper understanding of how they interact with one another.

Previous literature has revealed a significant role of anhedonia in reduced reward sensitivity (Liu et al., 2016), a component of the decision-making process that leads individuals to take risks. Based on this knowledge, we hypothesized negative linear relationships between anhedonia and risk-taking behavior, such that individuals scoring higher on anhedonia (or lower on pleasure) would display less risky behavior. While several processes – including reward learning, reward valuation, and motivation – are necessary for risk-taking behavior, this study focuses primarily on overall risk propensity, sub-optimal risky behavior, and response to punishment. Additionally, we were interested in how the social and physical dimensions of anhedonia might separately influence this relationship and so included measures that looked at each of these. As a secondary component of our analysis, we hypothesized that this relationship would be driven primarily by lower reported anticipatory pleasure based on prior literature indicating a relationship between anticipatory pleasure and reward-seeking behavior in clinical populations (Gard et al., 2007; Kring and Barch, 2014). We also explored whether there were differences in this relationship when we focused on the three distinct aspects of the tested risky behavior outlined above. Investigating anhedonia in this way may increase our understanding of the differential impact of anhedonia on other illness domains (e.g., risk-taking, cognition) in individuals with and without psychiatric illness. This work has the potential to open the door to further research on how 'mild' and 'severe' anhedonia can impart different functional outcomes regardless of official diagnosis.

METHODS

Participants

Ninety-seven undergraduate students at the University of California, Los Angeles (UCLA) were recruited using an online system through the Psychology Department. This study was approved by the UCLA Institutional Review Board, and participants were compensated with course credit. For inclusion in the study, participants were required to speak English fluently. Participants were excluded if they self-reported a neurological disorder, significant head injury, or ongoing treatment for a major mental illness. Of 97 students who completed testing, eight were excluded due to missing or incomplete data, seven due to scoring more than 1.96 standard deviations beyond the sample mean on either the Chapman Physical Anhedonia Scale (CPAS) or the Chapman Social Anhedonia Scale (CSAS), and one due to being an outlier on age. This left a total of 81 participants for inclusion. Estimated age was calculated based on year of birth and testing date (Table 1).

Mean Estimated Age (SD, range)	**20.71 (1.33, 18–23)**
Gender, %F	76.5
Race, n (% of sample)	
African American	2 (2.5)
Asian	30 (37.0)
Native American	3 (3.7)
Native Hawaiian/Pacific Islander	1 (1.2)
White	27 (33.3)
More than one race	12 (14.8)
Not reported	6 (7.4)

Note. Total sample size n = 81. + p < .10, *p < .05, **p < .01, ***p < .001.

Table 1. Sample demographics.

Anhedonia and Pleasure Questionnaires

Participants completed the CPAS (Chapman et al., 1976), the CSAS (Eckblad et al., 1982), and the Temporal Experience of Pleasure Scale (TEPS (Gard et al., 2006)). The CPAS and CSAS measure the experience of pleasure during typically enjoyable activities. The CPAS focuses on individual activities and experiences (e.g., "When eating a favorite food, I have often tried to eat slowly to make it last longer"), while the CSAS focuses on social norms and activities (e.g., "Having close friends is not as important as many people say"). Participants rate the statements as true or false, and higher scores on these scales indicate more pronounced anhedonia.

The TEPS measures both the experience of pleasure in the moment and pleasure taken from looking forward to future events. This scale contains 18 statements that the participant rates on a Likert-type scale from *very false for me* (1) to *very true for me* (6) (e.g., "When I hear about a new movie starring my favorite actor, I can't wait to see it" for anticipatory pleasure; "I enjoy taking a deep breath of fresh air when I walk outside" for consummatory pleasure). Higher ratings on the TEPS indicate a higher level of reported pleasure.

Previous work shows a negative correlation between subscales of the TEPS and the two Chapman scales (Chan et al., 2012). That said, when used together (e.g. (Tso et al., 2014),), they demonstrate distinct properties (i.e., temporal versus activity type). As the TEPS questions center around physical activities (rather than social), some overlap between TEPS scores and the CPAS is expected (Gard et al., 2007). However, the TEPS adds a unique component by distinguishing between the temporal components of pleasure.

Balloon Analogue Risk Task

Participants completed a 40 trial version of the Balloon Analogue Risk Task (BART (Lejuez et al., 2002)). Because of the BART's extensive use in multiple populations both with

(Hevey et al., 2017; Reddy et al., 2014) and without (Li et al., 2020) psychiatric illness, we employed it as an estimate of the risk-taking behaviors in a clinically diverse sample. In this version of the BART, participants key-pressed to inflate a virtual balloon until either they cashed out (stopped inflating) or the balloon exploded. Participants gained points for each successful inflation but lost all points on the trial if the balloon exploded. The task was probabilistic, with each balloon having a 1/32 chance of exploding at each key press.

Three BART outcomes were assessed. Mean Adjusted Pumps (MAPs) were calculated by averaging the inflations made on BART trials that did not terminate with an explosion. MAPs are a commonly used measure of risk propensity (Koscielniak et al., 2016; McCormick and Telzer, 2017). Total Explosions (TEs) were calculated by summing the number of trials with explosions. TEs represent how frequently a participant behaved in a way that was sub-optimally risky and punitive as it results in lost points (Hunt et al., 2005). Mean Adjusted Pumps After Explosion (PAEs) were calculated by averaging the number of inflations on each trial immediately succeeding an explosion. PAEs represent the degree to which a negative outcome of a previous risky decision impacts current behavior. These three outcomes were selected to provide us with an understanding of the impact of anhedonia on both the reward-seeking (MAPs) and punishment-oriented (TEs, PAEs) components of risk-taking behavior.

Statistical Analysis

Comparisons across demographic groups were made using independent t-tests for sex, one-way ANOVAs for race, and Pearson correlations for estimated age. Pearson correlations were also used to assess the relationships among the predictors (TEPS, CPAS, and CSAS), and among the outcome measures (MAPs, TEs, and PAEs). Given the expected overlap within the predictors and outcome measures, we followed these correlations with an exploratory factor

analysis (EFA) to investigate the level of uniqueness that each measure brought to the primary analyses. To determine the relationship between anhedonia (using the TEPS, CPAS, and CSAS) and risk-taking (using MAPs, TEs, and PAEs), a series of three-step hierarchical linear regressions were used. These included a base model of estimated age and sex predicting risk-taking, with measures of anhedonia added at subsequent steps: the TEPS at the second and the CPAS and CSAS at the third. This allowed for a stepwise analysis of the contribution of each measure of anhedonia on the outcomes of interest prior to and after the influence of subsequent predictors. Given our particular interest in understanding the impact of anticipatory and consummatory aspects of pleasure on risk-taking behaviors, the TEPS was included in an earlier step than either the CPAS or CSAS to see both how it independently impacted the three risk outcome measures and how its impact was affected by the addition of other anhedonia scales. Unstandardized local effect sizes are represented by Cohen's f^2 coefficients (Lorah, 2018) and reported without confidence intervals, as these are not typically used in hierarchical regression. All analyses were conducted in Stata version 16.1.

RESULTS

Demographics

Female participants had higher TEPS scores ($t(79) = -2.982$, $p = .004$), fewer MAPs ($t(79) = 2.840$, $p = .006$), fewer TEs ($t(79) = 3.638$, $p < .001$), and fewer PAEs ($t(79) = 2.370$, $p = .020$). Male and female participants did not significantly differ on CPAS or CSAS scores (both $p > .05$) (Table 2). Participants did not significantly differ on any of these outcomes based on race or estimated age (all $p > .05$). Given these significant sex differences and the developmental nature of this sample, sex and age were included as covariates in the primary

analyses. Because race was not a significant predictor in these preliminary analyses, it was not included as a covariate in later analyses.

	Male (n = 19)	Female (n = 62)	Total (n = 81)	t (p-value)	Effect Size (Cohen's *d*)
TEPS	71.32 (10.18)	78.71 (9.23)	76.98 (9.91)	−2.98 (.004)**	−0.78
TEPS-A	36.32 (6.82)	40.48 (5.90)	39.51 (6.33)	−2.60 (.011)*	−0.68
TEPS-C	35.00 (4.93)	38.23 (5.34)	37.47 (5.40)	−2.34 (.022)*	−0.61
CPAS	11.21 (4.53)	10.26 (4.30)	10.48 (4.34)	0.84 (.41)	0.21
CSAS	8.16 (3.89)	7.19 (4.43)	7.42 (4.31)	0.85 (.40)	0.22
MAPs	11.26 (2.38)	9.10 (3.04)	9.61 (3.03)	2.84 (.006)**	0.75
TEs	16.53 (2.89)	12.68 (4.31)	13.58 (4.33)	3.64 (.0005)**	0.95
PAEs	10.11 (2.18)	8.19 (3.31)	8.64 (3.18)	2.37 (.02)*	0.62

Table 2. Sex differences.

Correlations within Predictors and Outcome Measures

Pearson Correlations

Pearson correlations between the TEPS, CPAS, and CSAS revealed weak to moderate correlations. TEPS was negatively correlated with CPAS (r = −0.472) and CSAS (r = −0.423), and CPAS and CSAS were positively correlated (r = 0.245). Pearson correlations between the three outcome measures revealed strong positive correlations. MAPs were positively correlated with TEs (r = 0.813) and PAEs (r = 0.912), and TEs were positively correlated with PAEs (r = 0.751). See Table 3 for a correlation matrix of these results.

	TEPS	CPAS	CSAS	MAPs	TEs	PAEs
TEPS	–	−0.472***	−0.423***	–	–	–
CPAS	−0.472***	–	0.245*	–	–	–
CSAS	−0.423***	0.245*	–	–	–	–
MAPs	–	–	–	–	0.813***	0.912***
TEs	–	–	–	0.813***	–	0.751***
PAEs	–	–	–	0.912***	0.751***	–

Table 3. Correlation matrix.

Exploratory Factor Analysis

Given the significant correlations among the anhedonia measures, an EFA was run with no limitations on the number of factors retained. The output yielded a single retained principal factor where all three anhedonia measures had moderate loadings onto this common factor. Additionally, each measure showed moderate levels of uniqueness, or variance in the measure not explained by the common factor. For each measure, the degree of uniqueness was greater than that of communality, or variance in the measure explained by the common factor (Table 4a). CSAS showed the most uniqueness and TEPS the least. A second EFA was run for the three outcome measures and yielded similar findings (Table 4b). The BART measures showed greater communality than the anhedonia measures, with TEs showing the most uniqueness of the three. Despite the higher degree of overlap between these risk-taking measures, they putatively index different constructs, and each was included as an outcome in its own hierarchical regression to pick up on subtle differences among them.

a.

	Factor Loading	Communality	Uniqueness
TEPS	−0.6738	0.4540	0.5460
CPAS	0.5667	0.3211	0.6788
CSAS	0.4944	0.2444	0.7556

b.

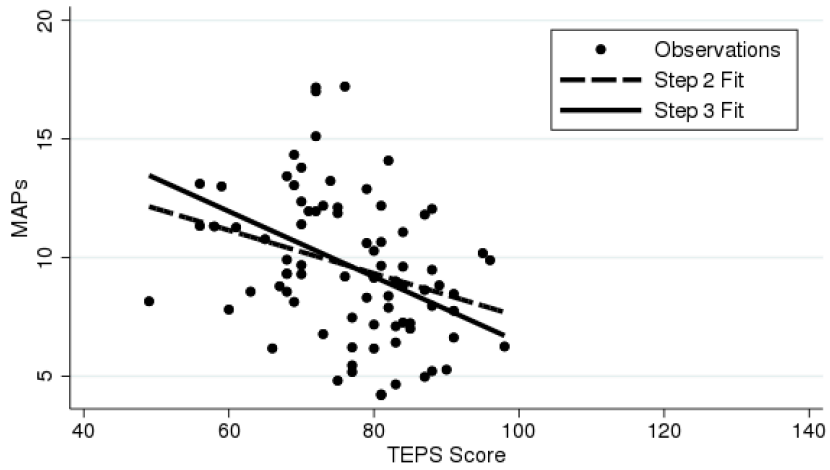
	Factor Loading	Communality	Uniqueness
MAPs	0.9570	0.9158	0.0841
TEs	0.8236	0.6783	0.3217
PAEs	0.9225	0.8510	0.1491

Table 4. Exploratory factor analysis.

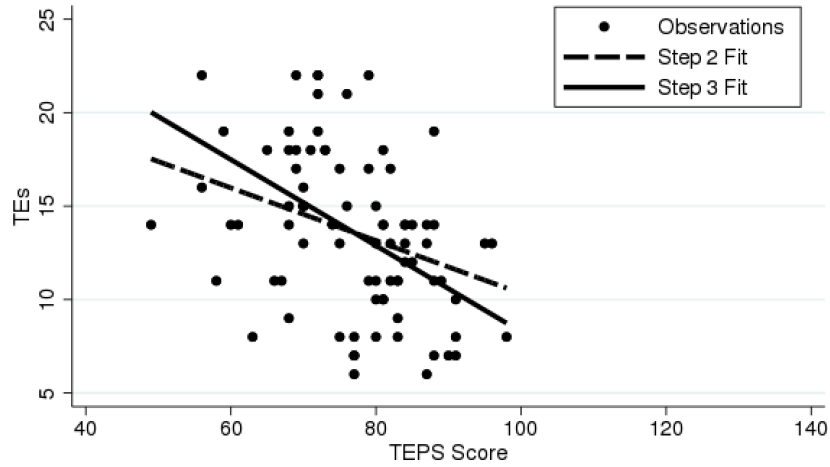
Relating pleasure and anhedonia to risk

TEPS, CPAS, and CSAS

Three hierarchical regressions were run, one for each of the three outcome variables of interest (MAPs, TEs, and PAEs). With MAPs as the outcome, TEPS score significantly predicted variance on MAPs above the effect of estimated age and sex ($b = -0.091$, $p = .008$). The local effect size of TEPS on MAPs was small ($f^2 = 0.086$). The addition of the CPAS and CSAS scores to this model did not significantly increase the variance explained by TEPS score alone ($p > .05$) (Figure 2a).



a.



