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Experiences of Discrimination and Psychosis Risk: Psychological and Neurobiological Mechanisms

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Experiences of Discrimination and Psychosis Risk: Psychological and Neurobiological Mechanisms

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy in Psychology

by

Logan Daniel Leathem

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ABSTRACT OF THE DISSERTATION

Experiences of Discrimination and Psychosis Risk:

Psychological and Neurobiological Mechanisms

by

Logan Daniel Leathem

Doctor of Philosophy in Psychology

University of California, Los Angeles, 2024

Professor Katherine H. Karlsgodt, Chair

Psychotic disorders disproportionately affect racial and ethnic minority groups, and prior research has shown that experiences of racial/ethnic discrimination can worsen symptoms and increase risk of developing psychotic disorders. However, psychological and biological mechanisms linking discrimination and psychosis have not been thoroughly explored. Further, while psychotic disorders are recognized as neurodevelopmental, there has been an absence of studies investigating how development interacts with discrimination and psychosis risk.

The social defeat hypothesis offers a potential mechanism to understand the link between discrimination and psychosis risk. It suggests that social disadvantage or acute social stress can increase dopamine signaling in the brain's striatum, a neural marker associated with psychosis. Human studies have shown altered dopamine function in the striatum can impact connectivity of the striatum and large-scale cortical networks, which has implications for experiences of

discrimination and patterns of functional connectivity observed in schizophrenia. Behaviorally, social defeat stress and altered dopamine function are linked to cognitive impairments and emotional disturbances, which in turn may elevate the risk of psychosis.

In the transition from childhood to adulthood, functional brain networks undergo significant maturation. Relative to young adults, adolescents show greater subcortical activation to social stressors. Further, stressors in adolescence have longer-lasting effects on the brain relative to those in adulthood. These patterns may be due to changes in the striatal DA system during adolescence. Maturation of striatal DA system and brain network organization likely creates a vulnerable period in adolescence for stressors to increase risk for psychosis.

The goal of this dissertation was to further our understanding of discrimination as a risk factor for psychosis by integrating psychological and neurobiological mechanisms as well as developmental processes. Study 1 investigated the psychological and behavioral mechanisms linking discrimination to subclinical psychotic-like experiences, focusing on cognitive and emotional disturbances. We found that discrimination predicts both positive and negative psychotic-like experiences, but via unique mechanisms. Study 2 sought to determine the effects of discrimination on functional brain connectivity in CHR youth. The primary finding was that discrimination did not impact connectivity patterns uniformly across adolescence and young adulthood. The relationship between reported discrimination and connectivity was moderated by age. Study 3 leveraged findings from the first two studies to improve the prediction of long-term outcomes in CHR youth, focusing on functional connectivity changes and psychological factors as mediators of discrimination's impact on outcomes. The functional connectivity patterns identified in Study 2 predicted negative symptoms and functioning outcomes. Connectivity patterns associated with risk and patterns associated with resilience were identified.

The dissertation of Logan Daniel Leathem is approved.

Carrie E. Bearden

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2024

This dissertation is dedicated to every person who has been made to feel less than, who has been denied opportunities, who has endured harassment and violence because of who they are, what they look like, what language they speak, and whom they love.

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1. Deng, W., Tuominen, L., Sussman, R., Leathem, L., Vinke, L. N., & Holt, D. J. (2024). Changes in responses of the amygdala and hippocampus during fear conditioning are associated with persecutory beliefs. *Scientific Reports*, *14*(1), 8173.
2. DeTore, N. R., Luther, L., Deng, W., Zimmerman, J., Leathem, L., Burke, A. S., Nyer, M.B., & Holt, D. J. (2023). Efficacy of a transdiagnostic, prevention-focused program for at-risk young adults: a waitlist-controlled trial. *Psychological medicine*, 53(8), 3490-3499.
3. Currin, D. L., Hart, K., Gupta, M., Patel, P. K., Leathem, L. D., & Karlsgodt, K. H. (2022). The role of anhedonia in predicting risk-taking behavior in university students. *Journal of Psychiatric Research, 155, 451-457.*
4. Leathem, L. D., Currin, D. L., Montoya, A. K., Karlsgodt, K. H. (2021). Socioemotional mechanisms of loneliness in subclinical psychosis. *Schizophrenia Research, 238*, 145-151.
5. Patel, P. K., Leathem, L. D., Currin, D. L., Karlsgodt, K. H. (2021). Adolescent neurodevelopment and vulnerability for psychosis. *Biological Psychiatry, 89*(2), 184-193.
6. Burke, A., Shapero, B. G., Baldelli, A., Nyer, M., Deng, Y. W., Namey, L., Leathem, L. D., Landa, C., Cather, C., Holt, D. J. (2020). Rationale, methods, feasibility and preliminary effectiveness of a transdiagnostic prevention program for at-risk college students. *Frontiers in Psychiatry, 10, 1030.*

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CHAPTER 1 | BACKGROUND

Racial Disparities in Psychotic Illness

Psychotic spectrum disorders such as schizophrenia are debilitating mental illnesses that create an annual economic burden of $150 billion dollars in the Unites States (Cloutier et al., 2016). The brunt of these disorders is placed on racial and ethnic minority communities. Racial and ethnic minority individuals are 2.5-3x more likely than their non-Hispanic white (NHW) peers to be diagnosed with a psychotic disorder (Schwartz & Blankenship, 2014). When diagnosed, racial and ethnic minority patients are less likely to receive adequate care, including a longer time to initiate treatment (Oluwoye, Davis, Kuhney, & Anglin, 2021), fewer average care visits (van der Ven, Susser, Dixon, Olfson, & Gilmer, 2020), and a lower likelihood of receiving evidence-based interventions once in treatment (Oluwoye et al., 2018) relative to NHW individuals, which contributes to poorer long-term outcomes (Morgan et al., 2017). These disparities highlight the need to understand the mechanisms that lead to increased psychosis symptomatology among minority groups, in order to inform intervention and prevention efforts.

Several factors have been hypothesized as explanations for these observed disparities or as mechanisms that may contribute to increased psychosis risk among minoritized populations, with the most research in the United States focusing on risk in African American and Latino males relative to risk in non-Hispanic white males (Anglin, 2023b). Clinician bias and poor understanding of cultural influence in psychosis presentation have potentially led to overdiagnosis of psychotic disorders, particularly schizophrenia, in ethnic and racial minority populations, which may partially, but not fully, explain these disparities (Schwartz & Blankenship, 2014). Other factors that have been proposed to contribute to the increased incidence of psychotic disorders among minority populations, including neighborhood

disadvantage and socioeconomic status, pollution, prenatal stress, and experiences of trauma and stress (Anglin et al., 2021).

One of the most validated factors shown to increase psychotic symptoms and psychosis risk among racial and ethnic minority individuals is the experience of discrimination (Pearce, Rafiq, Simpson, & Varese, 2019). Reported experiences of discrimination have been associated with psychosis incidence both cross-sectionally (Anglin, Lighty, Greenspoon, & Ellman, 2014; Oh, Cogburn, Anglin, Lukens, & DeVylder, 2016) and prospectively (Janssen et al., 2003). Discrimination has further been shown to be associated with increased psychotic-like experiences (PLEs), abnormal and often distressing beliefs or perceptual experiences that aren't as severe as a full disorder symptom, in non-clinical populations, and to predict conversion to diagnosed disorder among individuals identified as at clinical high risk for psychosis (Anglin, Lui, Espinosa, Tikhonov, & Ellman, 2018; Stowkowy et al., 2016). Despite associations with psychosis across the spectrum of severity, few studies have investigated possible mechanisms linking experiences of discrimination to psychosis risk.

Social Stress and Social Defeat Models of Psychosis

Many forms of social disadvantage and stress have been associated with the emergence of psychotic symptoms and disorders, including immigrant status (Bourque, van der Ven, & Malla, 2011; Kirkbride et al., 2017), low SES (Hur, Choi, Yun, Chon, & Kwon, 2015; Werner, Malaspina, & Rabinowitz, 2007), and traumatic events (Craig Morgan & Fisher, 2007; Read, van Os, Morrison, & Ross, 2005). Various forms of social disadvantage and stress, including experiences of discrimination share a common physiological mechanism linking them to psychosis risk: biological cascading effects, including activation of the HPA axis and autonomic nervous system, altering cortisol release and heart-rate variability, respectively (Berger &

Sarnyai, 2015). Individuals with psychosis reported greater number of stressful events relative to controls (Phillips, Francey, Edwards, & McMurray, 2007) and a greater reactivity to those events, assessed both subjectively (Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001) and via cortisol response (Cannon et al., 2008). These physiological effects, along with alterations of the brain's stress response system, including acute activation of the amygdala and modulation of the salience network (Van Marle, Hermans, Qin, & Fernández, 2010), result in altered emotional processing and increased negative affect, increased sensitivity to threat or hypervigilance, and aberrant salience, the tendency to assign importance to unimportant stimuli, or to discount the importance of important stimuli (Berger & Sarnyai, 2015). An ecological momentary assessment study found support for both disrupted affect and altered threat processing, but not aberrant salience, in explaining the link between social stress and increased psychotic experiences across the psychosis spectrum (discrimination was not measured) (Klippel et al., 2017). Exposure to chronic stress and chronic activation of the HPA axis may sensitize the mesolimbic dopamine (DA) system (Cannon et al., 2008), creating a vulnerability for the onset of psychosis. Childhood and adolescent trauma, predictors of later psychotic symptoms and disorders (Read, Perry, Moskowitz, & Connolly, 2001), have been linked to altered striatal DA function in healthy adults (Oswald et al., 2014).

Social defeat has been proposed as a specific model linking social stress to psychosis (Selten, van der Ven, Rutten, & Cantor-Graae, 2013). Social defeat is a paradigm in rodents that traditionally involves an acute social stressor resulting in a loss of territory or resources (Golden, Covington III, Berton, & Russo, 2011). Social defeat paradigms reliably cause acute striatal DA release and have been found to modulate DA long-term function in the striatum and prefrontal regions (Novick, Forster, Tejani-Butt, & Watt, 2011; Tidey & Miczek, 1996). In humans, social

stressors have been associated with acute DA release, in both healthy individuals (Pruessner, Champagne, Meaney, & Dagher, 2004) and in individuals with psychosis (Mizrahi et al., 2012). Social defeat stress may impact functional connectivity as well, as racial discrimination has been associated with altered striatal function and functional connectivity in racial minority adults (Akdeniz et al., 2014). Adolescent social defeat in rodents is also associated with impaired cognition (Jin et al., 2015; Von Frijtag et al., 2000) and increased social avoidance into adulthood (Zhang, Yuan, Shao, & Wang, 2016), common features of psychotic disorders that have also been linked to functional network dysfunction (Barch & Ceaser, 2012; Blanchard, Mueser, & Bellack, 1998; Kwapil, 1998; Simpson, Kellendonk, & Kandel, 2010). Cognitive impairment and poor social functioning have also been shown to increase risk for conversion to a psychotic disorder among those identified at clinical high risk over a 2-year period (Cannon et al., 2016). While social defeat is unlikely to explain the entirety of the racial minority experience or effects of racism, this model offers a promising neurobiological mechanism.

Functional Brain Development and Stress in the Psychosis Spectrum

Psychotic disorders are commonly considered neurodevelopmental disorders, with peak onset in late adolescence (Marenco & Weinberger, 2000; Patel, Leathem, Currin, & Karlsgodt, 2021). Additionally, peak incidence of subclinical PLEs occurs in early adolescence (Linscott & Van Os, 2013a), suggesting that adolescence is a crucial period for both the initial emergence of PLEs and progression to full disorder. The effect of race-based stressors on psychosis risk is similarly moderated by developmental stage. Racial minority immigrants to Great Britain are at highest risk of developing psychosis if they immigrated during childhood, and were thus exposed to racial minority stressors during adolescence (Kirkbride et al., 2017). Diathesis-stress and two-hit models of psychosis suggest that genetic factors, as well as the prenatal and early postnatal

environment, can contribute to initial vulnerability that increases risk for psychosis (Maynard, Sikich, Lieberman, & LaMantia, 2001; Walker, Kestler, Bollini, & Hochman, 2004). Then, a secondary stressor, potentially in adolescence, alters the typical trajectory of neural development, leading to psychosis (Karlsgodt, Jacobson, Seal, & Fusar-Poli, 2012). Adolescence is a period of ongoing structural and functional brain development, which may open a period of increased vulnerability to the effects of stressors (Romeo, 2010).

In the transition from childhood to adulthood, functional brain networks undergo significant maturation, with cortical networks becoming more integrated and hierarchical (Ernst, Torrisi, Balderston, Grillon, & Hale, 2015). While cortical networks strengthen over development, functional connections between subcortical and cortical regions weaken (Menon, 2013). In particular, stress-related functional circuitry develops throughout adolescence, with amygdala-prefrontal connections becoming inversely related (Gabard-Durnam et al., 2014; Gee et al., 2013) and striatal regions becoming more functionally specialized in their connections into adulthood (Greene et al., 2014; Porter et al., 2015).

Relative to young adults, adolescents also show greater subcortical activation to social stressors, particularly in the striatum (Vijayakumar, Cheng, & Pfeifer, 2017). Further, stressors in adolescence have longer-lasting effects on the brain relative to those in adulthood (Romeo, 2010), and social defeat in adolescence leads to opposite, and persistent, effects on cortical function relative to social defeat in adults (Watt et al., 2014). For those that experience social defeat in adolescence, prefrontal release of DA is reduced, an effect that persists into adulthood (Watt et al., 2014) while at the same time, striatal DA function is increased into adulthood (Novick et al., 2011), which mirrors dopaminergic abnormalities seen in schizophrenia (Howes, McCutcheon, Owen, & Murray, 2017; McCutcheon et al., 2019; Selten et al., 2013). In contrast,

in mature rodents, social defeat leads to increased prefrontal DA function that persists over a similar time period (Watt et al., 2014). These patterns may be due to maturation of the striatal DA system during adolescence (Matthews, Bondi, Torres, & Moghaddam, 2013) and modulation of the DA response to stress by pubertal hormones (Sinclair, Purves-Tyson, Allen, & Weickert, 2014). Maturation of striatal function and brain network organization likely creates a vulnerable period in adolescence for stressors to alter striatal function.

Social stress experienced during adolescence may have widespread effects on the functional connectivity of the developing brain. The striatum has dopaminergic connections to core regions of the salience/ventral attention network (e.g., anterior insula and dorsal anterior cingulate cortex) (Meador-Woodruff et al., 1996; Williams & Goldman-Rakic, 1998), and dopamine has been found to be integral to salience attribution processes and modulation of salience network activity during tasks (Ko et al., 2009; Pignatelli & Bonci, 2015). The aberrant salience hypothesis of psychosis suggests that dysfunction of the salience network and connectivity between the salience and other networks impairs switching between task-negative functional networks, like the default network, and task-oriented functional networks, like the frontoparietal control network (Howes & Nour, 2016; McCutcheon et al., 2019; Palaniyappan & Liddle, 2012). This dysfunction theoretically gives rise to psychotic symptoms as salience to certain stimuli is misattributed or internal stimuli, like thoughts, are treated as salient external stimuli, like voices (Howes & Nour, 2016; Palaniyappan & Liddle, 2012). Dysconnectivity across large scale networks, including the salience, default, and frontoparietal networks, is well documented in individuals with schizophrenia (Li et al., 2019; Yuan et al., 2022), and functional dysconnectivity across these three networks has been linked to experiences of racism and discrimination among adolescents and adults exposed to trauma, victimization, and racism (Corr

et al., 2022; Saxena, Liu, Handley, & Dodell-Feder, 2024; Webb et al., 2022). Despite these links to risk factors and the pathophysiology of psychosis, no study has investigated the neurobiological mechanisms of social defeat stress on the development of psychosis or the potential of adolescence as a vulnerable period for such stressors.

In this dissertation, three related studies were conducted in a targeted effort toward improving our understanding of risk for psychotic disorders following experiences of discrimination. In **Study 1**, a sample of diverse young adults enrolled at the University of California, Los Angeles reported on their recent experiences of discrimination as well as subclinical psychotic-like experiences. In this study, two facets of discrimination were measured: the type of discrimination, or the identity that was targeted by the perpetrator, and the form of the discrimination, which includes the context of the discrimination as well as the characteristics of the perpetrator. This information was then used to predict positive and negative psychotic-like experiences. Further, three mechanisms hypothesized to link experiences of discrimination to psychotic symptoms were evaluated simultaneously: negative affectivity, subjective cognitive concerns, and behavioral and emotional regulation. This study offers insight into qualities of discrimination that may place an individual at greatest risk and into processes that contribute to risk following discriminatory experiences.

In Studies 2 and 3, the impact of racial/ethnic discrimination specifically is the focus of investigation. In **Study 2**, the impact of discrimination on brain function was evaluated in a sample of youth and young adults, aged 12-35, identified as being at clinical high risk for developing a psychotic disorder, as well as typically developing peers. The effect of experiences of racial and ethnic discrimination on striatal dopaminergic functioning was estimated by modeling the resting state functional connectivity of the striatum with cortical brain networks.

Additionally, the potential associations between discrimination and large scale dysconnectivity were investigated by estimating the effect of discrimination on between-network connectivity of large-scale cortical functional networks like the frontoparietal, default, and ventral attention networks. Finally, given the developmental nature of psychotic disorders and the brain's response to stress, age was evaluated as a moderator for the relationship between discrimination and connectivity. This study provides novel information on the effect of acute stressors like discrimination on the developing functional architecture of the brain during adolescence and young adulthood.

Finally, in **Study 3**, an integrative model of psychological and neurobiological effects of racial/ethnic discrimination was built to predict symptom and functioning outcomes among youth and young adults identified as being at clinical high risk for psychotic disorders. Constructs identified in Study 1 as linking experiences of discrimination and subclinical psychotic symptoms were evaluated in this more clinically severe at-risk sample. In addition, functional connectivity patterns associated with experiences of discrimination, as described in Study 2, were tested for their ability to predict symptomatology and functioning at a follow-up visit. This study represents the first to comprehensively integrate psychological variables and functional neuroimaging to understand mechanisms of psychosis risk and functional outcome following discrimination.

Taken together, these three studies will provide greater understanding of the mechanisms by which discrimination increases psychosis risk, which may improve our ability to detect and intervene early in the course of psychotic illness, reducing disparities and improving outcomes among minoritized populations.

CHAPTER 2 | STUDY 1: Dimensions of unfair treatment and psychological mechanisms in a diverse undergraduate sample

INTRODUCTION

Discrimination and Psychosis Risk

Ethnic and racial minority (ERM) individuals in the United States are at increased risk of developing psychotic disorders (up to 2-3x) relative to non-Hispanic white (NHW) peers (Schwartz & Blankenship, 2014). Exposure to interpersonal and systemic stressors, including poverty and resource disadvantage, at both the individual and neighborhood levels; increased rates of perinatal complications; and more prevalent collective trauma among communities and families, confers excess risk for psychosis on ERM individuals (see (Anglin, 2023a; Anglin et al., 2021) for review). Among minoritized individuals, one of the most well-supported risk factors for psychosis outcomes is perceived interpersonal discrimination (Pearce et al., 2019). Experiences of discrimination have been associated with concurrent and prospective psychosis symptoms across the psychosis spectrum (Anglin & Lui, 2023; Michaels et al., 2023; Pearce et al., 2019). ERM individuals may additionally face unfair treatment due to factors other than their race and ethnicity, such as other marginalized identities which they may hold, and intersecting minoritized identities can compound these experiences (e.g., women of color experience sexism of different form and frequency compared to NHW women (Calabrese, Meyer, Overstreet, Haile, & Hansen, 2015)). Overall levels of minority stress (Hackett, Ronaldson, Bhui, Steptoe, & Jackson, 2020; Pascoe & Richman, 2009) may increase vulnerability for psychosis (Berger & Sarnyai, 2015).

Endorsement of psychotic-like experiences (PLEs) during adolescence and young adulthood has been shown to increase risk for psychotic disorders and other psychopathology

(Linscott & Van Os, 2013b; Mennigen & Bearden, 2020). While the majority of individuals who endorse PLEs do not go on to develop a psychotic disorder, PLEs are also associated with psychological distress, functioning, and suicidality (Kelleher et al., 2015; Staines et al., 2022). PLEs encompass attenuated positive psychosis symptoms, such as unusual beliefs or perceptual experiences (Chapman, Chapman, Kwapil, Eckblad, & Zinser, 1994; Phillips, Yung, & McGorry, 2000; Van Os, Hanssen, Bijl, & Ravelli, 2000) as well as negative symptomatology, including avolition/anhedonia (Strauss & Cohen, 2017) and reduced emotional expression (i.e., affective flattening, alogia) (Chapman et al., 1994; Kwapil, Miller, Zinser, Chapman, & Chapman, 1997). Further, negative symptoms are predictive of social and occupational functioning (Devoe et al., 2021; Riehle & Lincoln, 2017). Negative symptom dimensions are reflected in the diagnostic criteria of a variety of disorders (Strauss & Cohen, 2017), so the study of these phenomena may also provide insight to the development of mood and stressor-related disorders, which have also been linked to experiences of discrimination (Bird et al., 2021; Carter, 2007; Kessler, Mickelson, & Williams, 1999).

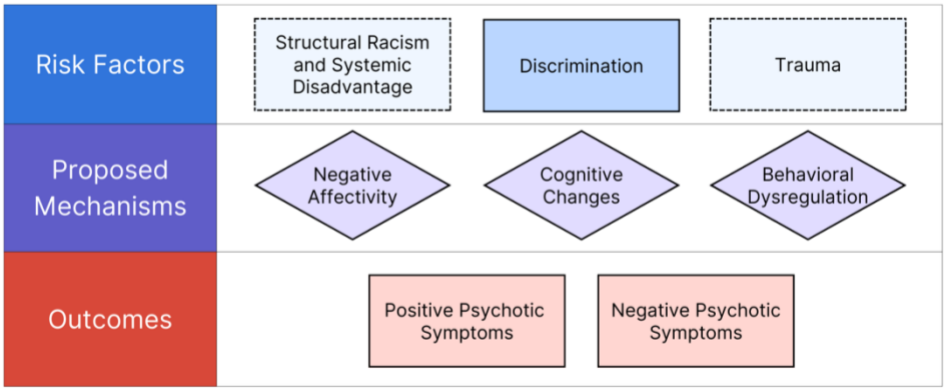


Figure 2.1. Proposed model of downstream psychological effects due to discriminatory stress. Additional risk factors (in light blue) contribute to disparities but are not of focus here.

Stress Mechanisms of Psychosis Risk

Experiences of discrimination are perceived as dehumanizing, distressing, and traumatic (Berjot & Gillet, 2011; Carter, 2007). Social stress has been shown to impact a variety of mechanisms that may increase risk for psychosis, including cognitive effects (Jin et al., 2015),

behavioral and emotional dysregulation (Badcock, Paulik, & Maybery, 2011; Tully & Niendam, 2014) and increased negative affect (Klippel et al., 2017) (see Figure 2.1), but research has yet to explore these pathways in the context of discrimination.

Negative Affectivity

Chronic and acute social stressors, including minority stress, have well-studied effects on negative affect and mood disorders (Duman & Monteggia, 2006; McEwen, 2003). In particular, prior studies have found that disrupted affect may mediate the relationship between social stress and negative health outcomes, including psychotic symptoms, across the psychosis spectrum (Ayduk et al., 2000; Klippel et al., 2017). Among minoritized individuals, experiences of discrimination predict momentary and sustained increases in negative emotion (Broudy et al., 2007; Livingston et al., 2020) as well as increased risk for mood disorders (Clark, Salas-Wright, Vaughn, & Whitfield, 2015; Noh & Kaspar, 2003). Emotional problems and mood disorders are highly comorbid in psychosis risk states and psychotic disorders and are believed to often precede the emergence of psychosis symptoms in at-risk individuals (Krabbendam et al., 2005; Mennigen & Bearden, 2020).