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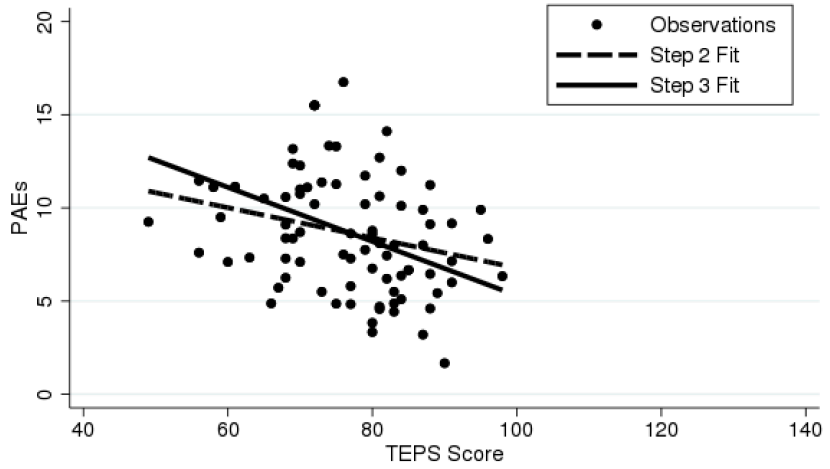


c.

Figure 2. The relationship between TEPS score and risk-taking outcomes. The relationships between (a) TEPS and MAPs, (b) TEPS and TEs, and (c) TEPS and PAEs at the second and third steps of the hierarchical linear regression. The dashed line (Step 2 Fit) represents the relationship between TEPS score and the risk behavior of interest, controlling for estimated age and sex. The solid line (Step 3 Fit) represents this relationship controlling for estimated age, sex, and the two Chapman scales.

With TEs as the outcome, TEPS score significantly predicted variance on TEs above the effect of estimated age and sex (b = −0.141, p = .003). The local effect size of TEPS on TEs was small-medium (f^2 = 0.108). The addition of the CPAS and CSAS scores to this model significantly increased its predictive power (R^2-change = 0.080, F(2,75) = 4.424, p = .015). While CPAS score significantly predicted variance above the effect of TEPS score (b = −0.253, p = .024), CSAS score did not have a significant effect (p > .05) (Figure 2b). The local effect size of CPAS and CSAS on TEs was small-medium (f^2 = 0.107).

With PAEs as the outcome, TEPS score significantly predicted variance on PAEs above the effect of estimated age and sex (b = −0.081, p = .029). The local effect size of TEPS on PAEs was small (f^2 = 0.060). The addition of the CPAS and CSAS scores to this model significantly increased its predictive power (R^2-change = 0.080, F(2,75) = 3.760, p = .028). While CPAS score significantly predicted variance above the effect of TEPS score (b = −0.203, p = .022), CSAS score did not have a significant effect (p > .05). The local effect size of CPAS and CSAS on PAEs was small (f^2 = 0.092). Full results for each of these models can be seen in Table 5, and a visual representation of results in Figure 2.

Predictor variables	**MAPs**	**TEs**	**PAEs**
Step 1: demographics			
Age	−0.035	0.221	0.142
Sex	−2.155**	−3.877***	−1.940*
R^2	0.093	0.148	0.070
F(2,78)	3.99*	6.77**	2.93+
Step 2: TEPS			
Age	−0.109	0.105	0.076
Sex	−1.474+	−2.819*	−1.333
TEPS	−0.091**	−0.141**	−0.081*
R^2	0.171	0.240	0.126

Predictor variables	MAPs	TEs	PAEs
R^2 change	0.079	0.092	0.056
F change (1,77)	7.299**	9.371**	4.954*
Step 3: Chapman			
Age	−0.145	0.374	0.016
Sex	−1.340+	−2.565*	−1.142
TEPS	−0.139***	−0.230***	−0.145***
CPAS	−0.134	−0.253*	−0.203*
CSAS	−0.093	−0.178+	−0.105
R^2	0.217	0.321	0.206
R^2 change	0.046	0.080	0.080
F change (2,75)	2.189	4.424*	3.760*

Table 5. Hierarchical regression analysis: TEPS, CPAS, and CSAS.

Anticipatory and Consummatory Pleasure

To further explore the relationship between the TEPS and the BART, three follow-up hierarchical regressions were analyzed in which the TEPS was split into its anticipatory (TEPS-A) and consummatory (TEPS-C) scales and added to steps two and three of the analysis, respectively.

In the model predicting MAPs, the inclusion of TEPS-A significantly increased how much variance was explained by the model (R^2-change = 0.065, $F(1,77) = 5.986$, p = .017). The local effect size of TEPS-A on MAPs was small ($f^2 = 0.072$). The inclusion of the TEPS-C in the subsequent step did not increase the model's predictive power, revealing that neither subscale significantly contributed to the model above the other. In the model predicting TEs, the inclusion of TEPS-A again significantly increased how much variance was explained by the model (R^2-change = 0.070, $F(1,77) = 6.895$, p = .010). The local effect size of TEPS-A on TEs was small ($f^2 = 0.082$). The inclusion of TEPS-C again reduced the individual contribution of each of the

two TEPS subscales. In the model predicting PAEs, the inclusion of TEPS-A did not significantly increase how much variance was explained by the model ($p > .05$). The inclusion of TEPS-C did not improve the overall predictive power of the model ($p > .05$). Full results for each of these models can be seen in Table 6.

Predictor variables	**MAPs**	**TEs**	**PAEs**
Step 1: demographics			
Age	−0.035	0.221	0.142
Sex	−2.155**	−3.877***	−1.940*
R^2	0.093	0.148	0.070
F(2,78)	3.99*	6.77**	2.93+
Step 2: TEPS-A			
Age	−0.104	0.118	0.082
Sex	−1.612*	−3.072**	−1.468+
TEPS-A	−0.128*	−0.190**	−0.111+
R^2	0.158	0.218	0.114
R^2 change	0.065	0.070	0.044
F change (1,77)	5.986**	6.895**	3.31*
Step 3: TEPS-C			
Age	−0.111	0.104	0.075
Sex	−1.472+	−2.818*	−1.332
TEPS-A	−0.104+	−0.146+	−0.087
TEPS-C	−0.074	−0.135	−0.072
R^2	0.172	0.241	0.126
R^2 change	0.014	0.022	0.012
F change (1,76)	1.290	2.251	1.053

Table 6. Hierarchical regression analysis: TEPS-A and TEPS-C.

Sex Differences

Given the significant difference in TEPS scores and BART outcome measure scores between female and male participants, the first set of hierarchical linear regressions were rerun to investigate whether one sex was the primary driver of the anhedonia and risk relationship. Thus, three supplementary models were analyzed including only male participants, and three including only female participants. These models otherwise included the same predictors, as well as estimated age as a covariate.

The models predicting MAPs, TEs, and PAEs in only male participants were all nonsignificant, with no predictors significantly contributing to the prediction of any outcome.

The models predicting MAPs, TEs, and PAEs in only female participants were all significant. The model including MAPs as the outcome revealed that TEPS score significantly predicted variance on MAPs above the effect of estimated age ($b=-0.117$, $p=.005$). However, the addition of the CPAS and CSAS scores did not significantly increase the variance explained by TEPS score alone ($p>.05$).

The female-only model including TEs as the outcome revealed that TEPS score significantly predicted variance on TEs above the effect of estimated age ($b=-0.175$, $p=.003$). The addition of the CPAS and CSAS scores significantly increased the model's predictive power (R^2 change=0.134, $F(2,57)=5.322$, $p=.008$). CPAS score ($b=-0.299$, $p=.021$) and CSAS score ($b=-0.244$, $p=.047$) significantly predicted variance above the effect of TEPS.

The female-only model including PAEs as the outcome revealed that TEPS score significantly predicted variance on PAEs above the effect of estimated age ($b=-0.119$, $p=.009$). The addition of CPAS and CSAS scores significantly increased the model's predictive power (R^2

change=0.136, F(2,57)=5.223, p=.008). CPAS score (b=-0.222, p=.028) and CSAS score (b=-0.198, p=.039) significantly predicted variance above the effect of TEPS.

DISCUSSION

Our study assessed the associations between anhedonia and risk-taking behavior in a non-clinical sample of university students. Previous research on the BART has primarily focused on risk propensity (operationalized as MAPs). However, this study additionally included sub-optimal risk-taking (TEs) and response to punishment (PAEs), revealing an interesting pattern. Individuals scoring higher on the index of pleasure (TEPS) presented with lower risk propensity, less sub-optimal risk-taking behavior, and less risk-taking immediately after punishment. Individuals scoring higher on the index of physical anhedonia (CPAS) also presented with less sub-optimal risk-taking and less risk-taking immediately after punishment. Taken together, these findings present a more complex relationship between physical anhedonia and risk than was predicted based on primarily clinical studies (Barch et al., 2014; Gard et al., 2007; Kring and Barch, 2014).

In line with previous work in schizophrenia, our study found negative relationships between TEPS scores and the Chapman scales (Gard et al., 2006; Gard et al., 2007; Strauss et al., 2011). An EFA revealed that while all three scales loaded onto a common factor, each contained a greater proportion of uniqueness, suggesting a more complex relationship among them than a simple inverse linear correlation. Including all three scales as predictors of risk-taking behavior suggested that each scale may explain a different part of risk-taking variability. These measures, therefore, may not be tapping into opposing constructs, but distinct components of anhedonia.

The two dimensions of anhedonia (social and physical) and the two components of pleasure (anticipatory and consummatory) demonstrated distinct relationships with risk-taking

behavior. The finding that physical (but not social) anhedonia significantly predicted risk-taking behavior was surprising given the importance of social interactions to typical adolescent development (Sawyer et al., 2012), and that social anhedonia is the dimension more typically studied in cases of the development of psychopathology (Cohen et al., 2020). However, some prior research in schizophrenia has shown the importance of physical anhedonia in real-world affect (Blanchard et al., 1994). Notably, a stark sex difference was revealed in the hierarchical models predicting BART outcomes. Models including only male participants were non-significant, while models including only female participants showed a similar, and occasionally stronger, relationship between anhedonia and risk as the full sample.

Within the TEPS, we investigated the contributions of anticipatory and consummatory pleasure to the prediction of risk-taking behavior. Anticipatory pleasure was a significant negative predictor of MAPs and TEs, in contrast to past research in schizophrenia samples noting a positive association between 'wanting' and reward-seeking behavior (Gard et al., 2007; Kring and Barch, 2014). However, the addition of consummatory pleasure to this model reduced the individual contributions of each below significant levels. These results imply not only a lack of significant association between 'liking' and risk-taking, but that in this non-clinical sample, considering 'wanting' and 'liking' separately may not be necessary or effective. While our results are in contrast to some prior research, other studies have found results similar to ours, particularly when investigating real-world risk-taking behaviors like bungee jumping (Michel et al., 1997) and riding a bicycle without a helmet (Testa and Steinberg, 2010). These studies, which link traits like thrill-seeking, boredom, and hopelessness to increased risk-taking, highlight the importance of considering anhedonia from multiple perspectives and in a variety of populations.

It is possible that the participants in this study with a lower experience of pleasure (i.e., lower TEPS scores) viewed the BART through a punitive lens, lending us one possible explanation of the pattern relating TEPS to BART performance. Previous work in health-related risk-taking behavior in individuals with depression found a similar relationship to that described here: participants higher in depression and anhedonia take more health-related risks (e.g. not wearing a helmet when riding a bicycle; Testa and Steinberg, 2010). These researchers theorized that risk-taking may have been a way to escape negative affect or express pessimism. In the current study, perhaps individuals reporting less pleasure were less sensitive to or mindful of the punishment they received. This is supported by the finding that lower experience of pleasure on the TEPS predicted more key presses on the BART immediately following a punishment (i.e., explosion). Despite evidence of adolescents basing behavior on their most recently experienced outcomes (Mitchell et al., 2008), the current findings indicate that, in line with the findings of Testa and Steinberg (2010), taking less pleasure from everyday experiences may relate to riskier behavior, seeking experiences higher in emotional salience (greater MAPs and TEs), and showing less sensitivity to emotional valence (greater PAEs).

The current body of literature on risk-taking, particularly the use of the BART, tends to focus uniquely on risk propensity (often operationalized as MAPs; Koscielniak et al., 2016; McCormick and Telzer, 2017). This tendency narrows our focus to determining how much risk individuals are willing to take in order to maximize gains (reward-seeking behavior). By broadening this lens, the current study has allowed for an expanded picture of the relationship between anhedonia and risk behavior. Notably, while the TEPS had similar power to predict each of the three risk-taking measures, subtle differences emerged with the Chapman scales, with only the two punishment-focused outcomes (TEs and PAEs) being significantly correlated. Finally,

significant relationships were revealed in the current study between sex and the reported experience of pleasure, as well as sex and risk-taking behavior.

These findings warrant additional research into the complexities of the relationship between anhedonia and risk-taking. The participants in this study, who would commonly be used as a control sample in clinical research, demonstrated significant variability in their levels of anhedonia and risk-taking. Thus, there may be real-life functional implications even for non-clinical levels of anhedonia, warranting closer study of our 'control samples' as part of the larger spectrum of mental health and illness. Additionally, these findings support the importance of studying late adolescence and early adulthood in a broader context. With this being a vulnerable window for the development of psychopathology characterized by anhedonia (Testa and Steinberg, 2010), further investigation of how the relationship between anhedonia and risk-taking may change over time (e.g., becoming stronger or even changing direction) has the potential to impact how we discuss psychopathology at different stages of life.

Limitations should be considered when interpreting the results of this study and developing future studies. This study was intended as a non-clinical sample, which has the benefit of providing data from a wide spectrum of anhedonia (as evidenced by the range of scores on anhedonia measures). However, much of the literature relating anhedonia to risk-taking has been done in clinically diagnosed samples, so comparison of the current study's results to prior literature should be done with careful consideration of the limits of generalizability, as well as potential differences (left unexplored here) in experiences of anhedonia in the presence versus absence of a clinical diagnosis. In terms of scale reliability, the internal consistency for responses on the CPAS (as reported by Cronbach's alpha) was 0.690, slightly below the commonly

accepted threshold of 0.70. The internal consistency for the CSAS and TEPS were 0.728 and 0.721, respectively.

Additionally, the BART employed in the current design was played for an accumulation of points rather than any concrete reward (e.g., money) based on performance. In many studies utilizing the BART, participants are provided with an external reward that is at least ostensibly related to task performance (Mitchell et al., 2008; Reddy et al., 2014). Thus, the lack of direct reward could be decreasing motivation on the BART and altering the level of risk that participants were willing to take. Finally, the analyses exploring the differences in male-only and female-only models should be considered in light of the small sample of male participants included in this study (n=19).

The current study provided support for the existence of a relationship between the experience of pleasure and engagement in risk-taking behaviors in a non-clinical sample, though a more intricate one than initially predicted. This work has uncovered complexity in how the experience of pleasure and anhedonia may affect individuals' relationships with the rewarding and punitive aspects of risk. Additionally, it may shed light on the similarities and differences between the TEPS and Chapman measures of anhedonia, such that these seemingly opposite measures may have unique contributions to predicting risk-taking behaviors. These results merit further study as we continue to unravel the unique roles of anhedonia and pleasure in understanding how late adolescents and early adults engage in risk.