Cognitive Changes

Executive functioning challenges are present in early, subclinical stages of psychosis (Mollon et al., 2016), in youth at CHR and high genetic risk (Agnew-Blais & Seidman, 2013; Bora & Murray, 2014; Fusar-Poli et al., 2012), and in diagnosed schizophrenia samples (Kerns, Nuechterlein, Braver, & Barch, 2008; Sheffield, Karcher, & Barch, 2018; Velligan & Bow-Thomas, 1999). Executive functioning encompasses a variety of cognitive processes, including maintaining and updating information related to the current task, inhibiting irrelevant information, and being able to shift from task to task (Diamond, 2013). Research on the impact

of social stress on these executive functions is mixed (Girotti et al., 2018; Plieger & Reuter, 2020), as moderate, controllable acute stress may improve executive functions, more intense and longer-lasting stress appears to have detrimental effects on working memory (Girotti et al., 2018) and cognitive flexibility (Girotti et al., 2018; Liston, McEwen, & Casey, 2009). Additionally, chronic stress and disadvantage have been shown to negatively impact executive functioning ability among patients with schizophrenia and unaffected individuals (Aas et al., 2012; Merz, Wiltshire, & Noble, 2019).

Self-Regulation

Effective coping and self-regulation are known to be protective against the effects of stress on mental health outcomes, including psychosis (Ered, Gibson, Maxwell, Cooper, & Ellman, 2017; Taylor & Stanton, 2007). However, while it may buffer negative outcomes, evidence suggests that self-regulation capacity is finite (Muraven & Baumeister, 2000). Moreover, while acute exposure to discrimination promotes self-regulation attempts (McGarrity, Huebner, Smith, & Suchy, 2020), repeated exposure to stress is thought to deplete long-term self-regulation capabilities (Fani, Carter, Harnett, Ressler, & Bradley, 2021). Consistent with this, discrimination exposure is predictive of later self-regulation difficulties among racial and sexual minority men (English, Rendina, & Parsons, 2018) and altered neural activity during emotion regulation among Black women (Fani et al., 2021). Negative social interactions can also reduce aspects of executive function such as cognitive control of emotion and distress tolerance (King, McLaughlin, Silk, & Monahan, 2018), and difficulty with cognitive control of emotion is associated with worsened positive psychosis symptoms and paranoia (Hooker et al., 2011; Horne et al., 2022) and may play a role in psychosis risk (Duggirala, Schwartze, Pinheiro, & Kotz, 2020; Tully & Niendam, 2014).

Dimensions of Discrimination

Most prior research investigating the connection between experiences of discrimination and psychosis risk has focused on the effects of discrimination attributed to singular identities, or *type* of discrimination (i.e., discrimination based on race, sex, weight, etc.), and often collapsing across the *forms* discrimination takes (e.g., being harassed by police, excluded from a social group, threatened, etc.) (Carter, 2007; Pearce et al., 2019). We know that experiencing multiple types of discrimination due to multiple stigmatized identities is associated with a higher likelihood of conversion to psychosis among individuals clinically identified as being at high risk for psychosis (CHR), even above other forms of stress, such as bullying and trauma (Stowkowy et al., 2016). However, we lack an understanding of the mechanisms that place multiply minoritized groups at increased risk for psychotic experiences. Similarly, experiencing more forms of discrimination across domains of life predicts increased subclinical positive psychotic-like experiences (PLEs) in sample of ERM young adults (Anglin et al., 2014). Certain forms of major discriminatory events, like police harassment (DeVylder, Cogburn, et al., 2017), have been linked to psychotic symptoms, independently of everyday forms of unfair treatment and microaggressions (Anglin & Lui, 2023). Yet, the limited study of specific forms of discriminatory treatment and the mechanisms linking them to psychosis among minoritized individuals (Carter, 2007) hampers our ability to intervene with affected youth.

Here we investigate specific effects of types and forms of discrimination in a sample of diverse young adults and investigate proposed mechanisms linking social stress to psychosis risk. This study examined multiple predictions. First, we predicted that ERM individuals will report more discrimination experiences across multiple types (identity attributions) and forms (domains of unfair treatment) compared to NHW young adults. Second, we hypothesized that increased

reports of discrimination would be associated with elevated PLEs. We explored the effects of reporting specific discrimination forms and the number of types on PLEs. Third, we hypothesized that the association between reported discrimination experiences and PLEs would be mediated by negative affectivity, cognitive changes, and behavioral dysregulation.

METHODS

Subjects

Undergraduate students provided informed consent to participate in this study in exchange for course credit as part of a large introductory psychology course, which enrolls approximately 5% of the student body each year. One hundred forty-eight students were enrolled in a cross-sectional study approved by the University of California Los Angeles IRB, between October 2018 and December 2020 in Los Angeles, California and reported discrimination and PLEs. Demographics are reported in Table 1. Forty participants identified as NHW and 108 as ERM, with the ERM group collapsing across all Hispanic/Latinx and non-White participants.

(N = 148)	**Number (%)**
Female	106 (71.6%)
Age	Mean = 19.6 (SD = 1.4)
Race and Ethnicity	
African American	3 (2.0%)
Asian	56 (37.8%)
Hispanic/Latinx	32 (21.6%)
Native American	1 (0.7%)
White	40 (27.0%)
More than one	16 (10.8%)

Table 2.1. Demographics

Measures

Discrimination. Experiences of unfair treatment were assessed via a two-stage self-report questionnaire adapted from the Everyday Discrimination Scale (Williams, Yu, Jackson, & Anderson, 1997). In the first stage, participants were asked to report which of 10 forms of unfair treatment they recently (i.e., “this quarter”) experienced to their gender, race or ethnicity, sexual orientation, gender expression, body weight, religion, because they spoke a second language or

spoke English with an accent, or because they or their parents were born in another country. Eight forms of discrimination from the original scale were included and revised for relevance to the college student population. These questions included "How often were you threatened by other young adults?" and "How often were you treated disrespectfully by authority figures (e.g., instructors at college, supervisors at work)?" We added two additional items applicable to the experience of this population: "How often did other young adults exclude you from their group or activities?" and "How often were you hassled by the police?" A total score was calculated by summing the number of discrimination forms endorsed (Chronbach's $\alpha = 0.64$).

In the second stage of the measure, participants were asked to report how frequently they faced discrimination due to the specific identities and attributes listed (e.g., race, gender, body weight, etc.). Responses were dichotomized to 0 "Never experienced" and 1 "experienced at least once" and summed to indicate the number of types of discrimination experiences endorsed ($\alpha = 0.80$). Table 2 provides the frequencies of each form and type endorsed in the current sample.

Type	**NHW (n=40)**	**ERM (n=108)**	**Total (%)**	**Chi-square**	
Racial or Ethnic	5 (12.5%)	44 (40.7%)	49 (33.1%)	10.51**	
Gender	13 (32.5%)	32 (29.6%)	45 (30.4%)	0.11	
Body Weight	9 (22.5%)	17 (15.7%)	26 (17.6%)	0.87	
Religious	8 (20.0%)	12 (11.1%)	20 (13.5%)	1.97	
Language/Accent	1 (2.5%)	18 (16.7%)	19 (12.8%)	5.24*	
Immigration	0 (0%)	17 (15.7%)	17 (11.5%)	7.11**	
Sexual Orientation	2 (5.0%)	5 (4.6%)	7 (4.7%)	0.01	
Gender Expression	0 (0%)	4 (3.7%)	4 (2.7%)	0.22	Regression Effects

Form					Positive PLEs	Negative PLEs
Disrespected	18 (45.0%)	48 (44.4%)	66 (44.6%)	0.00	0.120	0.173
Excluded by peers	13 (32.5%)	35 (32.4%)	48 (32.4%)	0.00	0.229*	0.292**
Treated poorly by service worker	5 (12.5%)	39 (36.1%)	44 (29.7%)	7.79**	0.151	0.175
Insulted	12 (30.0%)	31 (28.7%)	43 (29.1%)	0.24	0.109	0.173
Treated suspiciously	3 (7.5%)	28 (25.9%)	31 (20.9%)	5.99*	0.245*	0.174
Teacher or professor treated as not smart	3 (7.5%)	28 (25.9%)	31 (20.9%)	5.99*	0.056	0.084
Disrespected by an authority figure	3 (7.5%)	24 (22.2%)	27 (18.2%)	4.24*	0.049	0.091
Treated unfairly by store clerk or security guard	2 (5.0%)	24 (22.2%)	26 (17.6%)	5.98*	0.043	0.137
Threatened	3 (7.5%)	10 (9.3%)	13 (8.8%)	0.11	0.070	0.088
Treated unfairly by police	1 (2.5%)	6 (5.6%)	7 (4.7%)	0.61	0.077	-0.056

Table 2.2. Endorsement rates for various types and forms of discrimination. Significant differences in rate of endorsement between ERM and NHW subjects are indicated. For Discrimination Forms, secondary analyses predicting CAPE Positive and Negative PLEs for each form, controlling age, sex, and ethnic/racial minority status. *, $p < .05$; **, $p < .01$.

Psychotic-like Experiences (PLEs) and Negative Affectivity. The Community Assessment of Psychic Experiences (CAPE (Stefanis et al., 2002)) was used to assess subclinical symptoms. The CAPE is a 42-item survey that assesses the frequency at which an individual experiences of a variety of subclinical experiences on a scale from 1 “Never” to 4 “Nearly Always.” The CAPE is divided into three scales: Positive PLEs (abnormal sensory experiences or unusual experiences), Negative PLEs (reduced experience of pleasure or motivation), and Depressive symptoms. For Positive and Negative PLEs, subjects were also asked the level of distress each endorsed item caused, allowing for the generation of a specific distress score. Positive and Negative PLE scores served as the outcomes of interest. The Depressive symptoms scale was

used as the measure of negative affectivity in mediational analyses (CAPE Positive scale α = .85; CAPE Negative scale α = .88; CAPE Depressive scale α = .83).

Cognitive Difficulties and Behavioral Dysregulation. Executive and self-regulation difficulties were assessed via the Behavior Rating Inventory of Executive Function (BRIEF) – Adult version (Gioia, Isquith, Guy, & Kenworthy, 2000). The BRIEF is a 75-item self-report scale divided into indices: the Metacognition Index (MI) and the Behavioral Regulation Index (BRI). The MI score was used to represent executive functioning and cognitive difficulties, while the BRI was used to index behavior regulation challenges. BRIEF items were scored on a 3-point scale, from 1 "Never" to 3 "Often." Due to a technical error, some participants were not presented the item "I get overwhelmed by large tasks," from the MI scale. This item was removed from all responses prior to score calculation. The MI scale retains good internal consistency with this item removed (MI α = .93; BRI α = .91).

Data Analytic Plan

To determine differences in frequency of endorsement between NHW and ERM students, chi-square tests were performed for discrimination types and forms. In the full sample, linear regressions predicting CAPE symptoms (Positive and Negative PLEs) were estimated from 1) total number of discriminated identities (type) and 2) sum total domains of discrimination (form) as the primary predictor and age, sex, and ethnic and racial minoritized group membership as covariates. Significant direct effects of discrimination predictors on Positive and Negative PLEs were then entered into mediation analyses, simultaneously evaluating the parallel indirect effects of discrimination on PLEs through Negative Affectivity (CAPE Depressive symptoms), Cognitive Difficulties (BRIEF Metacognition Index), and Behavioral Dysregulation (BRIEF Behavioral Regulation Index). In exploratory analyses, significant overall effects for total

experienced discrimination domains were further interrogated by estimating the specific effects of each discrimination domain. To determine specific effects of certain discrimination forms, additional regressions were performed predicting Positive and Negative PLEs from endorsement of each discrimination form, controlling for age, sex, and ERM status. The alpha value for these exploratory analyses was set at $\alpha = .005$ to account for the number of comparisons (across 10 forms). All analyses were performed in SPSS version 28.0, and indirect effects were estimated using PROCESS version 4.0 with 5000 bootstrapped iterations.