CHAPTER 3 | STUDY 2: The impact of variability in anhedonia on risk-taking and working memory in adolescents

INTRODUCTION

Adolescence is a period of development in a number of areas, with cognition being one of the most critical. Multiple models have been proposed to illustrate the trajectory of adolescent cognitive development, one of the most prevalent and influential of them being the dual systems model proposed by Steinberg, which has itself been adapted several times (Shulman et al., 2016). Despite their differences, the primary takeaway from these models of cognitive development is the distinction between affective (hot) and non-affective (cold) cognition. The implication of these models is that due to early maturation of affective systems, adolescence is a time of increased reward sensitivity, sensation seeking, and risk-taking behavior, at least until development of the cognitive control system catches up to the socioemotional system (Shulman et al., 2016; Steinberg, 2008). Drawing this distinction has provided us with the opportunity to thoroughly investigate the development of hot and cold processes in typically developing adolescents, including increased rates of risk-taking behavior in adolescents as compared to children and adults (Braams et al., 2015). Importantly, a triadic model has also been introduced that distinguishes the roles of hot cognition (cognitive impulsivity and risk-seeking), cold cognition (regulation and control), and emotional intensity and lability (avoidance) (Ernst, 2014). In the current study, we focus our attention on the hot and cold cognition components.

In addition to the dynamic changes occurring in socioemotional and cognitive control systems, adolescents as a whole experience a greater vulnerability to the development of various psychiatric disorders, including psychosis (Patel et al., 2021), substance use disorders (Gray & Squeglia, 2018), and depressive disorders (Shorey et al., 2022). Additionally, the transdiagnostic symptom of anhedonia is known to increase in occurrence across adolescence, and its presence

tends to stabilize within individuals towards later adolescence (Bennik et al., 2014; Yang et al., 2022). Anhedonia, or the loss of the experience of pleasure from previously enjoyed activities, is a symptom not only experienced by adolescents in the context of a major psychiatric diagnosis (including depression, psychosis, substance use disorders (Stull et al., 2022), and even ADHD (Babinski et al., 2019)), but also seen, although at lower levels, in adolescents who have not been diagnosed with any major mental health challenges. In the general population of adolescents, anhedonia has been shown to predict later onset of mood disorders like major depressive disorder (Wilcox & Anthony, 2004), and was shown to be present in roughly 15-30% of a sample of adolescents regardless of diagnostic status (Bennik et al., 2014).

Cold cognition, which refers to non-affective cognitive abilities including working memory and cognitive control, is the slower to develop of the two systems in the dual systems model during typical adolescence. Working memory, a commonly studied deficit in various mental disorders including psychosis spectrum disorders and ADHD (Kofler et al., 2019; Lett et al., 2014), typically shows a curvilinear developmental trajectory that increases at a slowing pace through childhood and early adolescence (Ahmed et al., 2022). In psychopathology, cold cognition is affected in various disorders typified by anhedonia, including psychosis (Lepage et al., 2014; Reichenberg & Harvey, 2007), depression (Fossati, 2018; Nikolin et al., 2021), ADHD (Kofler et al., 2019), and substance use disorders (Paul & Bhattacharyya, 2021; Stavro et al., 2013), in that individuals who experience these mental health challenges typically suffer from impaired cold cognitive abilities.

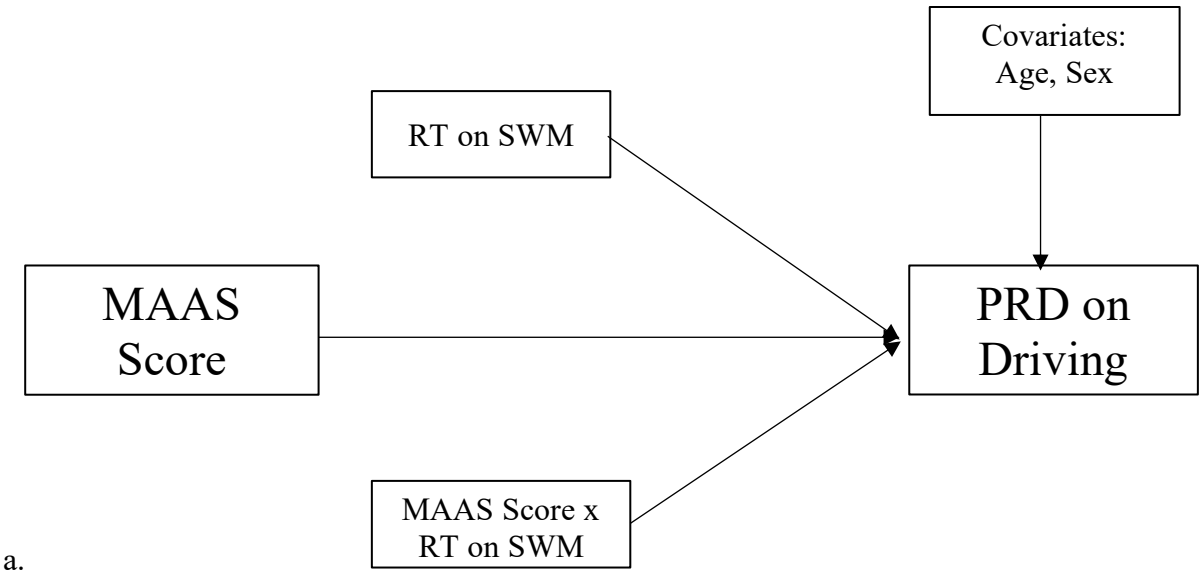
Hot cognition, which refers to affective cognitive abilities such as reward function, is the more rapidly developing aspect of the dual systems model, reaching its peak while cold cognition undergoes its slow increase. In adolescents, this is often typified as the relationship

between teenagers and risk-taking behaviors (Blakemore & Robbins, 2012). Though risk-taking behavior is often perceived as a maladaptive behavior in teenagers, the adaptive aspects of risk-taking should not be overlooked, as they are essential for important tasks of adolescence, such as establishing independence (Blair et al., 2018). However, individuals with a diagnosis of a mental disorder have been shown to exhibit alterations in risk-taking behaviors (e.g., psychosis (Cheng et al., 2012), depression (Follett et al., 2023; Testa & Steinberg, 2010), ADHD (Dekkers et al., 2020), and substance use disorders (Ashenhurst et al., 2014)) that represent alterations in the hot cognitive system. Though all of these are disorders characterized by anhedonia, the ways in which risk-taking behaviors are impacted vary across them; for instance, individuals with schizophrenia tend to show impaired reward processing (Cheng et al., 2012), while individuals with alcohol use disorder tend to show diminished reactivity to losses (Ashenhurst et al., 2014). Notably, research on the impact of these various disorders on risk-taking behaviors during adolescents is limited.

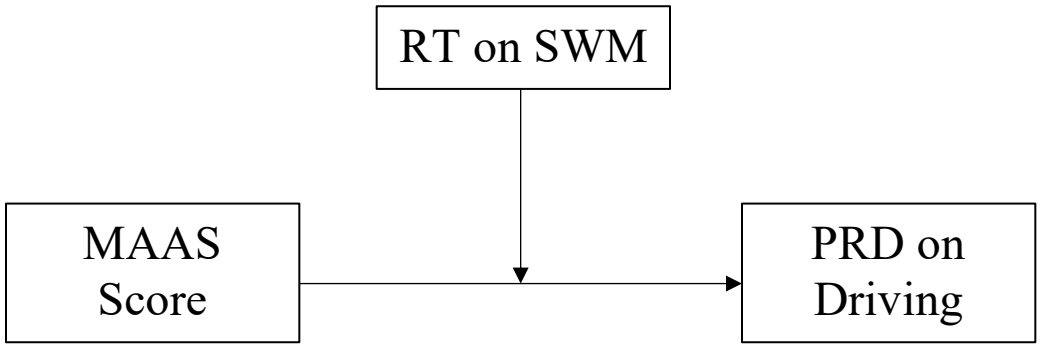
Our understanding of the interactions between hot and cold cognition in psychopathology has grown over the past few decades of research, with researchers investigating the impact of hot and cold cognition in depression (Ahern et al., 2019), bipolar disorder (Roiser et al., 2009), and problematic substance use (Savulich et al., 2021). These studies acknowledge that both affective and non-affective cognition are impacted in individuals with psychopathology, though they approach this idea in different ways regarding whether and how the two are thought to interact. In the case of major depressive disorder, researchers theorized that cold cognition deficits are necessary for hot cognition to be impacted, and that this interaction further exacerbates depressive symptoms (Ahern et al., 2019). In bipolar disorder, cold cognition appeared intact while hot cognition was impacted across patients (Roiser et al., 2009). In substance use, the

presence of hot cognition alterations seemed more prevalent across those who used novel psychoactive substances ("club drugs") than those without significant substance use history, with cold cognition deficits appearing to highlight the distinction between recreational and problematic substance use (Savulich et al., 2021). These findings suggest a complex relationship between cold and hot cognition in the context of various types of psychopathology and highlight the lack of a unifying model as to the mechanism that ties psychopathology, hot cognition, and cold cognition together.

The current study aims to fill this gap by elucidating such a mechanism, and will do this by shifting the focus away from the impacts of hot and cold cognition on particular diagnoses and towards their impact on individuals experiencing the transdiagnostic symptom of anhedonia. Given that anhedonia, cold cognition, and hot cognition all have a peaking prevalence or continued development during adolescence, the current study investigates adolescence specifically. Thus, the primary aim of this study is to elucidate a potential mechanism for the interaction of hot and cold cognition in a community sample of adolescents experiencing varying levels of anhedonia. Based on previous literature, we approached this aim with two hypotheses. First, we hypothesized that adolescents reporting higher levels of anhedonia will engage in more risk-taking behaviors (Currin et al., 2022). Second, we hypothesized that this relationship would be stronger in adolescents who experienced greater working memory deficits (Ahern et al., 2019; Savulich et al., 2021). See Figure 3 for visual representations of the proposed model.



a.



b.

Figure 3. Statistical and theoretical models of anhedonia (MAAS Score), working memory (RT on SWM), and risk-taking behavior (PRD on Driving Game). a. Proposed statistical model. b. Proposed theoretical moderation model.

METHODS

Participants

Adolescent participants were recruited from across the United States using a combination of social media (Twitter, Instagram, Facebook) posts, physical flyer advertisements in the Los Angeles area, and word of mouth. See Figure 4 for a visual representation of the geographic distribution of participants. Participants were eligible if they were between the ages of 12 and 21, were fluent in English, and did not have a history of traumatic brain injury or psychosis.

Participants (and, in the case of minors, their parent or guardian) completed an informed consent session via videoconference with a research assistant. Age was verified by checking government IDs for those who had them, and school or other IDs for younger participants. The participants then completed the approximately 60-minute study independently using the provided link from the research assistant. This study was approved by the UCLA Institutional Review Board, and participants were compensated with a $25 e-gift card.

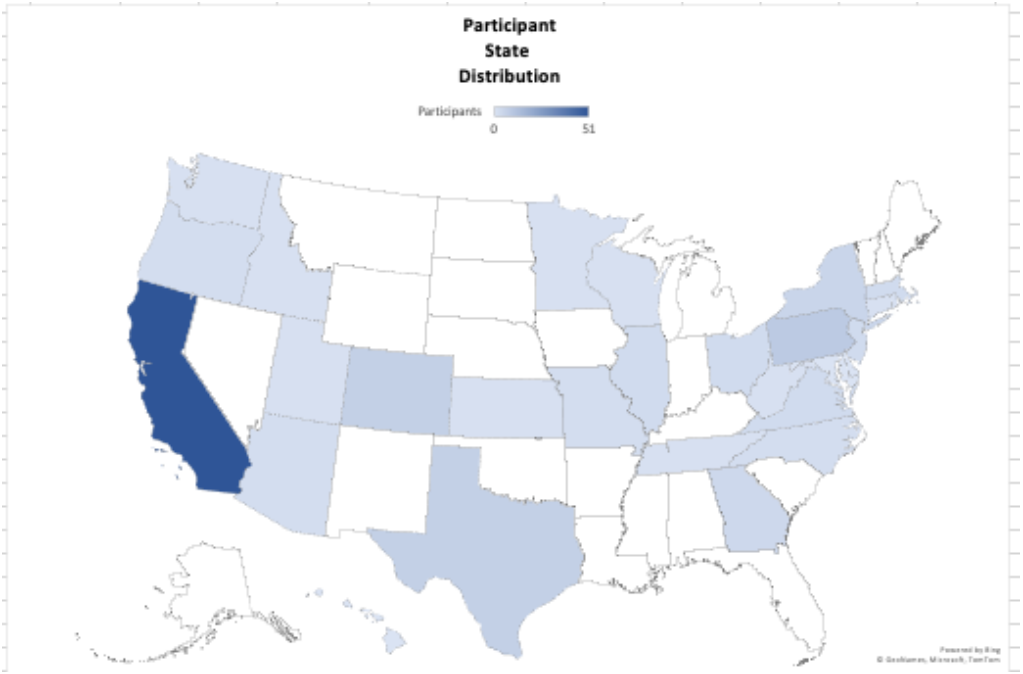


Figure 4. Geographic distribution of participants. The top 5 contributing states were California (51), Pennsylvania (9), Colorado (7), Texas (7), and New York (5).

A total of 123 valid data files were collected. After the data-cleaning process, a total of 83 participants were included in final analyses. See Figure 5 for details on how data were cleaned.

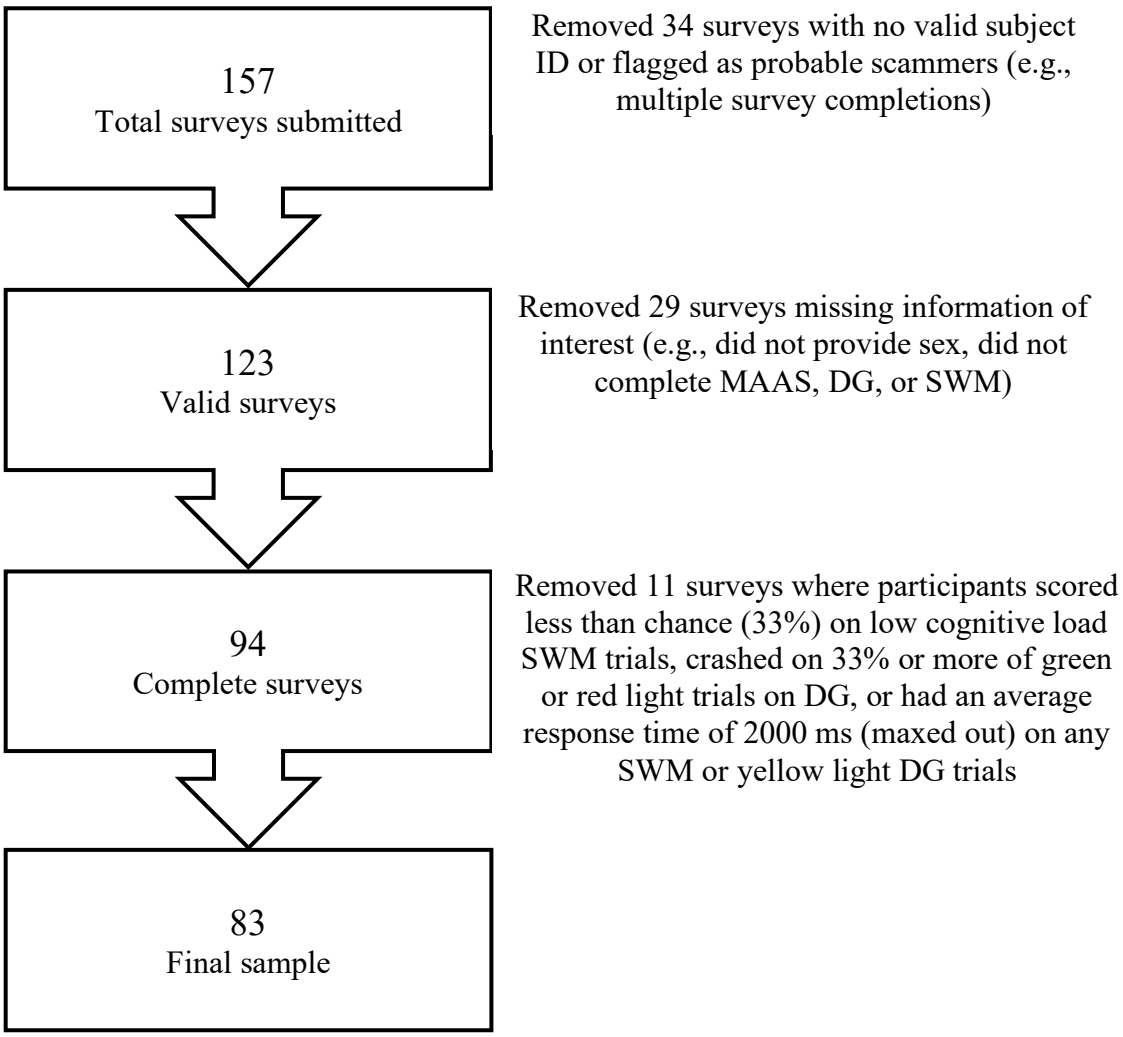


Figure 5. Data cleaning process.

The final sample consisted of 25 male (30.12%) and 58 female (69.88%) participants with ages ranging from 12 to 21 (mean age = 17.05, standard deviation = 2.996). The racial and ethnic breakdown of the sample is represented in Figure 6.

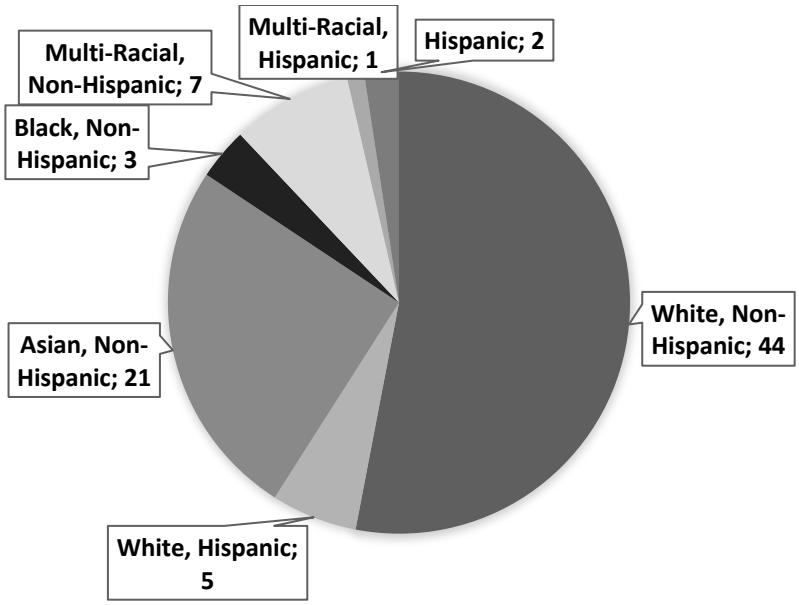


Figure 6. Racial/ethnic background of participants.

Surveys and Tasks

Participants completed several surveys and computerized tasks online from their personal computers using PsyToolkit software (Stoet, 2010; Stoet, 2016). A subset of the administered tasks were included in analyses for the current study.

MAAS

The Multidimensional Adolescent Anhedonia Scale (MAAS) is a 24-item questionnaire specifically designed to be appropriate for adolescents (Zareian et al., 2021a, 2021b). In addition to overall anhedonia, the MAAS assesses the experience of anticipatory, consummatory, and recall pleasure. In total, the MAAS provides four scores, where higher scores indicate a higher level of reported anhedonia. For the current study, the primary outcome of interest was the total anhedonia score, with each of the three subscales included as additional analyses.

Driving Game

The Driving Game is a 40-trial computerized task designed to probe risk-taking behaviors in participants (Baker et al., 2020; Chein et al., 2011) and is used in the current study as a

measure of hot cognition. In each trial, participants view a screen from the perspective of a person driving a car and are told to complete the task as quickly as possible while earning points based on their decisions. As they approach a stoplight, the color of the light is revealed to be either green, red, or yellow, and the participant must decide whether to continue driving forward or to hit the brakes. Whereas the "correct" response is made clear to participants 100% of the time for the green and red light trials, the yellow light trials present an equal chance of crashing the car or proceeding through the light quickly if participants choose to proceed, or a 100% chance of safely crossing the intersection if they choose to stop and wait a few seconds. The outcome of interest for the Driving Game is the proportion of risky decisions (PRD), which was calculated as the number of times the participant chose to drive through the yellow light (regardless of crash status) divided by the total number of yellow light trials.

Spatial Working Memory Task

The Spatial Working Memory Task (SWM) is a 40-trial Sternberg-style task used in the current study as a measure of cold cognition (Rawdon et al., 2013). In each trial, participants view an array of fishbowls, followed by the same array with a subset of bowls containing fish, followed by a target stimulus in which one fishbowl contains a fish. Participants must then select whether the fishbowl in the target stimulus was previously occupied by a fish. Of the 40 total trials, 20 included an array of nine fishbowls and three fish to hold in working memory (low cognitive load), and 20 included an array of 16 fishbowls and five fish to hold in working memory (high cognitive load). The outcome of interest for this task is response time (RT) in the high load condition (RT-h), which was calculated as the average response time in milliseconds for each participant across the 20 high load trials.

Benthin Risk Perception Measure

The Benthin Risk Perception Measure (BRPM; (Benthin et al., 1993)) is a five-item scale that assesses risk perception, risk seriousness, risk aversion, peer influence on risk-taking, and weighting of the costs and benefits of risk-taking for five risky behaviors (riding in a car driven by someone who has been drinking, having unprotected sexual intercourse, drinking alcohol, getting into a fight, and stealing something desirable). The primary outcome of interest for this measure included risk aversion, which was calculated as the average rating on the question "How scary do you find this activity?".

Statistical Analysis

All statistical analyses were completed using SPSS v28. Preliminary analyses were conducted to assess the direct effect of anhedonia on risk-taking behavior and working memory separately. Following this, a moderation model was run to assess whether the interaction of anhedonia and working memory significantly impacted risk-taking (see Figure 3). Given that this is a developmental sample, all analyses included sex and age as covariates. Additional analyses were run to investigate the impacts of risk aversion and age on these models.

RESULTS

Demographics

Within the dataset, there were no significant differences between male and female participants on MAAS scores, PRD, or RT-h. Female participants were significantly older than male participants (mean female age = 17.66, mean male age = 15.64; $t(81)=-2.94$, $p=.004$).

Linear Regression: Anhedonia and Risk-Taking

With PRD as the outcome, the overall linear regression model including total MAAS score as the predictor was trending but not significant [$F(3,79)=2.37$, $p=.077$]. However, within this trending model, total MAAS score was a significant positive predictor (ß=.291, p=.011) of PRD. Given

this significant coefficient, three further linear regression models were run. The models including anticipatory and recall anhedonia as predictors were not significant (both *p*s>.2). However, the linear regression model including consummatory MAAS score as the predictor was significant [$F(3,79)=4.03$, $p=.01$], with consummatory MAAS score as a significant positive predictor (ß=.372, $p<.001$) of PRD (see Figure 7). This model, which included age and sex as covariates, predicted approximately 10% of the variance in PRD (adj. $R^2=.100$). Neither sex nor age were significant covariates.

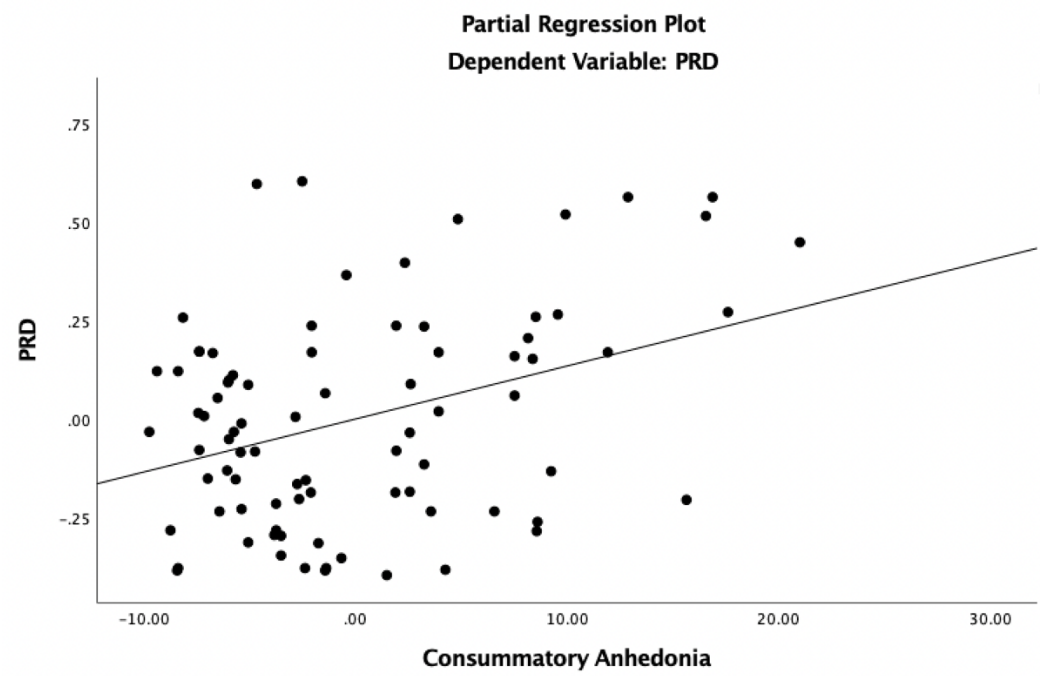


Figure 7. The relationship between consummatory MAAS score and risk-taking behavior. Age and sex have been partialled out.

Linear Regression: Anhedonia and Spatial Working Memory

With response time in the high cognitive load condition of the SWM task (RT-h) as the outcome, two linear regression models were run: one with total MAAS score as the primary predictor, and one with consummatory MAAS score as the primary predictor. Age and sex were included as

covariates in both models. Both linear regression models significantly predicted RT-h [total: $F(3,79)=5.37$, $p=.002$; consummatory: $F(3,79)=5.56$, $p=.002$]. However, total MAAS score ($p=.10$) and consummatory MAAS score ($p=.075$) were only trending positive predictors. Rather, the significant negative predictor in both of these models was age [total: ß=-.420, $p<.001$; consummatory: ß=-.416, $p<.001$]. See Figure 8 for a visualization of this relationship.

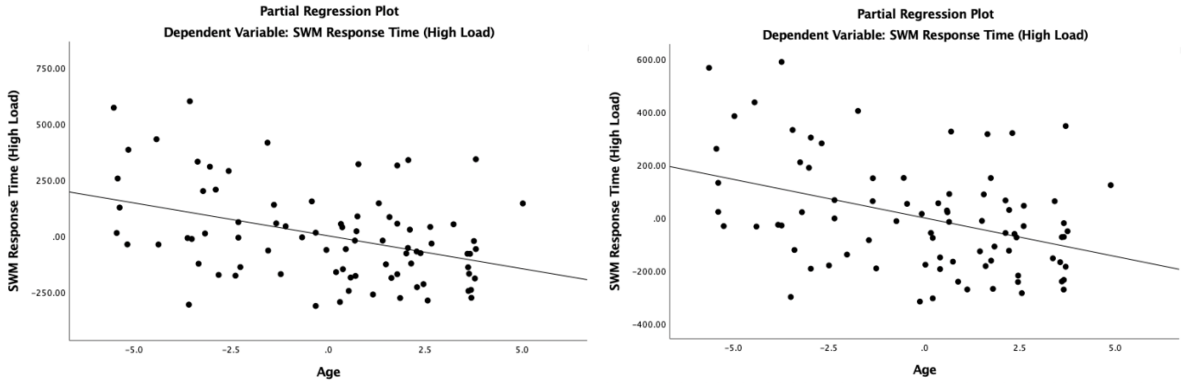


Figure 8. The relationship between age and response time on a spatial working memory task. Anhedonia (total on left, consummatory on right) and sex have been partialled out.

Moderation Model

Using the PROCESS macro (v43) for SPSS, a moderation model was run (model 1) to test the hypothesized impact of working memory on the relationship between anhedonia and risk-taking (see Figure 3). Given that only the consummatory subscale of the MAAS yielded both a significant model and anhedonia as a significant predictor, this subscale was included as the primary predictor. While the overall moderation model was significant [$F(5,77)=2.49$, $p=.038$], this was driven by the predictive value of the consummatory MAAS score ($p=.0017$) rather than the interaction between this score and RT-h ($p>.2$). A visual representation of this non-significant interaction can be seen in Figure 9.