RESULTS

Racial Differences in Discrimination Experiences. As predicted, ERM individuals reported higher rates of recent discrimination across multiple types (identity attributions), including race-based discrimination ($\chi^2 = 10.51$, $p = .001$), as well as discrimination due to speaking English as a second language or with an accent ($\chi^2 = 5.24$, $p = .022$) and due to being a first- or second-generation immigrant ($\chi^2 = 7.11$, $p = .008$) compared to non-Hispanic White participants (Table 2). ERM respondents were also more likely to report disrespect from authority figures ($\chi^2 = 4.24$, $p = .039$); being treated unfairly by security guards or store clerks ($\chi^2 = 5.99$, $p = .014$) and by restaurant workers ($\chi^2 = 7.79$, $p = .005$); and being treated suspiciously due to any aspect of their identity ($\chi^2 = 5.99$, $p = .014$), relative to NHW peers (Table 2.2).

Discrimination and Associations with PLEs. In linear regressions predicting PLE scores, total number of discrimination types endorsed predicted Positive PLE scores, above the effects of age, sex, and minoritized group membership, in the full sample ($\beta = 0.22$, $p = .008$). Total number of discrimination types was not significantly associated with Negative PLEs ($p > .05$).

In linear regressions estimating the effects of forms of discrimination controlling for age, sex, and race in the full sample, total number of forms of unfair treatment experienced was positively associated with Positive PLEs (β = 0.23, p = .006) and Negative PLEs (β = 0.26, p = .002). In exploratory analyses investigating the specific forms of discrimination and their associations with Positive and Negative PLEs, endorsement of social exclusion and being treated with suspicion were each associated with higher reported Positive PLEs (ß = 0.229, p < .005 and ß = 0.245, p = .003, respectively). Only social exclusion was significantly related to Negative PLEs (ß = 0.292, p < .001, see Table 2.2).

Significant main effects predicting PLEs were then entered into mediation models predicting PLEs with Behavioral Regulation, Cognitive Difficulties, and Negative Affectivity as simultaneous predictors (Figure 2.2; models summarized in Table 2.3). Total number of discrimination types endorsed predicted all three putative mediators ($ß_{BRI}$ = 0.252, p = .003; $ß_{MI}$ = 0.219, p = .009; $ß_{Depressive}$ = 0.207, p = .012), controlling for age, sex, and ERM status. However, only the indirect effect from number of discrimination types to Positive PLEs through Behavioral Regulation difficulties was significant ($ß_{BRI}$ = 0.083, $CI_{95\%}$ = [0.025, 0.176]; $ß_{MI}$ = -0.006, $CI_{95\%}$ = [-0.062, 0.038]; $ß_{Depressive}$ = 0.050, $CI_{95\%}$ = [-0.002, 0.110]). Total number of discrimination types was not associated with Negative PLEs, so no mediation model was estimated.

Predictor	Outcome	Direct Effect (*c*)	Mediator	Path *a*	Path *b*	Indirect Effect (*ab*)	Direct Effect (*c'*)
Total Discrimination Type	Positive PLEs	0.22**	BRI	0.252**	0.328**	0.083†	0.064
			MI	0.219**	-0.025	-0.006	
			Depressive	0.207*	0.241*	0.006	
	Negative PLEs	0.13	BRI	-	-	-	-
			MI	-	-	-	
			Depressive	-	-	-	
		0.23**	BRI	0.267**	0.323**	0.086†	0.069

Total Discrimination Form	Positive PLEs		MI	0.270**	-0.018	-0.005	
			Depressive	0.211*	0.230*	0.048	
	Negative PLEs	0.26**	BRI	0.267**	-0.156	-0.042	0.035
			MI	0.270**	0.439***	0.119†	
			Depressive	0.211*	0.622***	0.131†	

Table 2.3. Regression and mediation models predicting psychotic-like experiences (PLEs) from total discrimination types and forms. All models include age, assigned sex at birth, and ethnic/racial minority status as covariates. *, $p < .05$; **, $p < .01$; *** $p < .001$. †, bootstrapped 95% confidence interval of indirect effect does not include zero. Indirect effects were not estimated for non-significant direct effects.

Total number of discrimination forms endorsed was also significantly associated with all three mediators ($ß_{BRI} = 0.267$, $p = .001$; $ß_{MI} = 0.270$, $p = .001$; $ß_{Depressive} = 0.211$, $p = .010$), controlling for age, sex, and racial minoritized group membership. In predicting Positive PLEs from total discrimination forms, only the indirect effect through Behavioral Regulation difficulties was significant ($ß_{BRI} = 0.083$, $CI_{95\%} = [0.025, 0.176]$; $ß_{MI} = -0.006$, $CI_{95\%} = [-0.062, 0.038]$; $ß_{Depressive} = 0.050$, $CI_{95\%} = [-0.002, 0.110]$). Conversely, in predicting Negative PLEs from total discrimination forms endorsed, the indirect effect through Behavioral Regulation was not significant ($ß_{BRI} = -0.042$, $CI_{95\%} = [-0.093, 0.014]$), while the indirect effects through Cognitive Difficulties and Negative Affectivity were each significant ($ß_{MI} = 0.119$, $CI_{95\%} = [0.040, 0.211]$; $ß_{Depressive} = 0.131$, $CI_{95\%} = [0.027, 0.246]$).

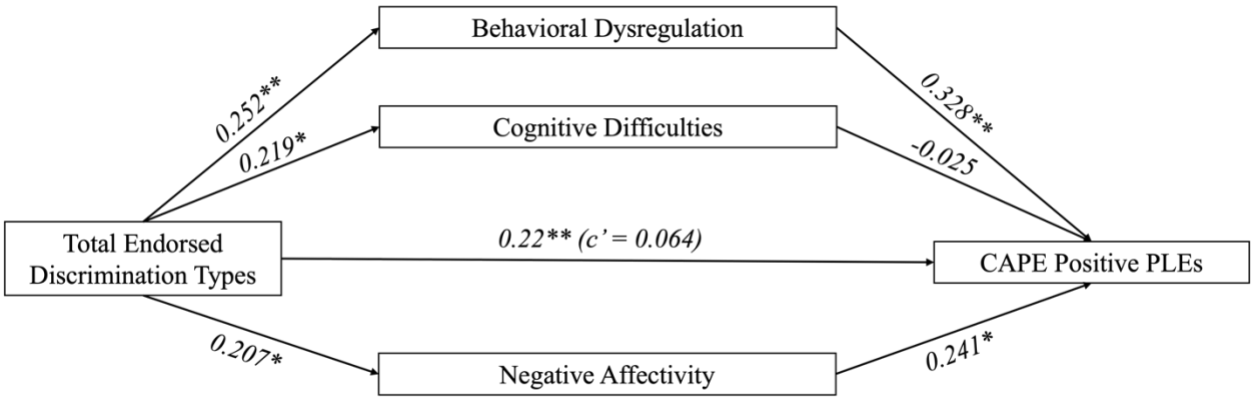


Figure 2.2. Multiple mediation model predicting CAPE Positive PLEs from total number of discrimination types experienced. Multiple pathways were evaluated, through BRIEF BRI scores (Behavioral Dysregulation) and MI scores (Cognitive Difficulties), and through CAPE Depressive symptoms (Negative Affectivity). *, p < .05; **, p < .01.

DISCUSSION

This study replicates findings that experiences of discrimination are a key predictor of psychotic symptoms among ERM individuals (Anglin et al., 2021; Pearce et al., 2019). Our results have highlighted the effects of discrimination on positive symptoms of psychosis, extending recent findings linking discrimination to positive symptoms, particularly paranoia/suspiciousness, in CHR youth (Michaels et al., 2023). These data also support the prediction that marginalization on the basis of multiple identities (i.e., reporting multiple types of discrimination) confers additional risk for psychotic-like symptoms, potentially in a dose-response fashion given the linear relationship between total discrimination types and Positive PLEs. This result bolsters previous findings that total number of discrimination types predicts likelihood of converting to a full psychotic disorder among individuals at high risk (Stowkowy et al., 2016) and extends it to subclinical symptoms. Utilizing a non-help seeking sample of college students has allowed us to target a developmental period that is both sensitive to the emergence of PLEs and psychotic disorders (Patel et al., 2021) as well as a crucial period for racial identity development (French, Seidman, Allen, & Aber, 2006; Phinney, 1989) in a social environment in which discriminatory experiences can be common and distressing (Carter, 2007). These results thus provide a possible early snapshot into mechanisms of risk for vulnerable populations while also showing that such experience can impact even otherwise healthy individuals.

These findings also highlight that experiencing discrimination across multiple domains is associated with higher endorsement of Positive and Negative PLEs. Additionally, specific forms of unfair treatment were identified as risk-factors for both Positive and Negative PLEs. Both peer exclusion and being treated suspiciously confer social threat and may signal deprivation of resources (in the form of social support or material resources). Social stress is core to many

etiological models of psychosis (and other psychopathology) (Walker et al., 2004). This may be especially true for young adults. Once of the major tasks of adolescence and early adulthood is to consolidate a sense of self and identity (Harter, 1990; Sebastian, Burnett, & Blakemore, 2008), which is often facilitated by social experimentation and updating our sense of self through feedback from others (Amiot, De la Sablonniere, Terry, & Smith, 2007). Facing discrimination in this way may foster negative self-esteem and self-schemas (Saleem et al., 2014), which are consistent with a cognitive model of psychosis (Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001).

Although there are limitations to cross-sectional associations and mediation analyses (Maxwell & Cole, 2007), we have provided preliminary support for the role of executive functioning as a mechanism from unfair treatment to subclinical PLEs. Executive functioning deficits have been well-described in individuals with schizophrenia (Barch & Sheffield, 2017; Goldman-Rakic, 1994), as well as individuals at risk for psychosis (Fusar-Poli et al., 2012). Cognitive and executive deficits may be associated with subclinical PLEs, as well (DeRosse & Karlsgodt, 2015), or even predict later development of psychosis (Barnett et al., 2012). Experiences of stress, particularly when they are repeated or chronic, have been shown to negatively impact a variety of cognitive abilities, including executive function (Merz et al., 2019; Sandi, 2013). Interpersonal stress has also been shown to be associated with less adaptive emotion regulation (Moriya & Takahashi, 2013), which is also partially captured by the BRI index. For ERM individuals, stressful experiences unfair treatment may reduce ability to effectively regulate their behavior and emotions, which, in turn, is associated with greater unusual experiences and risk for psychosis.

In contrast to the mediation effects found in models with Positive PLEs as the outcome, models predicting negative symptoms suggested that both self-reported meta-cognitive difficulties and depressive symptoms are possible mechanisms linking discrimination to negative symptoms. Further, since all three mediators were included simultaneously, these indirect effects may represent distinct pathways to symptomatology. These separable mechanisms are consistent with our current understanding of the etiology of negative symptoms, which suggests that negative symptoms transdiagnostically arise due to both altered hedonic responses and "cold" cognitive changes (Strauss & Cohen, 2017). Stress, including minority stress and victimization, are associated with deficits in reward learning and anticipation (Auerbach, Admon, & Pizzagalli, 2014; Pachankis et al., 2015) as well as observed difficulties with working memory and attention (Klein & Boals, 2001; Liston et al., 2009; Schoofs, Preuß, & Wolf, 2008). However, the exact point or points of disturbance in these processes contributing to negative symptomatology following experiences of discrimination requires additional study.

Future research will help uncover mechanisms of risk as well as effective resilience factors and possible points of intervention. We found that, within a diverse sample of young adults, experiences of discrimination and unfair treatment were reported more frequently among ERM individuals and contributed to subclinical PLEs in this diverse young adult sample. This study further elucidates the effect of discriminatory experiences on ERM youth and will help better understand racial and ethnic disparities in serious mental illness.

Limitations

This study was constructed to explore the specific effects of discrimination on PLEs among diverse young adults. However, interpersonal acts of prejudice and unfair treatment captured in our measure of discrimination only captures one part of the struggles minoritized

individuals face due to structural racism, sexism, heterosexism, xenophobia, etc. These other stressors and disadvantages, such as exposure to community violence, poor prenatal care, and pollution, have been linked to psychosis risk (Anglin et al., 2021) and may covary or interact with interpersonal discrimination. Direct measures of socioeconomic status and other risk factors would provide a fuller understanding of disparities in psychosis risk among minoritized individuals.