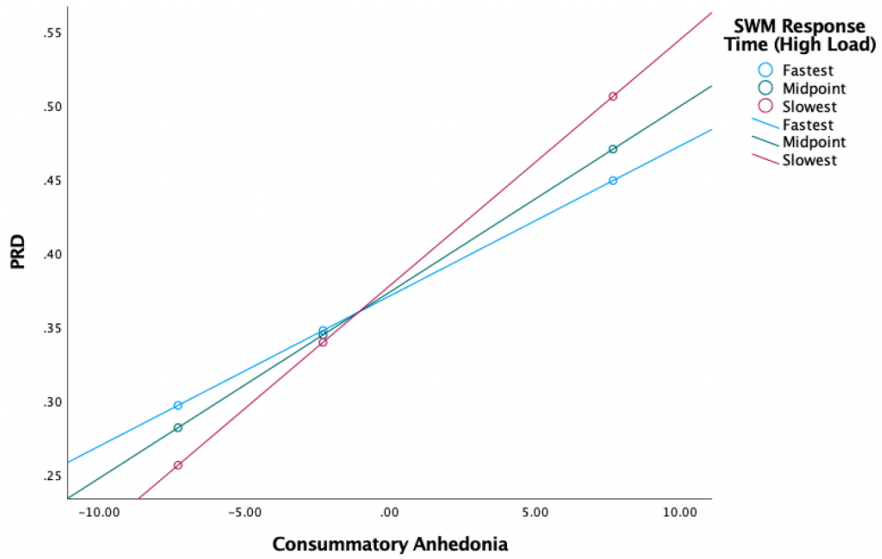


Figure 9. The relationship between consummatory anhedonia and risk-taking behavior at three levels of working memory performance (i.e., fastest response time, midpoint response time, and slowest response time).

Impact of Risk Perception on Anhedonia and Risk-Taking

In addition to risk-taking behavior as seen in the Driving Game, we were also interested in better understanding adolescents' risk perception; hence the inclusion of the Benthin Risk Perception Measure (BRPM). The five subscales from this measure included risk perception, risk seriousness, risk aversion, peer influence on risk-taking, and weighting of the costs and benefits of risk-taking. Based on response distribution and overall skewness, we prioritized risk aversion ("How scary do you find this activity?") as the BRPM outcome of interest. See Figure 10 for a representation of these data.

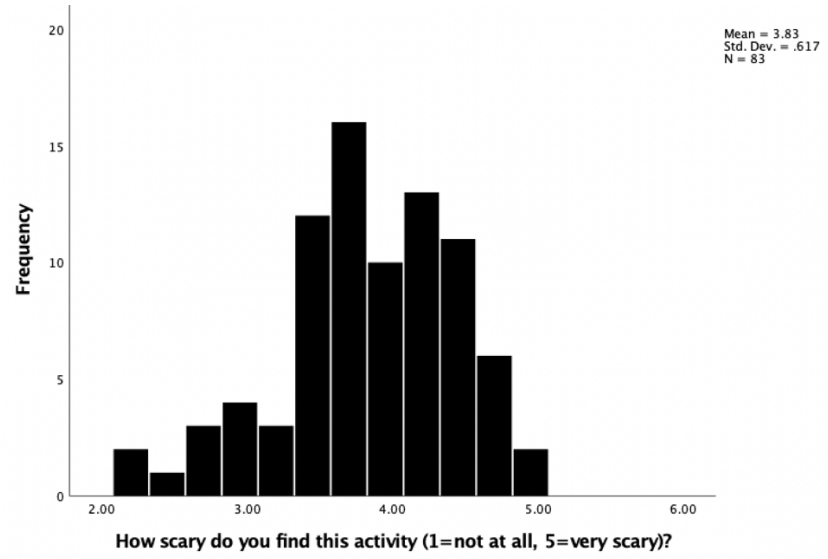


Figure 10. Frequency of average response to risk aversion question across five activities.

With risk aversion as the outcome, the linear regression model including total MAAS score as the predictor was not significant [$F(3,79)=2.34$, $p=.080$]. Within this trending model, total MAAS score was a trending negative predictor ($p=.073$) of risk aversion. The linear regression models including consummatory and recall MAAS score as the predictors, respectively, were also not significant, nor were consummatory or recall MAAS score significant predictors (all $p>.10$). However, the model including anticipatory MAAS score as the predictor was significant [$F(3,79)=2.89$, $p=.041$]. Within this model, anticipatory MAAS score was a significant negative predictor (ß=-.242, $p=.030$) of risk aversion (see Figure 11).

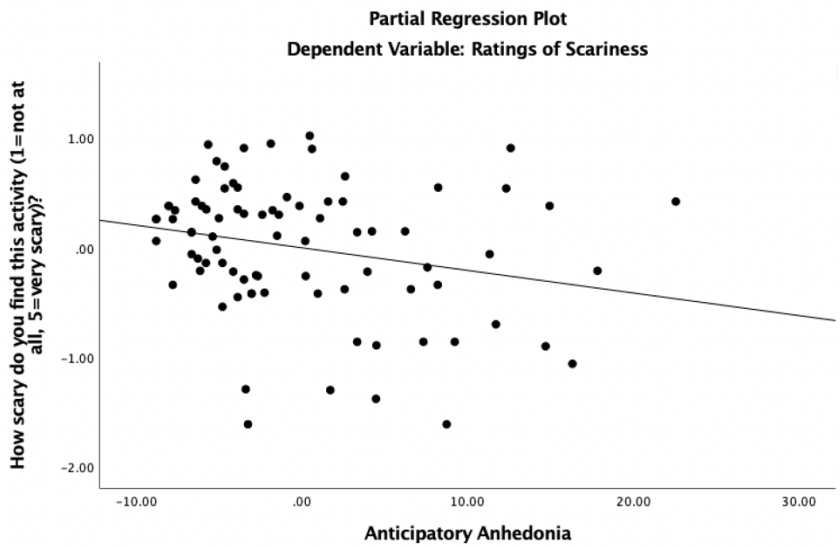


Figure 11. The relationship between anticipatory anhedonia and risk aversion. Sex and age have been partialled out.

Linear regression models were run to investigate risk aversion's predictive power concerning risk-taking behavior (PRD) and working memory (RT-h). Risk aversion was not a significant predictor in any of these models (all *p*s>.10).

Age Differences: Full Dataset

Given the significance of age especially in the models predicting working memory performance, additional moderation models were run to explore the possibility that anhedonia (specifically, total and consummatory anhedonia) and age might interact to predict either risk-taking behavior or working memory performance. The model including PRD as the outcome and total MAAS score as the predictor was not significant (*p*>.10). The other three models were significant, but none included a significant interaction between anhedonia and age. Sex was included as a covariate in all models. See Table 7 for details of these four moderation models.

Predictor Moderator Outcome	Model *F* value (*p* value)	Anhedonia coefficient	Age coefficient	Interaction (anhedonia x age) *F* value (*p* value)
Total MAAS Age PRD	1.75 (.15)	.0043*	-.0059	0.0053 (.94)

Consummatory MAAS Age PRD	3.00 (.02)*	.0138*	-.0070	0.0540 (.82)
Total MAAS Age RT-h	3.99 (.005)*	2.155	-29.95*	0.0401 (.84)
Consummatory MAAS Age RT-h	4.35 (.003)*	6.254*	-31.12*	0.7643 (.38)

Table 7. Moderation models. *=p<.05; all coefficients are unstandardized

Age Differences: 16 and older only

Given a) the bimodal age distribution of the dataset (see Figure 12), b) that one of the tasks involved driving, an activity that usually commences around age 16, and c) that age has emerged as a significant predictor in multiple models, a subset of participants – those at or over the age of 16 – were separated out and included in additional analyses.

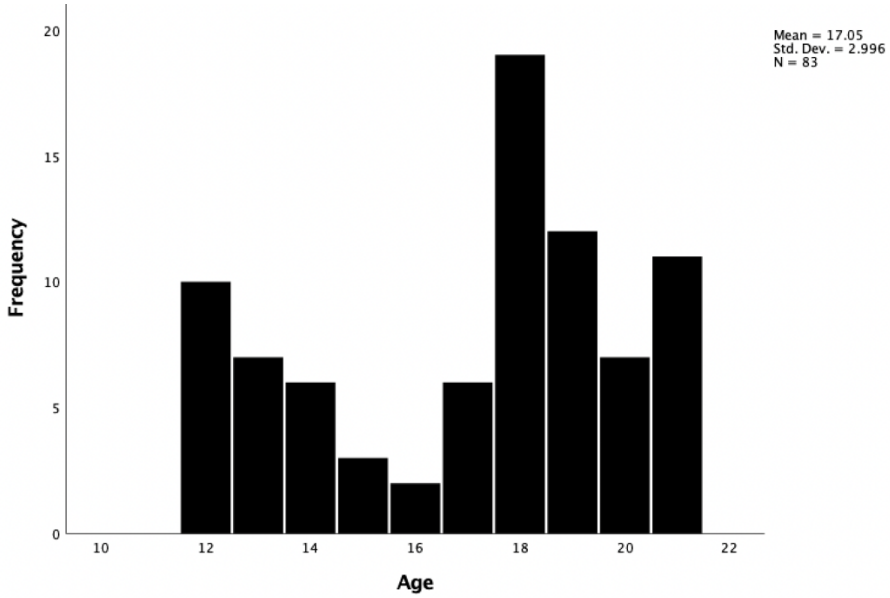


Figure 12. Age distribution of the full dataset.

The new smaller dataset (n=57), included 13 male and 44 female participants. The average age was 18.86, with a standard deviation of 1.41. Four linear regression models were run with sex as a covariate to investigate the power of anhedonia (total MAAS score and its three subscales) to predict risky decision-making (PRD). The linear regression model including total MAAS score

as the predictor was significant [$F(2.54)=3.74$, $p=.030$]. Within this model, total MAAS score was a significant positive predictor (ß=.347, p=.009) of PRD (see Figure 13, left). This model predicted approximately 9% of the variance in PRD (adj. $R^2=.089$). The model including recall anhedonia as the predictor was not significant ($p>.2$). The model including anticipatory anhedonia as the predictor was not significant [$F(2,54)=2.75$, $p=.073$]. However, within this trending model, anticipatory MAAS score was a significant positive predictor (ß=.301, $p=.024$) of PRD. The model including consummatory MAAS score as the predictor was significant [$F(2,54)=5.49$, $p=.007$], with consummatory MAAS score as a significant positive predictor (ß=.412, $p=.002$) of PRD (see Figure 13, right). This model predicted approximately 14% of the variance in PRD (adj. $R^2=.138$).

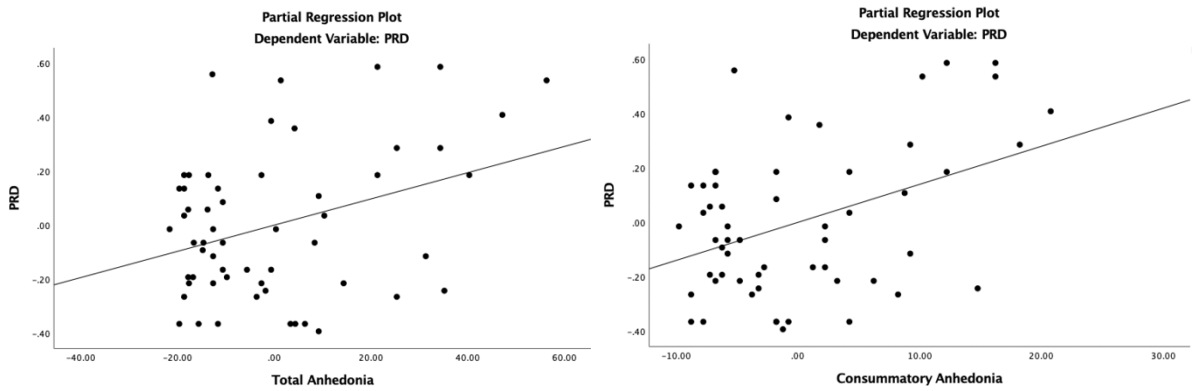


Figure 13. The relationship between anhedonia (total on left, consummatory on right) and risky decision-making.

Two moderation models were run to test the hypothesized impact of working memory on the relationship between anhedonia and risk-taking (see Figure 3) in this sample of older adolescents. The first model included total MAAS score as the primary predictor, and the second included consummatory MAAS score as the primary predictor. Both included RT-h as the moderator, PRD as the outcome, and sex as a covariate. With total MAAS score as the predictor, the overall model was not significant [$F(4,52)=.119$]. With consummatory MAAS score as the predictor, the overall model was significant [$F(4,52)=2.77$, $p=.037$]; however, this was driven by

the predictive value of the consummatory MAAS score (p=.0062) rather than the interaction between this score and RT-h (p>.2). A visual representation of this non-significant interaction can be seen in Figure 14.

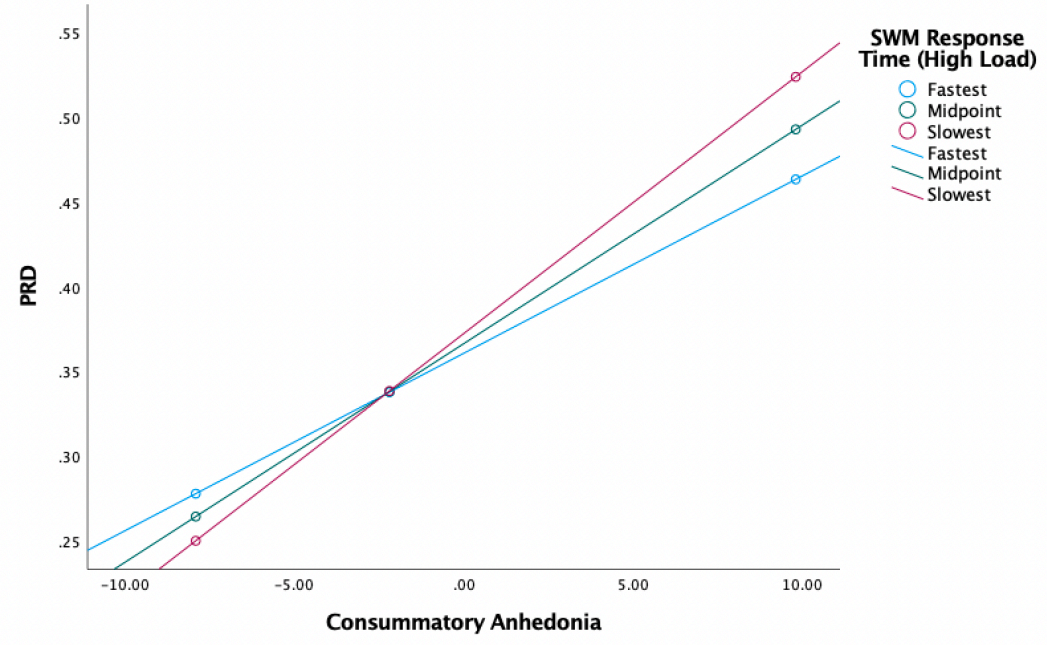


Figure 14. The relationship between consummatory anhedonia and risk-taking behavior at three levels of working memory performance (i.e., fastest response time, midpoint response time, and slowest response time).