Primary analyses reported here combine participants from all non-white racial backgrounds and Hispanic participants into the ERM group. Minority stress and experiences of discrimination are not uniform across ethnic and racial groups, and the relationships between minority stress and psychotic symptoms may vary by racial group and other cultural factors (Booth, Leigh, & Varganova, 2012; Yang & Chen, 2018). For instance, acculturative stress has been associated with auditory and visual hallucinations among Asian-American immigrants to the United States but only auditory hallucinations among Latino-American immigrants (DeVylder et al., 2013). The current study is not sufficiently powered to estimate moderation models evaluating unique effects across different ERM groups. Further, certain experience deemed as psychotic-like on the CAPE may also be culturally normative (e.g., belief in voodoo or witchcraft) (Larøi et al., 2014) or adaptive at non-clinical levels. For example, baseline cultural distrust or hypervigilance (which exist on a putative continuum with paranoia) may promote physical safety and protect self-esteem in the context of interpersonal discrimination or structural racism (Whaley, 1998, 2001).

There is a significant amount of variance shared among the three mediators evaluated in this study (rs > .40, ps < .001). This is likely due to both the shared method (i.e., self-report) and to construct overlap and association. Both the MI and BRI subscales of the BRIEF assess aspects

of executive functioning. While the two indices capture conceptually separable facets of executive functioning, they are highly interrelated (Hofmann, Schmeichel, & Baddeley, 2012; Miyake et al., 2000). Depression has also been shown to be associated with executive functioning difficulties, such as impairments in attention, working memory, and emotion regulation (Moritz et al., 2002). This should be taken into account when considering the "true" relationships among these variables and between these variables and discrimination and PLEs. Future studies that utilize multiple methods may be able to interrogate further the effects found here.

The data analyzed here were collected cross-sectionally, thus no causal or directional claims can be made about the observed relationships. While other studies have illustrated interpersonal and minority stress preceding increased psychosis risk (Dykxhoorn, Lewis, Hollander, Kirkbride, & Dalman, 2020; Van Der Ven & Selten, 2018), individuals experiencing psychotic symptoms are also subject to significant stigma, unfair treatment (Crisp, Gelder, Rix, Meltzer, & Rowlands, 2000; Schulze & Angermeyer, 2003), and may be more likely to experience and perceive negative social interactions (Patel et al., 2021), which may be indirectly captured in our measure of discrimination.

Although this sample was large enough to detect effects for certain forms of discrimination, our study may have been underpowered to detect subtler effects and effects specific to infrequently endorsed discrimination types and forms. In other samples, perceived discrimination based on sexual orientation and gender orientation have been shown to be associated with psychosis risk (Gevonden et al., 2014; Thoroughgood, Sawyer, & Webster, 2017). Exposure to police violence, as well as other forms of "major discriminatory events" have been linked to PLEs in the United States (DeVylder, Oh, et al., 2017; Oh et al., 2016) but may be

linked to PLEs independently of more common unfair treatment and microaggression, like those captured more frequently here (Anglin & Lui, 2023). Studies that are sufficiently powered to detect the effects of infrequent events or those that impact a smaller proportion of the population, and the longitudinal mechanisms of these effects on psychosis symptoms, are needed to better understand this phenomenon.

Conclusions

In a sample of diverse young adults, this study was able to identify multiple marginalization and social discrimination in the form of exclusion as particular predictors of subclinical PLEs. Additionally, a possible mechanism was described, by which experiences of discrimination are associated with psychotic experiences through self-reported difficulties with behavioral and emotional regulation. Given the high incidence of psychotic and other psychological disorders during early adulthood, efforts to reduce social discrimination and bolster social belongingness and emotion regulation are crucial for supporting the wellness and well-being of minoritized young adults.

CHAPTER 3 | STUDY 2: Effects of Discrimination on Functional Connectome Development in High-Risk Youth

INTRODUCTION

Psychotic disorders are commonly considered neurodevelopmental disorders, with peak onset in late adolescence (Marenco & Weinberger, 2000; Patel et al., 2021). Additionally, peak incidence of subclinical PLEs occurs in early adolescence (Linscott & Van Os, 2013a), suggesting that adolescence is a crucial period for both the initial emergence and identification of psychosis risk and the progression to full disorder.

Adolescence is also a period of substantial change in both the structure and function of the brain, as gray matter undergoes a reduction associated with synaptic pruning (Shaw et al., 2008), and white matter volume steadily increases with ongoing myelination (Lebel, Walker, Leemans, Phillips, & Beaulieu, 2008). Functionally, the architecture of the resting brain undergoes significant reorganization, with cortical networks becoming more integrated, specialized, and hierarchical (Ernst et al., 2015; Grayson & Fair, 2017). Functional organization development is most prominent in task-oriented (i.e., salience and control) and default networks (Grayson & Fair, 2017; Gu et al., 2015). Further, while cortico-cortical networks strengthen over development, functional connections between subcortical and cortical regions often weaken (Menon, 2013; Sato et al., 2015). The significant brain development ongoing during adolescence may open a period of increased vulnerability to the effects of stressors (Romeo, 2010) and conferring risk for psychopathology (Cannon et al., 2003; Patel et al., 2021; Selemon & Zecevic, 2015).

Dysconnectivity models of psychosis posit that the symptomatology and deficits associated with psychotic disorders arise from abnormal communication between brain regions –

including altered functional connectivity (Friston, 1998; Pettersson-Yeo, Allen, Benetti, McGuire, & Mechelli, 2011). Compared to healthy controls, individuals with chronic schizophrenia display a broad pattern of functional connectivity differences (Li et al., 2019). While both hyper- and hypoconnectivity patterns have been found in patients relative to controls, patients with schizophrenia frequently show reduced resting state functional connectivity both within networks like the Default, Salience, Frontoparietal, and Temporal Networks and between networks (Harikumar et al., 2023; Li et al., 2019; Yuan et al., 2022). Individuals with schizophrenia have been found to display abnormal connectivity between the Default network and task-positive frontoparietal networks at rest and during tasks (Whitfield-Gabrieli et al., 2009), as well as reduced integration of the Salience/Ventral Attention network (Dong, Wang, Chang, Luo, & Yao, 2018), which may impair appropriate task-oriented activity and connectivity (Harikumar et al., 2023; Palaniyappan & Liddle, 2012)

Diathesis-stress and two-hit models of psychosis suggest that these functional brain abnormalities are the result of a genetic liability for psychosis that interacts with a secondary stressor, potentially experienced during adolescence, to alter the typical trajectory of neural development, leading to psychosis (Karlsgodt, Jacobson, Seal, & Fusar-Poli, 2012; Maynard et al., 2001; Walker et al., 2004). Experimental work has shown that, in rodents, stressful experiences during adolescence have led to long-term changes in the structure and function of the brain (Watt et al., 2014).

In humans, adolescent brains process social stressors, such as rejection, differently than those of young adults, with adolescents showing greater subcortical activation to social stressors, especially in regions of the striatum (Vijayakumar et al., 2017). Despite this, little work has

investigated how environmental stressors during adolescence affect brain function among those identified as being at risk for psychosis.

Experiences of racial discrimination contribute to overall levels of stress and have cascading effects on physiological and neural stress systems (Berger & Sarnyai, 2015). Discrimination is perceived as a form of social threat that stimulates immediate stress responses from the body, activating the autonomic nervous system and hypothalamic-pituitary-adrenal axis, stimulating release of norepinephrine, epinephrine, and cortisol (reviewed in Berger & Sarnyai, 2015; Goosby, Cheadle, & Mitchell, 2018; Hobson, Moody, Sorge, & Goodin, 2022). Midbrain regions and salience network regions contain glucocorticoid receptors that upregulate salience network activity during acute stress (Hermans, Henckens, Joëls, & Fernández, 2014). Chronic exposure to racism increases allostatic load (Rodriguez et al., 2019), prolongs cortisol secretion (Hobson et al., 2022), and alters salience network activity and connectivity (Akdeniz et al., 2014). These physiological and neurobiological effects contribute to psychotic symptoms and severity (Klippel et al., 2017). Additionally, this effect may be especially salient for adolescents and young adults, given the ongoing changes to functional brain networks. Despite the documented effects of discrimination on physiological stress responding and psychotic symptoms, no study to date has evaluated the effects of discrimination on neurodevelopment and psychosis in adolescents.

Social defeat and social stress hypotheses suggest that social stressors lead to altered dopamine release in the striatum (Selten et al., 2013; Veling et al., 2008) which is a central feature in neurobiological models of psychotic disorders (Howes & Kapur, 2009). Striatal dopamine release then modulates large scale functional networks (McCutcheon, Nour, et al., 2019). Adult psychosis patients commonly show altered functional connectivity (Liu et al., 2008;

Lynall et al., 2010), including in striatal regions (Quidé, Morris, Shepherd, Rowland, & Green, 2013; Tu, Hsieh, Li, Bai, & Su, 2012), relative to healthy individuals. Striatal connectivity patterns distinguish patients from controls (Sullivan et al., 2020), are associated with symptom severity (Tu et al., 2012), and predict antipsychotic treatment response (Sarpal et al., 2015), suggesting the importance of striatal connectivity to psychotic disorder outcomes. Given the heterogeneity in outcomes, both for CHR individuals (Allswede et al., 2020) and for individuals exposed to stressful events (Alisic et al., 2014), identifying neural markers of discriminatory stress exposure may improve understanding of differential trajectories.

Striatal DA function is further associated with network organization in major cortical networks, including the salience and default networks (McCutcheon, Nour, et al., 2019). Although atypical striatal connectivity patterns are seen in CHR (Hubl et al., 2018) and subclinical psychosis spectrum populations (Jacobs et al., 2019), changes in striatal network function due to psychosis risk and the effect of stressors like discrimination unknown.

In contrast to Study 1, this study focuses on racial/ethnic discrimination, rather than discrimination across types and forms, to provide targeted insight into the impact of race-based discriminatory experiences. As social defeat stressors, like discrimination, alter DA function, potentially long-term, we expect to see alterations in striatal connectivity in individuals who experience discrimination that are similar to alterations associated with CHR status and for these to be particularly evident in CHR individuals reporting recent discrimination. Additionally, we expect alterations in cortical network connectivity among the Frontoparietal, Salience/Ventral Attention, and Default Networks following reported experiences of discrimination. Finally, given the neurodevelopmental model of psychosis risk and hypothesized disruptions of typical neurodevelopment following a stressor, we predicted that discriminatory experiences will

moderate age-related changes to functional connectivity during this developmental period.

METHODS

This project used data collected as part of the NIH-funded North American Prodrome Longitudinal Study 2 (NAPLS 2, (Addington et al., 2015)), a large consortium study in which baseline neuroimaging and longitudinal clinical data was collected at 8 sites spanning the United States and Canada: University of California, Los Angeles (UCLA; Los Angeles, California); Emory University (Atlanta, Georgia); Harvard University (Cambridge, Massachusetts); University of North Carolina, Chapel Hill (UNC; Chapel Hill, North Carolina); Yale University (New Haven, Connecticut); University of California, San Diego (UCSD; San Diego, California); Zucker Hillside Hospital (New York City, New York); and University of Calgary (Calgary, Alberta).

Sample. Baseline measures were collected from 764 CHR adolescents and young adults and 280 TD controls. Prodromal symptoms were assessed by trained graduate student raters using the SIPS and the Scale of Prodromal Symptoms (Miller et al., 2003). 227 CHR and 138 TD youth were included in connectivity analyses (see Pre-processing below). Subjects were ages 12-35, to fully capture the age range of typical onset for psychotic disorders. CHR participants were help-seeking individuals who met criteria for one of four prodromal syndromes, defined by the Structured Interview for Prodromal Syndromes (SIPS): attenuated positive symptom syndrome (83.9% of CHR), genetic risk and deterioration (4.4%), brief intermittent psychotic symptoms (0.8%), or schizotypal personality disorder, if under age 19 (2.7%). Some met criteria for multiple syndromes (8.1%). Participants were excluded from the CHR group if prodromal symptoms were clearly caused by an Axis I disorder or medical issue.

Criteria for TD: TD individuals were excluded if they met criteria for a current prodromal

syndrome or a Cluster A personality disorder, had a family history of psychotic disorders, or were taking any psychotropic medication.

Exclusion criteria for all participants: Evidence for a current or lifetime psychotic disorder, an IQ < 70, a history of central nervous system disorder, or substance dependence in the previous 6 months.

	TD (n = 138)	CHR (n = 227)	
Age	19.6	18.9	$t = 1.655$
Sex	76M (55%)	133M (59%)	$\chi^2 = 0.43$
Race First Nations East Asian South Asian SE Asian Black Central/S. American SWANA White Multi-racial	 2 8 6 3 32 4 1 69 13	 2 2 5 6 41 8 3 132 28	$\chi^2 = 12.40$
Hispanic/Latino	20 (14.5%)	44 (19.4%)	$\chi^2 = 1.42$
Discrimination Past Year	0.85	1.87	$t = -5.551$***
Discrimination Lifetime	1.80	2.91	$t = -5.419$***
Education – Father	6.49	6.28	$t = 1.096$
Education – Mother	6.72	6.37	$t = 2.110$*

Table 3.1. Comparisons between Clinical High Risk (CHR) and Typically Developing participants on key variables. *, $p < .05$; ***, $p < .001$.

Measures

Surveys. At baseline, in a 9-item questionnaire, subjects reported experiences of various types of discrimination: discrimination based on their skin color, ethnicity, gender, sexual orientation,

age, physical appearance, disability, or religion in the past year or ever in their lifetime. Individuals reporting discrimination based either on skin color or ethnicity were included in the recent racial discrimination group (see Table 2.1). Measures similar to this one have been shown to predict psychotic symptoms and disorder incidence (Chakraborty, McKenzie, & King, 2009; Janssen et al., 2003). Six CHR and eight TD subjects were missing discrimination data, so these individuals were not included in analyses.

Subjects reported the highest level of education achieved by each of their parents on a scale from 1 = "No schooling" to 9 = "Completed graduate/professional school." Reports for each parent were entered as separate covariates. Parental Education variables were included as indices of generalized social and economic disadvantage and included as covariates to better estimate specific effects of perceived discrimination. In the full sample, there were significant group differences on Parental Education between ERM and NHW subjects (father: t = -2.90, p = .004; mother: t = -2.60, p = .010), and between CHR and TD subjects (father: t = -1.47, p = .142; mother: t = -2.88, p = .004). Thirteen CHR and five TD subjects were missing educational data from at least one parent and were not included in analyses.

Neuroimaging Procedures. 8 3T MR scanners with 3 different models were used: Siemens Trio scanners at Emory, Harvard, UCLA, UNC and Yale, GE HDx scanners at UCSD and Zucker Hillside Hospital, and a GE Discovery scanner at Calgary. Siemens sites employed a 12-channel head coil and the GE sites an 8-channel. Five-minute open-eyes resting-state fMRI (rs-fMRI) scans were performed using gradient-recalled-echo echo-planar imaging (GRE-EPI) sequences with identical parameters at all sites: TR/TE 2000/30 ms, 77° flip angle, 30 4-mm slices, 1-mm gap, 220-mm FOV. They also acquired high-resolution T1-weighted images with the following sequence: (1) Siemens scanner: MPRAGE sequence with 256 mm × 240 mm × 176 mm FOV,

TR/TE 2300/2.91 ms, 9° flip angle; and (2) GE scanners: SPGR sequence with 260 mm FOV, TR/TE 7.0/minimum full ms, 8° flip angle. Given the variability in scanners across sites, study site will be entered as a covariate in all analyses.

Pre-processing rs-fMRI data. Previously reported (Anticevic et al., 2015) preprocessing steps include 1) slice-timing correction, de-banding, and intensity normalization, 2) removal of first 5 volumes of run, 3) rigid-body registration and registration to first volume in run, and 4) co-registration to Talariach-transformed T1 structural image. Rigorous quality control procedures were then applied. Framewise displacement (FD) across all 6 rigid body motion correction parameters was calculated for each frame relative to the previous. Root mean square (RMS) differences in intensity between frames were computed and normalized to the time series median. Frames with FD > 0.5mm or RMS > 1.6 were flagged. All flagged volumes were scrubbed from analyses. Runs with > 50% frames flagged were fully removed from analyses. Following quality control, 365 subjects were included with complete predictor and covariate data: 227 CHR and 138 TD youth. While this represents a notable drop-off in sample size, given the substantial effects of motion on connectivity (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012), and high levels of motion in developing (Satterthwaite et al., 2012) and clinical samples (Makowski, Lepage, & Evans, 2019), we have followed this quality assurance plan to ensure confidence in our metrics and potential findings. No differences in covariate data were observed between included and excluded subjects (Table 3.2).

	TD – Excluded	TD – Included		CHR – Excluded	CHR - Included	
Age	19.86	19.62	t = 0.474	18.35	18.86	t = -1.514
Sex	65M (46.1%)	76M (55.1%)	χ^2 = 2.246	303M (56.4%)	133M (58.6%)	χ^2 = 0.305
Discrimination Past Year	0.88	0.85	t = 0.173	1.86	1.87	t = -0.064

Discrimination Lifetime	1.67	1.80	t = -0.617	2.72	2.91	t = -1.026
Education – Father	6.59	6.49	t = 0.498	6.23	6.28	t = -0.408
Education - Mother	6.94	6.72	t = 1.182	6.32	6.37	t = -0.345

Table 3.2. Comparisons between subjects excluded from analyses and subjects included in analyses by diagnosis group. No significant differences detected. Total sample sizes for excluded TD = 114 and CHR = 537. Sample sizes vary for each comparison due to missing data.

Following preprocessing and quality control, each subject's resting state scan was parcellated into functionally defined regions. Surface data was parcellated using the Yeo et al. (2011) 7 network parcellation. This parcellation was developed by clustering functional connectivity data from 500 young adult individuals, confirmation of these clusters in an additional 500 individuals, with reliability and validity tests of the defined regions using seed-based fcMRI and histological data (Yeo et al., 2011). Striatal data was parcellated according to Choi et al. (2012). This parcellation was developed by assigning striatal voxels to the cortical networks defined in Yeo's 7 network parcellation. From there, the time course data from each cortical network and striatal region were extracted and correlated using the Connectome Workshop (Marcus et al., 2013) and transformed using Fisher's *r*-to-*z* transformation before export.

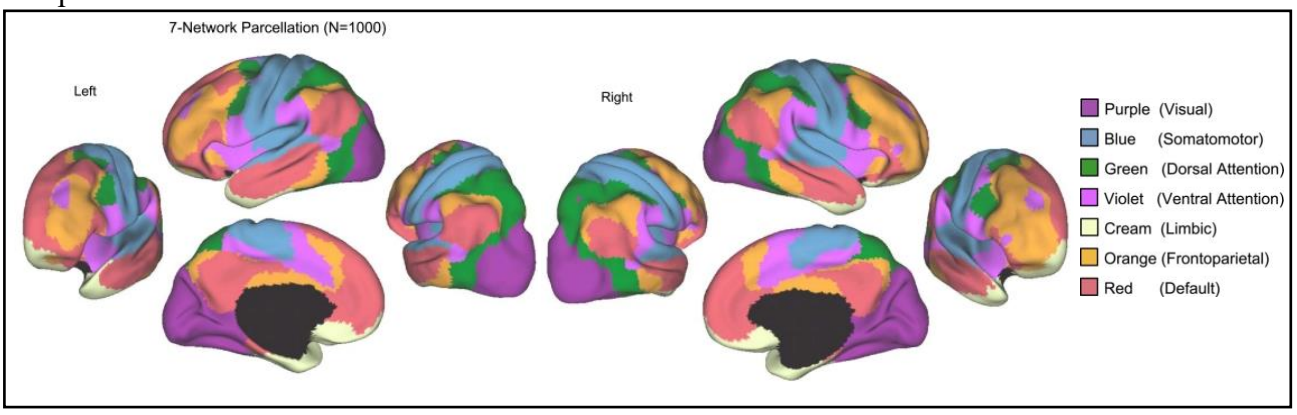


Figure 3.1. Network parcellation used to calculate between network connectivity matrices. Image taken from Yeo et al. 2011.

Primarily analyses were performed using MANCOVAs to reduce the number of analyses and possible Type 1 error. Each model was estimated on a set of connectivity metrics

corresponding to a target network (e.g., all network connections to the Frontoparietal network). Age, reported sex, ethnic/racial minority status, parental education, and study site were entered as covariates. Main effects of group were estimated for clinical groups: CHR vs TD and discrimination groups: reported discrimination vs no reported discrimination.

To estimate age effects and interactions, standardized correlation coefficients were entered into a general linear model, with CHR status, ethnic minority group membership, sex and parental education as covariates. Two age effects were estimated for each model: linear age effects model incremental age-related change and quadratic effects model age-specific effects (i.e., connectivity patterns that peak within the age range). The highest order significant age term and all lower order age terms were included in following analyses.

To model age-related changes in connectivity due to recent racial/ethnic discrimination, linear Age X Discrimination interaction terms were entered into MANCOVA models. Quadratic Age X Discrimination effects were evaluated in a second model including linear age interaction terms and all covariates.

RESULTS

Main effects of CHR status

Multivariate linear regressions were estimated for correlations grouped by network with age, sex, racial minority status, education level of each parent, and study site as covariates. The effect of CHR status was significant in the model predicting connectivity patterns between the Ventral Attention network and other cortical networks ($F = 3.577$, $p = .002$). Post-hoc between-subject tests revealed that CHR and TD individual differed significantly on connectivity between the Somatomotor (SMN) network and the Ventral Attention network (VAN, $F = 13.725$, $p < .001$). CHR status did not significantly predict connectivity patterns for the Frontoparietal

network (FPN, $F = 1.935$, $p = .074$), or the Default network ($F = 1.120$, $p = .350$).

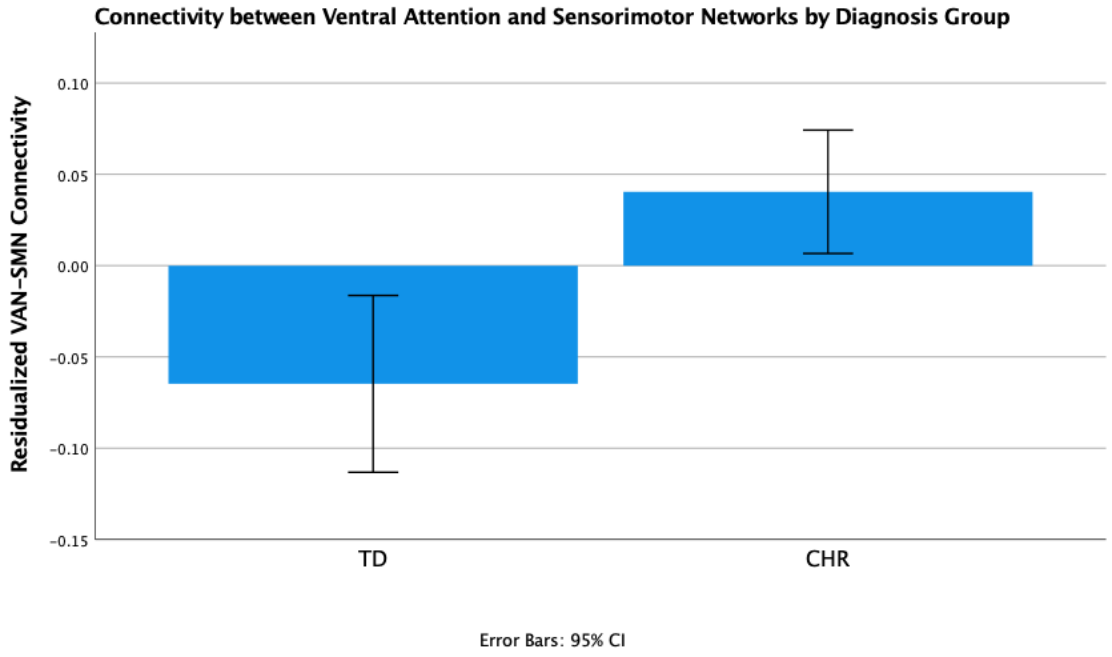


Figure 3.2. Significant main effect of group on connectivity. Standardized correlation coefficients residualized on age, sex, racial/ethnic minoritized group status, and parental education.