DISCUSSION

The current study aimed to assess a model that described the relationships among anhedonia, cold cognition (working memory), and hot cognition (risk-taking behavior) in adolescents. The first hypothesis was that there would be a positive relationship between anhedonia and hot cognition in that adolescents who self-reported higher levels of anhedonia would also engage in more risk-taking behaviors. This hypothesis, which was aligned with recent findings (Currin et al., 2022) (see Study 1), was supported. The second hypothesis was that this relationship between anhedonia and risk-taking behavior would be stronger in adolescents with working memory deficits. This hypothesis, which was aligned with literature suggesting a hot-

cold cognitive model in depression (Ahern et al., 2019), was not supported. Additional analyses were conducted to investigate various other relationships between anhedonia and cognition beyond those initially hypothesized. These analyses yielded significant relationships between age and spatial working memory, as well as anhedonia and risk aversion. No tested moderation models emerged as significant.

The current study and Study 1 (Currin et al., 2022) suggest a different relationship between anhedonia and risk-taking than has previously been seen, as the experience of anhedonia is often considered to blunt reward sensitivity and thus decrease risk-taking behavior (Follett et al., 2023; Frost & Strauss, 2016; Liu et al., 2016). What this study and Study 1 (Currin et al., 2022) suggest is that anhedonia may alter the lens through which adolescents view risk-taking behaviors, such that those experiencing more anhedonia may be experiencing less responsiveness to punishment (Mitchell et al., 2008) or more sensation-seeking behaviors (Testa & Steinberg, 2010). The current study further supports this finding with the addition of a measure to assess attitudes towards risk (the Benthin Risk Perception Measure), which revealed that those adolescents self-reporting increased levels of anhedonia also self-reported viewing real-life risky activities as less scary.

Notably, the current study found that consummatory anhedonia, or a lack of pleasure taken from engaging in an enjoyable activity ("liking"), was the primary type of anhedonia that predicted risk-taking behavior; past research found that anticipatory anhedonia, or a lack of pleasure taken from imagining or preparing for a future enjoyable activity ("wanting"), was the most significant predictor (Currin et al., 2022). The difference in these findings may be due in part to differences in the samples collected in each study. The wider age range of 12-21 may capture a different picture of adolescence than the prior study's 18-22 age range. In the current

study, while consummatory anhedonia was the only significant predictor of risk-taking behavior in the full sample, anticipatory anhedonia emerged as a significant predictor of risk-taking behavior (albeit in an overall trending linear regression model) in a subsample including only participants aged 16 or older. As adolescents become older and cold cognition abilities further develop (Steinberg, 2008), sensitivity to time-dependence of pleasurable and risky behaviors may play a larger role in engagement with these behaviors. This can be seen in the current study with the result of older adolescents showing significantly increased working memory skills (operationalized as response speed in a spatial working memory task) as compared to younger adolescents.

These findings add to the evidence that the relationship between anhedonia and cognition in adolescence is a complex one. The moderation models tested here did not yield significant results when predicting risk-taking behavior from the interaction of anhedonia and spatial working memory, or from the interaction of anhedonia and age. Additionally, while anhedonia predicted risk aversion, risk aversion did not in turn predict risk-taking behavior. This implies that moderation may not be the most representative way to understand how anhedonia, hot cognition, and cold cognition relate to one another during adolescence. However, it is important to note that there are limitations to the current study that could impact results. Firstly, the study was conducted remotely, meaning that adolescents completed the study in an uncontrolled environment without being observed by research staff. This could introduce numerous confounding factors, such as environmental distractions or even multiple people working together on the study. These factors have the potential to bias or invalidate the results in either random or systematic ways. However, we did do careful quality control to try to remove problematic data, including removing surveys where participants scored below chance on low

cognitive load SWM trials, where they crashed on 33% or more of green or red light trials on the Driving Game, or had an excessive response time on any SWM or yellow light DG trials. The sample collected was unevenly distributed in terms of age and sex, such that there were more older adolescents than younger adolescents, and more female than male participants. These factors were included as covariates in all analyses where they were not a predictor of interest, but there may be other ways in which they bias or add noise to the results.

The current study adds to the growing body of literature on how adolescents experience anhedonia, risk-taking, and working memory. Future research can expand on these findings in numerous meaningful ways, from including data on participants' driving habits (to assess potential noise in Driving Game performance) and substance use (to contextualize responses to the Benthin Risk Perception Measure), to conducting follow-up studies to track changes in hot and cold cognition not only cross-sectionally across participants but longitudinally within participants. Given the non-significance of the moderation models tested in the current study, further investigation is warranted to explore other possible models beyond simple moderation to relate different types of anhedonia with different types of cognition across adolescence.

CHAPTER 4 | STUDY 3: Psychosis, anhedonia, and white matter development across adolescence

INTRODUCTION

Adolescence is a time of not only functional and behavioral changes (Braams et al., 2015), but also of neurodevelopment, particularly with regard to structural connectivity (Peters et al., 2012). In recent years, there has been an increased focus on understanding how white matter typically develops during the adolescent years, as well as what differences in white matter exist in individuals with varying psychopathologies. Diffusion tensor imaging (DTI) is a non-invasive tool that allows for in-vivo visualization of white matter tracts throughout the brain, and it has been frequently used in developmental studies. This research has shown a multitude of changes in white matter during adolescence, with many honing in on changes in two key DTI metrics, mean diffusivity (MD) and fractional anisotropy (FA) (Bava et al., 2010; Herting et al., 2017; Lebel & Deoni, 2018). FA, which provides information about the directional flow of water in the brain, putatively serves as an index of white matter "integrity" and is commonly used as a proxy for the strength of the connections between different regions within the brain.

Individual white matter tracts show differences in their rate of development, with certain tracts, particularly long-range association tracts, showing a more protracted developmental trajectory that continues through adolescence and lasts into early- or even mid-adulthood (Lebel et al., 2019; Olson et al., 2015). Long-range association tracts connect regions that span large areas of the brain, and are often associated with higher-level functions including cold cognition. Cold cognition is typically defined as non-affective or emotion-independent cognition, and includes such tasks as working memory and verbal learning. One tract associated with cold cognition is the superior longitudinal fasciculus (SLF), which connects frontal and parietal regions. The SLF has been shown to correlate with executive functions and working memory

performance in children and adolescents (Peters et al., 2012; Vestergaard et al., 2011). The integrity of the SLF is believed to reach its peak value when a person is in their third decade of life (Lebel et al., 2019)). Frontostriatal tracts are another class of white matter tracts with continued development during adolescence. These tracts specifically connect frontal and striatal regions of the brain, and have been associated with hot cognition (Achterberg et al., 2016; Ikuta et al., 2018). Hot cognition is typically defined as affective or emotion-laden cognition, and includes such tasks as risk-taking and reward learning. The accumbofrontal tract (AF), connecting the nucleus accumbens and orbitofrontal cortex is an example of a frontostriatal tract that has been connected to risk taking and decision making in adolescents (Karlsgodt et al., 2015; Uy & Galvan, 2020). Its integrity is believed to peak earlier in life than the SLF, in middle adolescence (Karlsgodt et al., 2015). Notably, taken together, these findings are consistent with the dual systems model of adolescent development (Shulman et al., 2016), in which executive functions mature more slowly than reward based functions, which peak in mid adolescence. Examining the development of these two tracts in particular, and white matter overall, represents an opportunity to better understand the structural mechanisms of adolescent development.

Adolescence is a life stage in which individuals show heightened vulnerability to the development of psychiatric diagnoses, including depressive and psychotic disorders. Research on white matter development has repeatedly shown disruptions in white matter connectivity as related to psychopathology (Vanes et al., 2020). In particular, regions related to both cold and hot cognition, both of which are impacted by many psychiatric disorders, show disruptions in white matter integrity and development in adolescents struggling with their mental health (Epstein et al., 2014; von Hohenberg et al., 2014). However, the longitudinal development of

these affected tracts over time in adolescents with psychosis spectrum disorders has not been thoroughly researched.

Anhedonia has been well-studied as a feature of multiple psychiatric disorders, including depressive disorders (Keedwell et al., 2005; Pizzagalli, 2014; Treadway & Zald, 2011) and psychosis (Gard et al., 2007; Kasanova et al., 2018; Kring & Barch, 2014; Strauss et al., 2011). In adolescents at high risk for psychosis or experiencing early stages of psychosis, anhedonia has become a topic of recent interest (Jhung et al., 2016; Pelizza et al., 2020). Part of this is due to the importance of anhedonia and negative symptoms of psychosis in predicting functional outcomes for adolescents and early adults (Cohen et al., 2020; Gabbay et al., 2015; Pelizza et al., 2020). Anhedonia is also of interest as it varies in a trait-like way across the general population, even in individuals whose symptoms do not reach a diagnostic threshold (Barkus & Badcock, 2019), consistent with models of mental illness as existing along a spectrum. Increasing understanding of the relationship between anhedonia and white matter development in adolescents with and without psychosis is an important step towards understanding and better addressing broader mental health challenges in adolescents.

The relationship between anhedonia and white matter integrity is another area of recent interest, with higher levels of anhedonia being associated with disrupted white matter integrity in tracts related to reward processing and cognitive functioning. In many cases, these disruptions follow a negative correlation pattern, with higher levels of anhedonia being associated with lower white matter integrity (Diaz et al., 2021; Henderson et al., 2013). However, some studies have found a positive correlation in patients with schizophrenia compared to controls, indicating the possibility of different neural mechanisms contributing to this correlation in those with and without schizophrenia (e.g., (Lee et al., 2014)). The current study aims to fit these three pieces

(white matter, anhedonia, and adolescent development) together from a dimensional perspective to determine the longitudinal interactions between anhedonia and white matter development in adolescents with and without a formal psychosis diagnosis. Of particular interest in this study are the SLF and AF tracts. As previously mentioned, these two tracts have been chosen for their known (SLF) or suspected (AF) disruption in psychotic disorders and continued development during adolescence, as well as their association with cold and hot cognition. Namely, the SLF is associated with working memory (Karlsgodt et al., 2008; Vestergaard et al., 2011), and the AF with risk-taking behavior and impulsivity (Ikuta et al., 2018; Uy & Galvan, 2020).

Based on previous literature, three hypotheses are proposed. First, participants with a psychosis diagnosis will show decreased FA in the SLF and AF as compared with healthy controls at baseline. This hypothesis aligns with prior research indicating decreased integrity in these two tracts in psychosis patients as compared to healthy controls (Vanes et al., 2020). Second, there will be a linear relationship between anhedonia and white matter integrity in these tracts at baseline such that those with higher levels of trait anhedonia will show decreased FA in the SLF (associated with cold cognition) and AF (associated with hot cognition). This hypothesis stems from the findings of Study 1 (Currin et al., 2022) and Study 2, which showed that adolescents with higher levels of anhedonia showed increased risk-taking (Study 1) and decreased risk perception (Study 2). Third, individuals with a psychosis diagnosis will show an altered trajectory of white matter integrity over the course of two years than those without a diagnosis such that in both tracts, individuals with a psychosis diagnosis will show a flattened trajectory. This hypothesis aims to expand on the body of research that has found both increases in white matter integrity across adolescence (Lebel et al., 2019; Olson et al., 2015) and decreases in white matter integrity in the presence of psychopathology (Vanes et al., 2020). In addition to

these hypotheses based in specific white matter tracts, there was an additional exploratory goal of investigating group and anhedonia-based differences in FA across the brain.

METHODS

Participants

Participants were assessed as part of a 2013-2018 longitudinal study at the Feinstein Institute for Medical Research in Manhasset, New York. Recruitment was-via posted flyers, Internet advertisements, outreach to educational centers, and referrals from previous study participants. The study protocol was approved by the Institutional Review Board of Northwell Health. Participants age 18 and over provided written informed consent, and minors provided written assent alongside parental written consent. Participants were eligible if they were between the ages of 10 and 25 at the time of the first visit, were fluent in English, had an IQ of at least 70, and had no history of neurological disorders or significant head trauma. For early psychosis participants, inclusion criteria included duration of illness less than three years, current treatment with atypical antipsychotic medication, and a primary psychotic illness diagnosis including Schizophrenia, Schizoaffective, Bipolar Disorder with Psychotic Features, Major Depressive Disorder with Psychotic Features, and Unspecified Psychotic Disorder. Diagnostic evaluations were done according to the Structured Clinical Interview for DSM-V (SCID), and finalized via case conference in the Zucker Hillside Hospital Research Division. Control participants had no DSM-V diagnoses, and no first degree relatives with schizophrenia spectrum disorders or bipolar disorder. Clinical symptom ratings were evaluated in the early psychosis group using the Brief Psychiatric Rating Scale (Overall & Gorham, 1962), the Scale for the Assessment of Negative Symptoms (Andreasen, 1989), and the Young Mania Rating Scale (Young et al., 1978). The final baseline sample (n=151) for this data included 68 patients and 83 unaffected controls. Between

the ages of 14 and 25 at baseline. The final sample across the three visits of the study (n=64) included 25 patients and 39 controls. See demographic information in Tables 8 and 9, and a plot of ages at the various study visits in Figure 15.

Group	**Patients (n=68)**	**Controls (n=83)**	**Total**
Sex			
Female	20	48	68
Male	48	35	83
Race			
Asian	9	18	27
Black	27	17	44
White	24	42	66
Other	8	6	14
Ethnicity			
Hispanic	11	10	21
Non-Hispanic	57	71	128
Indian	0	2	2
Age at Baseline			
Mean	20.80	19.52	20.10
Standard deviation	2.52	2.36	2.51

Table 8. Demographics at baseline visit for cross-sectional analysis (N=151).

Group	**Patients (n=25)**	**Controls (n=39)**	**Total**
Sex			
Female	9	21	30
Male	16	18	34
Race			
Asian	4	6	10
Black	11	6	17
White	7	26	33
Other	3	1	4
Ethnicity			
Hispanic	4	5	9
Non-Hispanic	21	33	54
Indian	0	1	1
Age at Baseline			
Mean	20.52	19.38	19.83
Standard deviation	2.80	2.36	2.58

Table 9. Demographics at baseline visit for longitudinal analysis (N=64).