CHR status did not significantly predict connectivity patterns between striatal regions and the Ventral Attention network ($F = 0.367$, $p = .921$), Frontoparietal network ($F = 1.044$, $p = .400$), or the Default network ($F = 0.628$, $p = .733$).

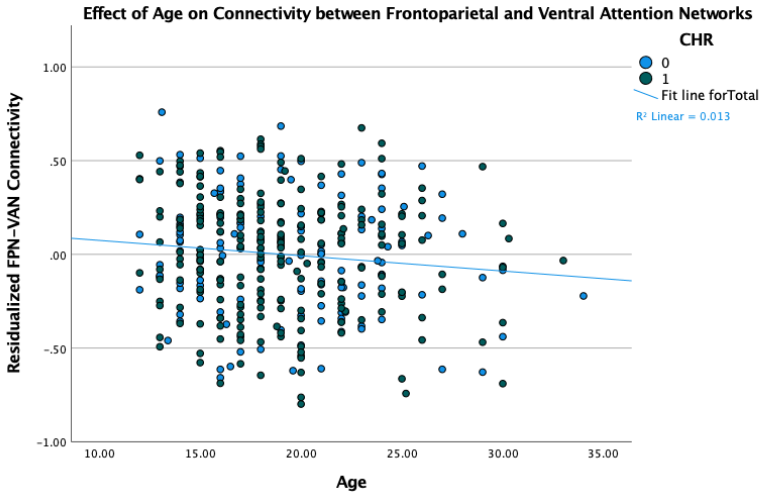
Main Effect of Recent Discrimination

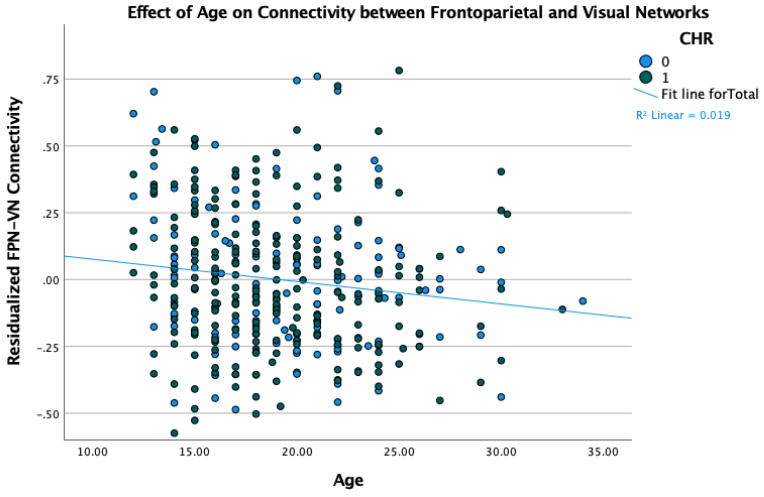
Recent discrimination status was not a significant predictor of connectivity patterns for cortical or striatal regions (cortical internetwork connectivity: Ventral Attention $F = 0.836$, $p = .543$; Frontoparietal $F = 1.127$, $p = .346$; Default $F = 0.608$, $p = .724$; cortical network-striatal connectivity: Ventral Attention $F = 0.869$, $p = .531$; Frontoparietal $F = 0.742$, $p = .636$; Default $F = 1.298$, $p = .250$).

Main Effect of Age

To determine the effect of age on connectivity, mean centered age and squared age were entered along with sex, CHR status, minoritized group membership, and mother and father

educational level. Age was associated with Ventral Attention connectivity ($F = 2.417$, $p = .027$). Post hoc analyses revealed a negative relationship between age and VAN – Frontoparietal network connectivity ($F = 6.092$, $p = .014$). Age was estimated to have a significant effect on Frontoparietal network connectivity ($F = 2.719$, $p = .014$). Post hoc analyses revealed a negative relationship between age and Frontoparietal – Visual network connectivity ($F = 8.088$, $p = .005$) and a positive relationship between age and Frontoparietal – Default network connectivity ($F = 5.488$, $p = .020$). Squared age was not associated with Frontoparietal connectivity ($F = 1.618$, $p = .141$) or Ventral Attention connectivity ($F = 0.355$, $p = .907$). Age was not associated with Default connectivity (linear: $F = 2.021$, $p = .062$, quadratic: $F = 0.814$, $p = .560$).





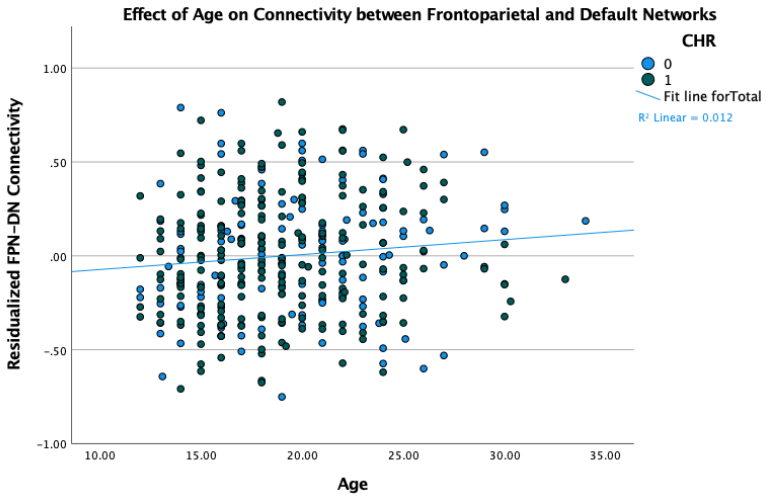


Figure 3.3. Significant main effects of age on between-network connectivity. Standardized correlation coefficients residualized on age, sex, CHR group status, and parental education.

In models predicting cortical network connectivity with striatal regions, the estimated effect of age was significant in the model predicting Ventral Attention network connectivity to the striatum, controlling for sex, CHR status, minoritized racial/ethnic group membership, and mother and father education level ($F = 2.887$, $p = .006$). Post-hoc analyses revealed specific negative effect of age on the connectivity between the Ventral Attention network and striatal regions assigned to the Ventral Attention network ($F = 6.003$, $p = .015$), as well as with striatal regions assigned to the Frontoparietal network ($F = 15.631$, $p < .001$). Squared age was not associated with Ventral Attention network connectivity ($F = 0.844$, $p = .551$). Age was not associated with connectivity between striatal regions and the Frontoparietal network (linear: $F = 0.480$, $p = .849$; quadratic: $F = 1.809$, $p = .084$) or the Default network (linear: $F = 1.371$, $p = .217$; quadratic: $F = 0.137$, $p = .995$).

Age by Discrimination Moderation Effects

To determine moderation effects of discrimination on the relationship between age and functional connectivity, interaction terms for linear age by discrimination and for squared age by discrimination were entered into multivariate models predicting connectivity patterns for each of

the three cortical networks of interest, as well as the connectivity patterns between those networks and striatal regions. As in other models, sex, CHR status, ethnic minority status, and maternal and paternal educational level were included as covariates. No significant moderation effect was found on the relationship between age and Frontoparietal connectivity (linear: F = 1.854, p = .088; quadratic: F = 1.949, p = .072). Endorsement of recent racial/ethnic discrimination did not moderate the effect of age on Ventral Attention network connectivity (linear: F = 1.222, p = .294; quadratic: F = 1.181, p = .316) or on Default network connectivity (linear: F = 0.799, p = .571; quadratic: F = 0.749, p = .611).

In models predicting cortical network connectivity to striatal regions, endorsement of recent racial discrimination did not significantly moderate the effect of age on connectivity for the Ventral Attention network (linear: F = 0.190, p = .987; quadratic: F = 0.305, p = .951) Frontoparietal network (linear: F = 0.301, p = .953; quadratic: F = 1.139, p = .338) or the Default network (linear: F = 0.256, p = .970; quadratic: F = 0.973, p = .451).

To determine if moderation effects are present within the at-risk sample, models predicting cortical internetwork connectivity were estimated with the subjects identified as CHR, with sex, racial minority status, and mother and father education level as covariates. Recent discrimination significantly moderated the association between squared age and Frontoparietal connectivity (F = 2.612, p = .018). In post-hoc analyses, recent discrimination moderated the associated between squared age and connectivity between the Frontoparietal network and the Ventral Attention network (F = 7.458, p = .007). The moderation effect of discrimination on the association between linear age and Frontoparietal connectivity was nonsignificant (F = 2.134, p = .051). In post hoc analysis of the linear interaction, discrimination was found to significantly moderate the effect of age on FPN-Limbic connectivity (F = 9.162, p = .003). Within the CHR

group, endorsement of recent racial discrimination did not significantly moderate the effect of age on connectivity for the Ventral Attention network (linear: $F = 0.832$, $p = .546$; quadratic: $F = 1.511$, $p = .176$) or the Default network (linear: $F = 0.713$, $p = .639$; quadratic: $F = 0.494$, $p = .813$).

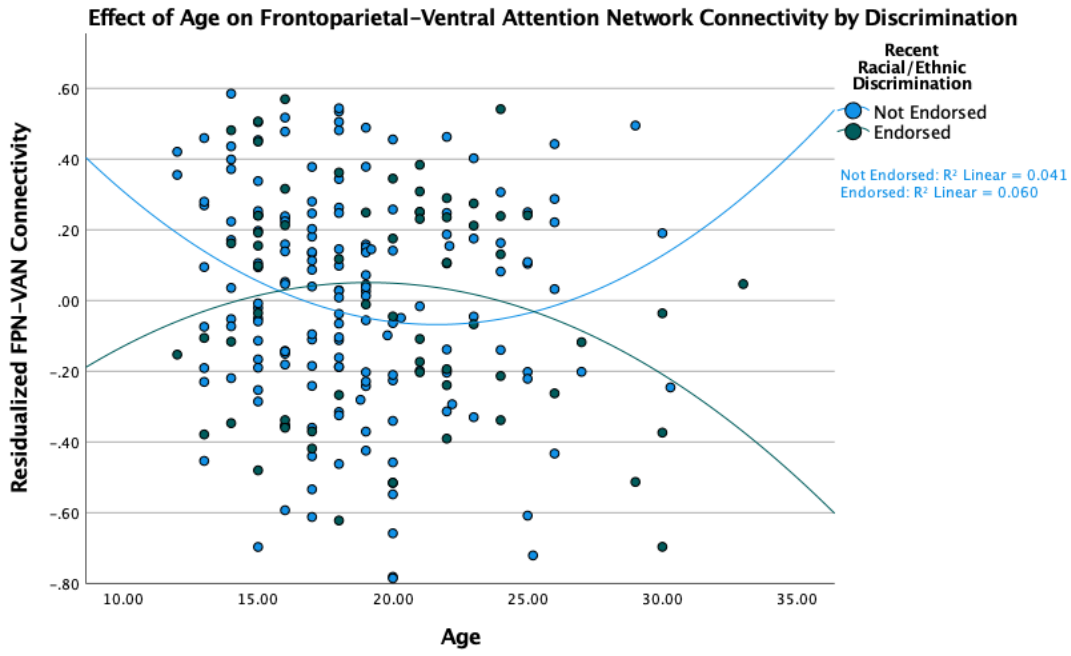


Figure 3.4. Significant interaction between discrimination and squared age on between-network connectivity within the CHR group. Standardized correlation coefficients residualized on, sex, racial/ethnic minoritized group status, and parental education.