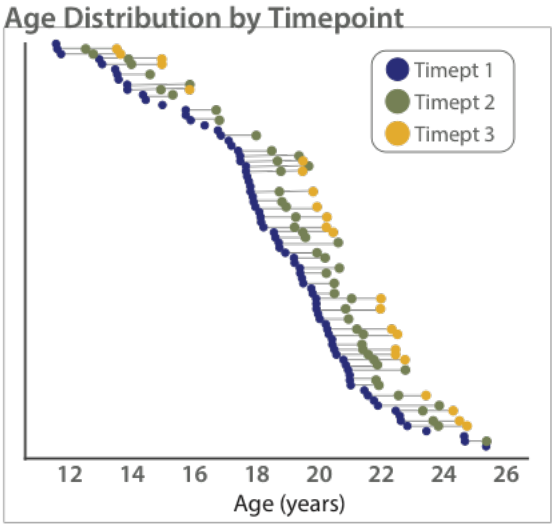


Figure 15. Representation of age at each visit. Each blue dot represents a participant at their first visit. Connected green and yellow dots represent subsequent visits of the same participant. Reproduced from Arkin (unpublished).

Data Collected

Participants in the MEND study completed a battery of questionnaires and neuroimaging scans in three visits set roughly one year apart (see Figure 16). Some sections of the battery were completed only in the patient sample, and others collected across patients and controls. In the current study, we focused on one self-report questionnaire and one set of imaging data, each of which were collected at baseline and the two follow-up visits in both patients and controls.

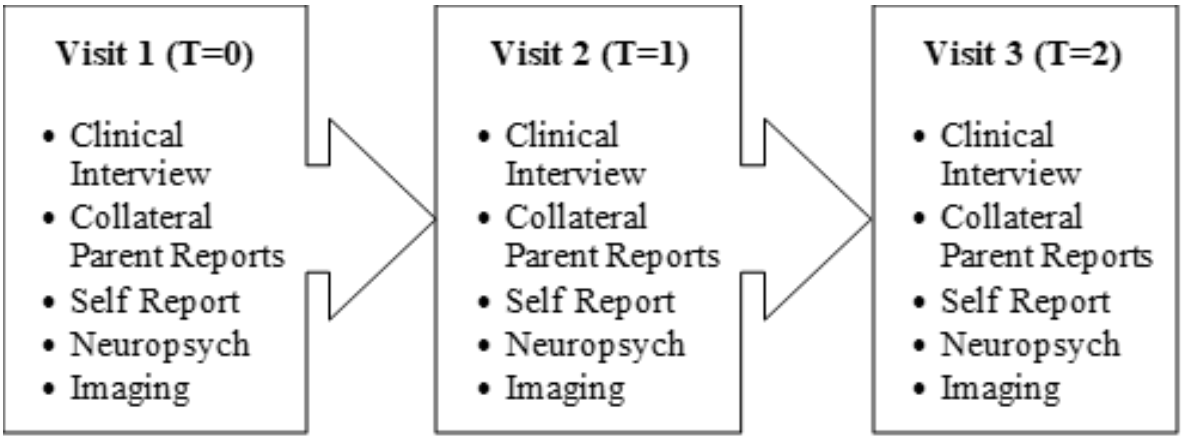


Figure 16. Data collected at each of three visits.

Beck Depression Inventory (BDI)

The Beck Depression Inventory (BDI) assesses a variety of symptoms typical of depression (Beck et al., 1961). An anhedonia subscale (calculated as the sum of the Loss of Interest, Loss of Pleasure, and Loss of Interest in Sex) has been used in previous research (Ballard et al., 2017; Joiner et al., 2003). For the purposes of this adolescent sample, this subscale has been reduced to the sum of scores on the Loss of Interest and Loss of Pleasure questions. A mean-centered score was calculated for the modified anhedonia subscale of the BDI (BDIa) for all participants.

Diffusion Tensor Imaging (DTI)

All imaging scans were collected on a 3T Siemens Verio magnetic resonance machine at Zucker Hillside Hospital in Long Island, NY. Scanning sessions included collection of high-resolution T1-weighted (TR/TE 2530/3.3ms, 1mm slice thickness, 7° flip angle, matrix 256*256mm, 1 average) and T2-weighted structural image data (TR/TE 1500/27ms, FOV 220*220mm, 0.5*0.5*3mm isotropic resolution, 1 average) and single shell DWI data (TR/TE 6000/87ms, FOV 240mm, 2.5mm isotropic resolution, 52 axial slices, 65 directions, b = 1000 s/mm2, paired phase encoding). FMRIB Software Library (FSL) was used to create a tract-based spatial statistics (TBSS) skeleton based on the existing fractional anisotropy (FA) data. Regions of interest representing the SLF and AF tracts were projected onto this skeleton and used to determine the FA per tract for each participant. The resulting FA values were used in subsequent statistical analyses. In addition to these ROIs, a whole-brain analysis was run on the baseline data to assess additional group differences in tract integrity across the brain.

Statistical Analysis

Statistical analyses were completed using SPSS v28. To test the first hypothesis (group differences in FA at baseline), a series of ANCOVAs were run comparing the FA values associated with the two tracts of interest (SLF and AF) in patients and controls at their initial baseline visit. Group status (patient or control) was the covariate of interest, and age and sex were included as additional covariates.

To test the second hypothesis (relationship between anhedonia and FA at baseline), a linear regression was run to test the predictive power of BDIa on the tracts of interest at baseline. Age and sex were included as covariates in this analysis.

To test the third hypothesis (group differences in trajectory of FA across adolescence), a linear mixed effects model (LMM) was utilized to investigate the difference in the trajectory of white matter development in the two tracts of interest based on diagnostic status across three visits. The fixed effects of this model included the group status, age, and sex. The repeated effects described the individual trajectories of each participant's FA values across the three visits.

Exploratory analyses were also conducted to investigate baseline group differences in FA across the whole brain based on group status (aligned with the first hypothesis) and level of anhedonia (aligned with the second hypothesis). The covariates included were age at baseline and sex.

RESULTS

Demographics at Baseline (N=151)

First, demographic information was assessed between groups. Within the dataset, there was a significant difference in sex across groups ($X^2(1,151)=12.20$, $p<.01$). There were also significant differences in race across groups ($X^2(3,151)=9.07$, $p=.028$). There were no significant differences

in ethnicity across groups ($X^2(2,151)=2.11$, p=.348). There was a significant difference in age across groups ($t(149)=-3.19$, $p=.002$).

Demographics for 3-Visit Sample (N=64)

Demographics were then assessed within the subset of participants who had data across three timepoints. Within the dataset, there was no significant difference in sex across groups ($X^2(1,64)=1.95$, p=.163). There were significant differences in race across groups ($X^2(3,64)=11.29$, p=.010). There were no significant differences in ethnicity across groups ($X^2(2,64)=0.75$, p=.687). There was no significant difference in age across groups ($t(62)=-1.758$, $p=.084$).

Attrition Demographics

Chi-square tests were completed to assess differences between those who completed all three visits (N=64) and those who did not (N=87). Patient status did not significantly differ across the two groups ($p=.206$). Sex did not significantly differ across the two groups ($p=.696$). Race did not significantly differ across the two groups ($p=.357$). Ethnicity did not significantly differ across the two groups ($p=.975$). Age also did not differ across the two groups ($p=.735$).

Comparison of Predictors (Diagnosis and Anhedonia)

An independent samples t-test was completed to look at the overlap in anhedonia across psychopathology (patients versus controls). This t-test revealed that there was a significant group difference in anhedonia at baseline ($t(149)=2.57$, $p=.006$), with patients having a significantly higher mean score (1.10) than controls (0.63).

ANCOVA: Group Differences in SLF and AF Integrity

Group differences were assessed in the baseline sample (N=151). With mean FA of the SLF as the outcome of interest, there was no significant group difference ($p>.2$). There was also no

significant difference based on sex (p=.19), and there was a trending difference based on age (p=.06).

With mean FA of the AF as the outcome of interest, there was a significant group difference [F(1,147)=3.92, p=.05]. There was no significant difference based on sex (p=.16) or age (p=.34). See Figure 17 for a visual representation of these data.

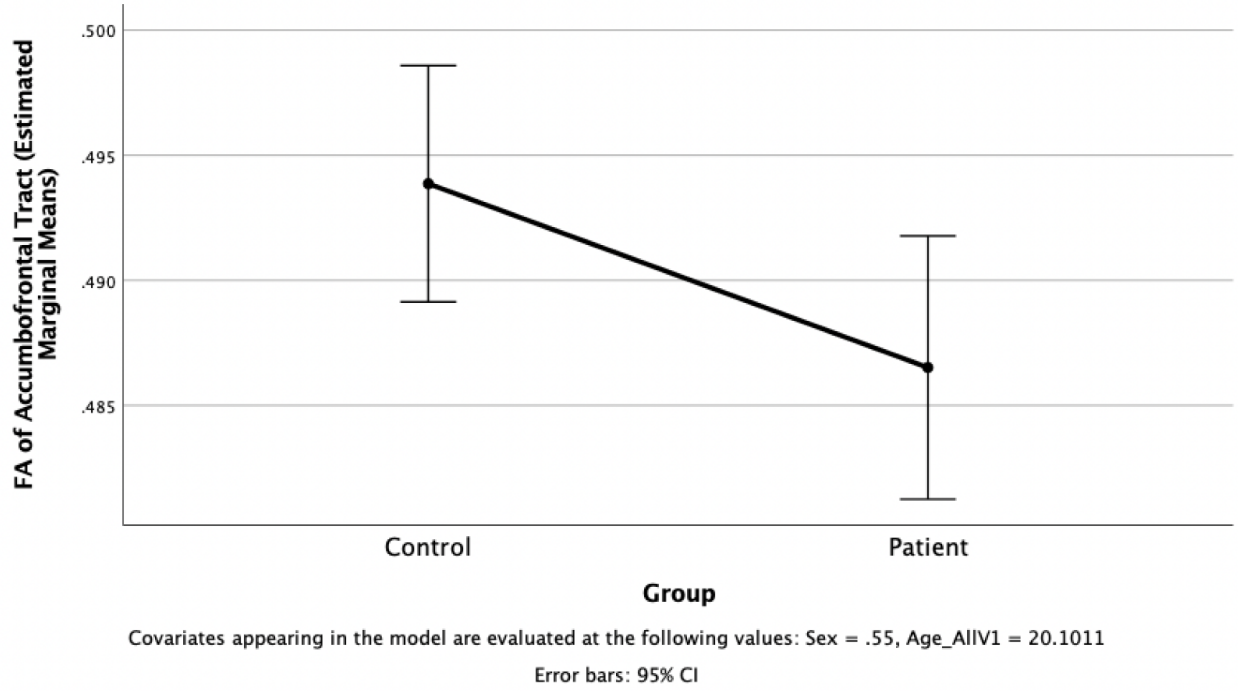


Figure 17. Group difference in AF FA, holding sex and age constant.

A whole brain analysis was completed to determine whether additional white matter tracts would emerge as demonstrating group differences in FA at baseline. No group differences emerged (whole brain p>.2).

Linear Regression: Anhedonia and SLF and AF Integrity

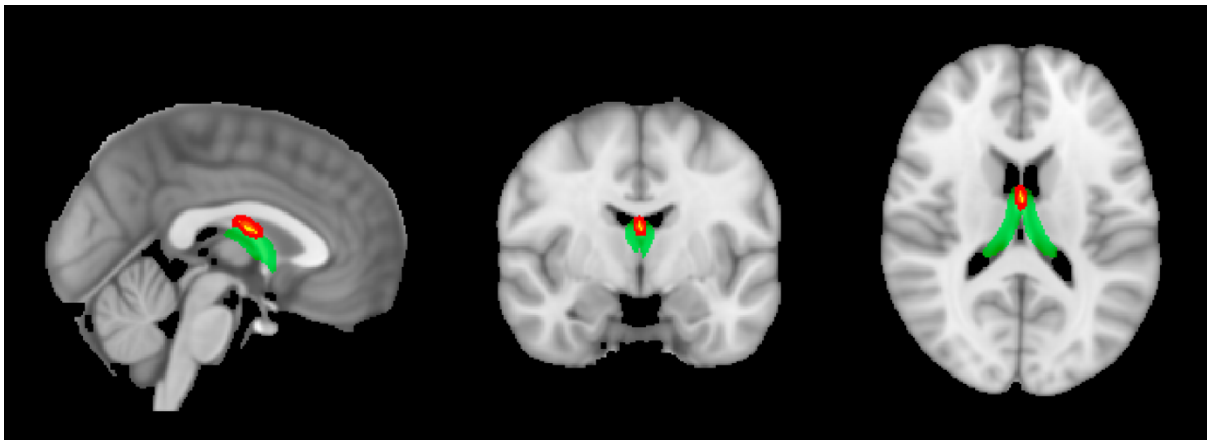
A linear association between anhedonia and white matter integrity was assessed across the full baseline sample (N=151) without regard to diagnostic status. With mean FA of the SLF as the

outcome, the linear regression model including BDIa as the predictor was not significant [$F(3,147)=1.715$, $p=.166$], and BDIa was not a significant predictor ($p>.2$).

With mean FA of the AF as the outcome, the linear regression model including BDIa as the predictor was not significant [$F(3.147)=0.351$, $p>.2$], and BDIa was not a significant predictor ($p>.2$).

A whole brain analysis was completed to determine whether additional white matter tracts would emerge as demonstrating variance in FA based on self-reported level of anhedonia (BDIa) at baseline. The fornix, a white matter tract connecting the hippocampus to several subcortical brain regions, emerged as a tract for which individuals with higher self-reported anhedonia demonstrated lower FA values (one-tailed $p=.04$). See Figure 18 for a visualization of this outcome.

a.



b.

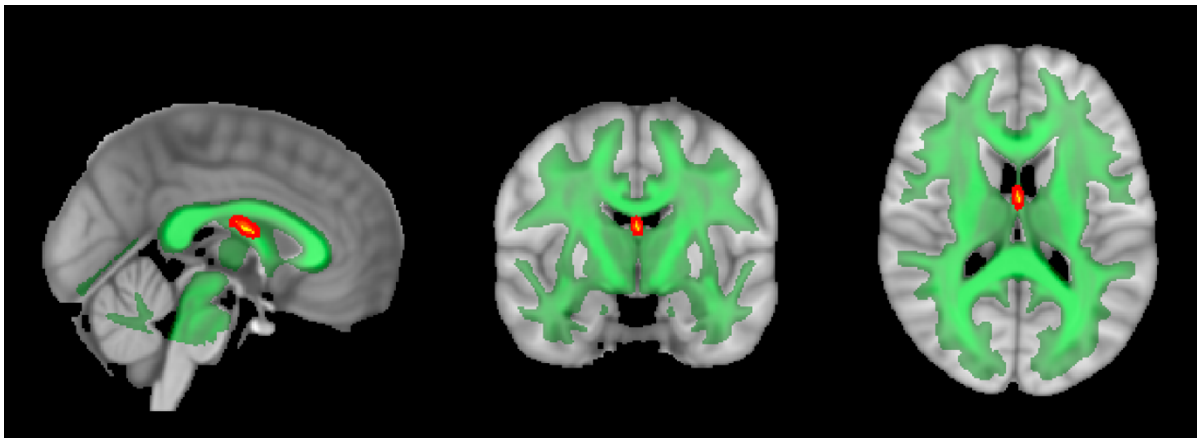


Figure 18. Significant areas demonstrating a negative relationship between anhedonia and FA highlighted in red. 4a: green represents the fornix as represented by FMRIB Software Library (FSL). 4b: green represents the mean FA map for the current sample.

Multilevel Modeling: Group Differences in SLF and AF Integrity Across Adolescence

Using the subset of participants who completed three visits, a linear mixed effects model (LMM) was estimated to assess group differences in white matter integrity in the two tracts of interest. With mean FA of the AF as the outcome, the LMM including group, age, and sex as fixed effects and visit number as the repeated effect showed that group was a significant predictor of AF FA (b=-0.016, p=.006). Age was a trending predictor of AF FA (b=.001, p=.075), and sex was not significant (p>.2). The correlation parameter of the repeated measures variable was relatively large (rho=.791), and the Wald test is significant (Z=21.032, p<.001), indicating that an autoregressive structure is appropriate for these data to account for within-subject correlation of FA values across visits. See Table 10 for a complete report of these findings, and Figure 19 for a visualization.

Predictor of AF FA	**Coefficient**	**Standard Error**	**t-value**	**p-value**	**95% Confidence Interval**
Group*	-0.016	0.006	-2.833	.006	(-0.027, -0.005)
Age^{+}	0.001	0.001	1.796	.075	(-0.000, -0.003)
Sex	-0.005	0.005	-1.030	.307	(-0.016, 0.005)
Repeated Measure	**rho**	**Standard Error**	**Wald Z-value**	**p-value**	**95% Confidence Interval**
Visit*	0.791	0.038	21.032	<.001	(0.705, 0.854)

Table 10. Estimates of fixed effects and covariance parameters. *p<.05, $^{+}$p<.10

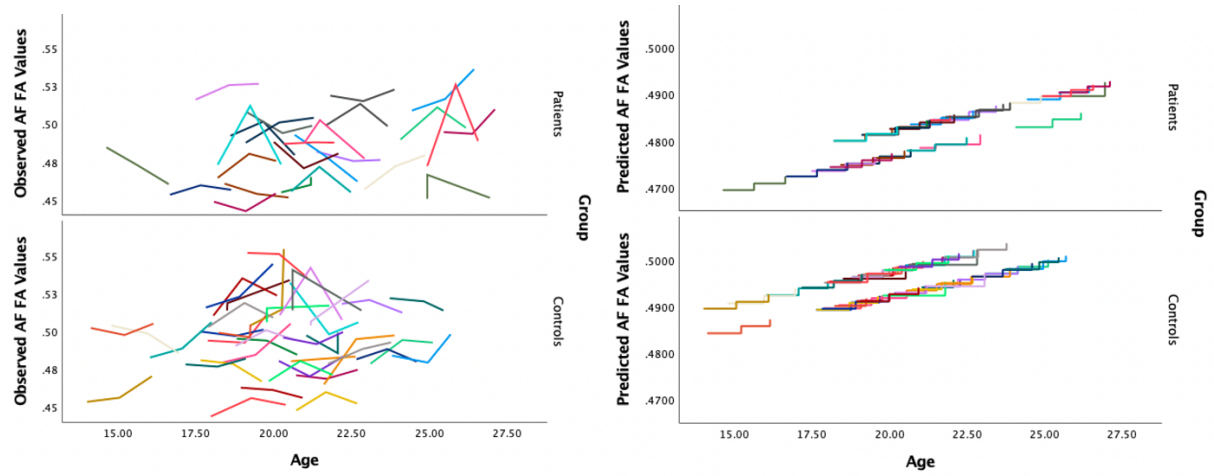


Figure 19. The relationship between AF FA values for each participant by age and patient status. Left top: Observed trajectory for each patient. Left bottom: Observed trajectory for each control. Right top: Predicted trajectory for each patient. Right bottom: Predicted trajectory for each control.

With mean FA of the SLF as the outcome, the LMM including group, age, and sex as fixed effects and visit number as the repeated effect showed that group, age, and sex were not significant predictors of SLF FA (all $p>.2$). As with the prior model, there was high correlation among the three visits within a single subject (rho=.765), and the autoregressive structure appeared to be appropriate for these data (Wald Z=18.762, $p<.001$).

DISCUSSION

The current study aimed to investigate the differences in white matter integrity across adolescent development as impacted by diagnostic status and by self-reported anhedonia experience. The first hypothesis was that there would be a significant group difference in white matter integrity as indicated by fractional anisotropy (FA) in two tracts of interest: the superior longitudinal fasciculus (SLF) and the accumbofrontal tract (AF). This hypothesis was partially supported, with significant group differences in the AF but not SLF. The second hypothesis was that there would be a negative linear relationship between anhedonia as measured by a subset of

questions on the Beck Depression Inventory (BDIa) and FA in these two tracts of interest, such that adolescents with higher levels of anhedonia would show decreased white matter integrity. This hypothesis was not supported, with no significant relationship between anhedonia and FA in either tract. The third hypothesis was that there would be longitudinal group differences in FA in the two tracts of interest. The linear mixed effects model tested here partially supported this hypothesis. While group significantly predicted AF FA across visits, age was trending, and neither group nor age predicted SLF FA across visits. In addition to these *a priori* hypotheses, whole-brain analyses were completed to determine if there were additional white matter tracts whose integrity differed by diagnosis or experience of anhedonia. These analyses revealed that individuals with higher self-reported anhedonia had lower white matter integrity in the fornix, a tract that is associated with cold cognition, specifically memory (Benear et al., 2020). Disruption of the fornix has been linked to anterograde amnesia and disruptions in verbal memory in schizophrenia (Fitzsimmons et al., 2009; Takei et al., 2008).

These findings provide a structural framework for investigating the role of hot and cold cognition in adolescents not only with psychosis diagnoses, but in those experiencing anhedonia more broadly. In the current study, the AF emerged as a tract that showed group differences in integrity, supporting prior literature indicating its disruption in schizophrenia. The AF is associated with risk taking and decision making, tasks involving hot cognition that are continuing to develop across adolescence. These findings support the idea that not only are these behaviors impacted by the presence of psychosis, but the structural integrity of regions associated with these behaviors are significantly altered. While the *a priori* tract of the SLF did not show any significant differences across groups or anhedonia, another region associated with cold cognition, the fornix, emerged as having altered integrity based on self-reported anhedonia.

Taken together, these disruptions in AF and fornix integrity align with the broader assertion made in this study that systems of hot and cold cognition, known to be disrupted in a variety of psychopathology presentations, show structural disruptions in adolescents experiencing psychosis or the transdiagnostic symptom of anhedonia.

Notably, there are limitations and other considerations to be taken into account in the current study. The small sample size of adolescents who completed three visits contributed to a somewhat underpowered analysis given the range of ages represented. Relatedly, the sample of adolescents was not evenly distributed in terms of age, such that the trajectory estimated by the linear mixed effects model has more room for error in estimating average FA in the tracts of interest, particularly at the lower and upper ends. This could have either flattened or steepened the true growth model if certain ages were not well-represented. While psychosis and anhedonia are presented here as two independent methods of measuring psychopathology in this sample of adolescents, an independent samples t-test revealed that patients had a significantly higher mean score (1.10) than controls (0.63). This could introduce concerns that the regression was more indicative of diagnosis than symptom presentation. However, the range of scores seen in each group was similar (0-5 for controls, 0-6 for patients), and the findings for the regressions were sufficiently different from the ANCOVAs to support the measurement of anhedonia being different than the assignment of a psychiatric diagnosis. In addition, while DTI is a broadly used analysis approach for diffusion weighted data, and has been the primary method used in schizophrenia work, recently developed advanced diffusion techniques may yield more subtle measures that could be more sensitive to small developmental changes.

The current study adds to the growing body of literature on psychosis, anhedonia, and white matter development, while adding a novel lens of considering the roles of hot and cold

cognitive development during adolescence. Further research could expand on these findings with the addition of more thorough measures of anhedonia such as the Temporal Experience of Pleasure Scale (TEPS, used in Study 1; (Gard et al., 2006)) or Multidimensional Adolescent Anhedonia Scale (MAAS, used in Study 2; (Zareian et al., 2021a, 2021b)) and hypotheses about other white matter tracts, including the fornix, which was not included in initial hypotheses but is nevertheless associated with the cognitive behaviors of interest here. As more research is done, additional models should be investigated to specify the relationships among psychosis, anhedonia, and white matter development.

CHAPTER 5 | General Discussion

The goal of the current dissertation was to investigate different aspects of adolescent development, including anhedonia, risk-taking, working memory, and white matter development, and present a broader understanding of how these pieces fit together in adolescents experiencing a range of psychiatric symptoms. Each of the three studies in this dissertation aimed to fit a different subset of these pieces together. In Study 1 (Currin et al., 2022), a complex relationship between anhedonia and risk-taking was assessed in late adolescence and early adulthood, in which participants who self-reported a lower experience of pleasure (i.e., higher experience of anhedonia) appeared to engage in more risk-taking behavior than those who self-reported a higher experience of pleasure. This was especially apparent when considering the anticipatory aspects of pleasure, or taking pleasure from imagining a future enjoyable experience.

In Study 2, this relationship of higher anhedonia predicting more risk-taking behavior was replicated in a sample representing a wider spectrum of adolescence and using different measures. This study utilized not only a broader sample, but also a different anhedonia measure and a different risk-taking task, providing further evidence that this relationship is generalizable. Differences emerged between this result and that of Study 1, specifically that in Study 2, the aspect of anhedonia that was most strongly associated with risk-taking behavior was consummatory, or a lack of taking pleasure from a current enjoyable experience, rather than anticipatory, which was the case in Study 1. Beyond this finding, Study 2 also introduced working memory as an aspect of cold cognition that develops during adolescence. While anhedonia did not predict working memory, age was a significant predictor, supporting the dual systems model of adolescent development (Shulman et al., 2016; Steinberg, 2008) that proposes a linear growth model in cognitive control across adolescence. Additionally, this study proposed

a moderation model in which deficits in working memory would strengthen the relationship between anhedonia and risk-taking behavior. However, this model was not supported. Finally, this study investigated the relationship between anhedonia and risk perception, finding that adolescents who reported higher levels of anticipatory anhedonia also reported lower levels of risk aversion, aligning with the Study 1 finding that higher anticipatory anhedonia predicted higher risk-taking behavior.

In Study 3, the relationship between anhedonia and cognition in adolescents was studied from a neuroscience perspective, specifically by investigating differences in the integrity of specific white matter tracts in the brain associated with hot and cold cognition. The sample studied here included adolescents who were diagnosed with a psychosis spectrum disorder as well as healthy controls. All participants self-reported their experience of anhedonia (using a different measure than Study 1 or Study 2) and completed a diffusion tensor imaging (DTI) scan. A subset of those participants completed two additional visits, each roughly a year apart, in which they completed the same measures. In this study, both diagnosis and anhedonia severity were considered as possible predictors of white matter integrity in one white matter tract associated with cold cognition (SLF), and another associated with hot cognition (AF). The first hypothesis of this study was that there would be a group difference in SLF and AF integrity; this hypothesis was supported for the AF, in that controls had greater AF integrity than patients, but not for the SLF. The second hypothesis was that higher levels of anhedonia would be associated with lower SLF and AF integrity; this hypothesis was not supported for either the SLF or the AF. However, exploratory analyses outside of the tracts of interest revealed a significant relationship between the experience of anhedonia and integrity of the fornix, a region that, like the SLF, is associated with cold cognition. Finally, the third hypothesis proposed a longitudinal model in

which patients and controls showed a significantly different trajectory of white matter development in the SLF and AF across visits; this hypothesis was not supported for the SLF, and only a difference in the intercepts (absolute group difference), but not the slopes (trajectory) was significant for the AF.

Taken together, these three studies present a complex picture of adolescence and open many doors for continued exploration. A relationship between anhedonia and cognition was found in all three studies in different ways: anticipatory anhedonia predicting hot cognition in Study 1, consummatory anhedonia predicting hot cognition and anticipatory anhedonia predicting risk aversion in Study 2, and anhedonia predicting integrity of a cold cognition-related tract in study 3. Notably, these studies benefitted from studying three distinct samples representing a wide and varied range of ages, diagnoses, racial and ethnic identities, and even geographic locations. The participants in these samples completed a varied set of self-report questionnaires and tasks, in both in person and remote settings, bolstering the generalizability of the findings. Even the unpredicted finding in Study 3 of a relationship between anhedonia and white matter integrity in the fornix fits the broader theme of anhedonia predicting cognition, given the role of the fornix in basic memory processes. The implications of this research extend beyond clinical samples to the broader adolescent population, in that adolescents with higher levels of anhedonia may be experiencing cognitive demands, whether remembering to complete a chore just assigned by a parent (cold cognition) or deciding whether to speed through a yellow light while driving (hot cognition), differently than their non-anhedonic peers. The more complex models (moderation and longitudinal) proposed in these three studies were, on the whole, not supported, highlighting the need for continued study to investigate the mechanisms relating all of these components of adolescent development.

Limitations and future directions for each individual study have already been discussed within their respective chapters. However, more generally speaking, future research in this field would benefit from investigating alternate models relating anhedonia to cognition and brain development across adolescence, as well as incorporating a variety of both cold and hot cognition tasks to further specify what facets of cognition are most impacted by anhedonia. This diversity of tasks will also help guide decisions about what white matter tracts are of primary interest when investigating brain development. Additional studies in other psychiatric populations beyond psychosis spectrum disorders, such as substance use, eating disorders, or ADHD, would also provide an opportunity to broaden the lens of this anhedonia-cognition link to other clinical populations with a significant adolescent constituent.

Anhedonia is a ubiquitous symptom experienced in the general population as well as those with diagnosed psychiatric disorders. The work done in this dissertation has shed light on not only how prevalent the experience of anhedonia in adolescence is even outside of typical clinical samples, but also how in those non-clinical populations, anhedonia can still have a significant impact on an adolescent's cognitive functioning. Additionally, this dissertation has shown that even after establishing these broader connections among anhedonia, hot and cold cognition, and white matter development, there is more work to be done to consolidate these findings into a unified theory binding these components together.

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