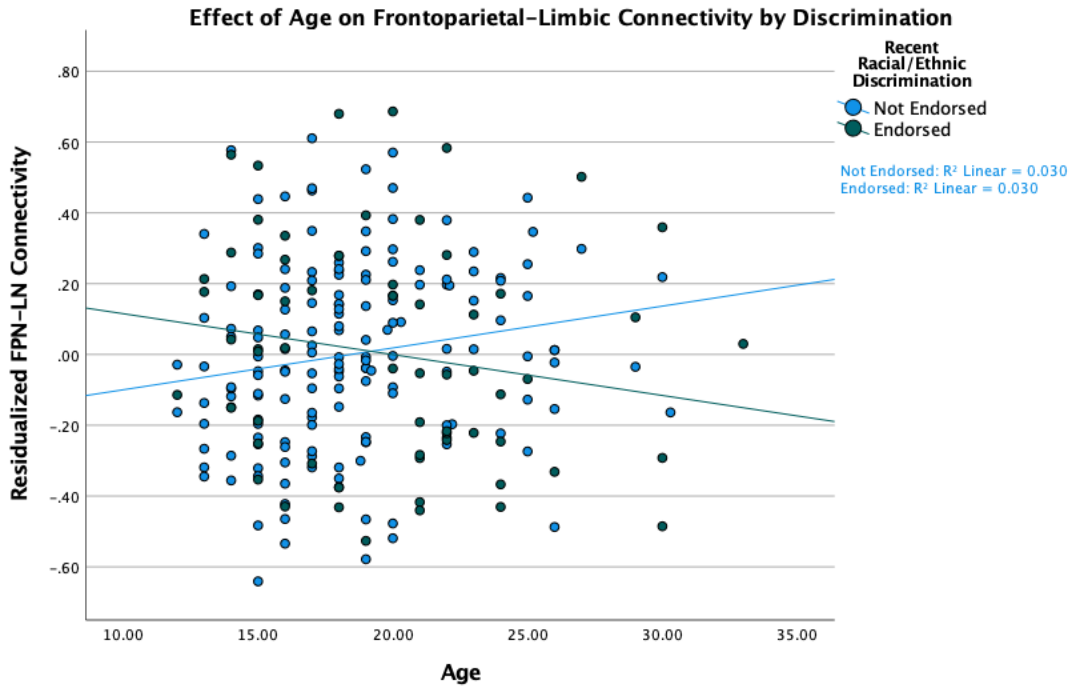


Figure 3.5. Significant interaction between discrimination and linear age on between-network connectivity within the CHR group. Standardized correlation coefficients residualized on, sex, racial/ethnic minoritized group status, and parental education.

Sensitivity analyses were performed to determine if antipsychotic use impacts the results within the CHR subjects. MANCOVAs evaluating Age X Discrimination and Age-squared X Discrimination interaction effects on FPN cortical internetwork connectivity were re-estimated with sex, ethnic/racial minority status, parental education, and study site as covariates. A binary value indicated antipsychotic use (n = 80) or not (n = 147), did not significantly predict the pattern of FPN connectivity ($F = 0.743$, $p = .615$). In this model, there was a significant interaction between squared age and reported recent discrimination ($F = 2.713$, $p = .015$), with post hoc analyses indicated specific effect of this interaction on connectivity between the Frontoparietal network and the Ventral Attention network ($F = 7.722$, $p = .006$). The moderation effect of recent racial/ethnic discrimination on the linear age and Frontoparietal connectivity relationship was not significant ($F = 2.128$, $p = .052$), but post hoc analysis revealed a significant moderation of discrimination on the association between age and FPN-Limbic connectivity ($F =$

9.079, $p = .003$).

DISCUSSION

This study is the first to model the effects of discrimination on functional connectivity patterns in a psychosis-spectrum sample, specifically a sample of youth at high risk for developing a psychotic disorder. Our first goal was to determine group differences between the CHR and TD groups on cortical network inter-connectivity and cortico-striatal connectivity. Contrary to our hypotheses that dysconnectivity would be found widely across cortical networks and specifically between network connectivity with the Default network, the only group difference detected was for the connectivity of the Ventral Attention network, seemingly driven by more positive correlations between the VAN and the Somatomotor network. Motor dysfunction is commonly observed in individuals with schizophrenia and in those at risk for psychotic disorders (e.g., abnormal involuntary movements, reduced voluntary movement (Walther et al., 2017)). These have been associated with abnormal dopaminergic function (Dean & Mittal, 2015) and patterns of connectivity, relative to healthy controls, in the cerebellar-thalamic-striatal-cortical motor loop (Walther et al., 2017). Motor network connectivity is also predictive of conversion to psychotic disorder in those at high risk (Masucci, Lister, Corcoran, Brucato, & Girgis, 2018; Mittal et al., 2011). Regions of the VAN/Salience network (i.e., dACC) that receive dopaminergic projections from the basal ganglia are implicated in motor control and dysfunction in schizophrenia (Walther et al., 2017). Hyperconnectivity between VAN and Somatomotor regions in schizophrenia has been observed during tasks of attentional control of motor function (Honey et al., 2005). The current results highlight sensorimotor network dysconnectivity and potentially motor dysfunction as markers for psychosis risk.

We then estimated the effect of recent discrimination on inter-network and cortico-striatal

connectivity. No main effects of reported racial/ethnic discrimination in the past year on functional connectivity were detected. These results do not support our hypotheses that racial/ethnic discrimination would alter functional connectivity patterns among adolescents and young adults. It is possible that we are not detecting effects of discrimination on functional connectivity for several reasons. The binary nature of the discrimination measure may be failing to capture variability among individuals who reported discrimination, as frequency and form of discrimination potentially play a role in the impact of these experiences on brain function. Dose-dependent effects of trauma and other stressors on brain function and connectivity have been observed in healthy (Frodl & O'Keane, 2013) and psychosis spectrum samples (Mayo et al., 2017; Read, Fosse, Moskowitz, & Perry, 2014). Additionally, the focus on racial/ethnic discrimination fails to account for individuals who have experienced other types of discrimination in the past year, which may impact the connectivity patterns studied here. Multiple marginalization (experiencing discrimination due to more than one minoritized identity factor), has been shown to be related to cortical thickness (Collins et al., 2021) psychotic experiences (see Study 1) and conversion to psychosis (Stowkowy, 2016). As the measure of discrimination collected also provides information about other types of discrimination (e.g., on the basis of gender, sexual orientation, etc.), additional analyses can be performed to investigate the effect of multiple minoritization on functional connectivity.

In our evaluation of age relationships with functional connectivity, we found modest support for a weakening of connectivity patterns between cortical regions and the striatum, as age was negatively associated with VAN connectivity to striatal regions. Connectivity between the Frontoparietal network and the Visual and Ventral Attention networks were also negatively associated with age, while connectivity between the Default and Frontoparietal networks was

positively associated with age. This supports the general developmental finding that cortical networks become more specialized and locally efficient into adulthood (Ernst, Torrisi, Balderston, Grillon, & Hale, 2015; Grayson & Fair, 2017)

Within the CHR group, recent racial/ethnic discrimination moderated linear age associations with connectivity patterns between the FPN and Limbic network. Among individuals reporting no racial/ethnic discrimination, a positive age association was found for FPN-Limbic connectivity, such that adults displayed stronger FPN-Limbic connectivity than early adolescents. Among individuals reporting recent discrimination, an opposite age-related effect was observed, such that adults displayed weaker FPN-Limbic connectivity relative to early adolescents. FPN connectivity with regions of the Limbic network have been implicated in reward learning (Camara, Rodriguez-Fornells, Ye, & Münte, 2009), decision making (Cohen, Heller, & Ranganath, 2005), and "hot" or emotional executive functioning (Friedman & Robbins, 2022; Salehinejad, Ghanavati, Rashid, & Nitsche, 2021) Each of these cognitive functions develop over adolescence (Blakemore & Robbins, 2012; Davidow, Foerde, Galván, & Shohamy, 2016; Zelazo & Carlson, 2012). Further, each of these have been shown to be impaired in psychotic disorders (Gold, Waltz, Prentice, Morris, & Heerey, 2008; Shurman, Horan, & Nuechterlein, 2005; Strauss, Waltz, & Gold, 2014) with reward learning processes potentially associated with development and severity of negative psychotic symptoms (Strauss et al., 2011). Further, discrimination and other forms of minority stress are also associated with development of post-traumatic stress disorder and major depressive disorder (Baams, Grossman, & Russell, 2015; Livingston, Berke, Ruben, Matza, & Shipherd, 2019) which also display alterations in hedonic processes (Nawijn et al., 2015; Pizzagalli, Iosifescu, Hallett, Ratner, & Fava, 2008). Interestingly, connectivity between the prefrontal regions and the amygdala (a subcortical limbic

region) may be protective against internalizing disorders in adolescents who have experienced adversity (Herringa et al., 2016). Connectivity between Frontoparietal and Limbic regions may warrant further investigation as a transdiagnostic mechanism or buffer of discriminatory stress.

The connectivity between FPN and VAN regions appear to show opposite quadratic associations with age, such that, for individuals reporting no racial/ethnic discrimination, the connectivity between these regions displays an age-related pattern of weakening connectivity from young adolescence to late adolescence, with a subsequent strengthening into young adulthood. For individuals reporting recent racial/ethnic discrimination, an age-related pattern of strengthening connectivity from young adolescence to late adolescence, with a subsequent weakening into young adulthood was observed in connectivity between the frontoparietal and vental attention networks. Abnormalities in FPN-VAN function have been robustly reported in psychosis spectrum samples (Li et al., 2019), and are theorized to be due to altered dopaminergic function (McCutcheon et al., 2019; Palaniyappan & Liddle, 2012). Disrupted connectivity between these regions is believed to impair "switching" between task-on states and task-off states and related to cognitive deficits, such as impaired sustained attention (Menon & Uddin, 2010).

We failed to find direct striatum-mediated evidence for the social defeat theory, as the main effect of discrimination and its interactions with age did not impact striatal connectivity with cortical networks. Although changes in dopaminergic functioning have been shown to impact striatal connectivity (Horga et al., 2016), functional connectivity is a proxy measure that may fail to detect certain changes in dopaminergic functioning. Further, we did not collect data on frequency or form of discriminatory experience, which are likely to affect the neural response.

We did, however, detect effects of discrimination on functional connectivity, specific to

stage of development. These findings support our hypothesis that discrimination would disrupt age-related patterns of connectivity from early adolescence into early adulthood. Adolescence is a significant period of development for functional network organization (Ernst et al., 2015; Grayson & Fair, 2017) and function of the dopaminergic system (Wahlstrom, White, & Luciana, 2010). This may make adolescents more vulnerable (or potentially more resilient) to the effect of acute stressors like discrimination, as measured here. Alternatively, the effects of stressors like discrimination may accrue and compound over adolescence, leading to the age-related patterns of connectivity seen here. Further longitudinal work is needed to disentangle such effects.

All imaging data analyzed here were collected at the baseline visit and are therefore cross-sectional. This limits interpretations for developmental trajectories and causation. However, multiple scan points are available for a subset of subjects, which would allow for follow-up analyses investigating within-person changes across age.

Due to the centrality of DA signaling to the social defeat hypothesis and to the pathophysiology of schizophrenia (Veling et al., 2008) and the impact of DA changes on cortical network connectivity (McCutcheon, Nour, et al., 2019), we have focused on cortico-striatal and cortico-cortical connectivity. However, other brain regions, such as the amygdala, are also implicated in social stress theories of psychosis (Aas et al., 2012). Patients show marked alterations in activation and connectivity of emotional processing regions (e.g., amygdala) for both nonsocial (Takahashi et al., 2004) and social (Mow, Gandhi, & Fulford, 2020) stimuli. Additionally, youth who exhibit subclinical PLEs and those at high risk for psychosis display altered developmental trajectories of amygdala and PFC activation (Gee et al., 2012) and connectivity (Jalbrzikowski, Murty, Tervo-Clemmens, Foran, & Luna, 2019) during emotional processing. Acute (van Marle, Hermans, Qin, & Fernández, 2009) and past childhood stress (van

Harmelen et al., 2013) have further been shown to modulate amygdala reactivity, suggesting that stressful experiences, such as discrimination may alter the development of amygdala reactivity and heighten vulnerability for psychotic symptoms and disorders. Thus, future analyses could include the amydala as another region of interest. Since measures of striatal connectivity were not found to be assocaited with discrimination in this study, the role of the amygdala should be considered.

Overall, this project offers the unique evaluation of alterations in age-related trajectories of brain maturation due to external stressors like discrimination. Evaluating the effects of development and potential developmental stage interactions will be crucial in understanding the emergence of psychotic disorders (Patel et al., 2021) and mitigating the impact of these disorders on vulnerable adolescents and their communities.

CHAPTER 4 | STUDY 3: Evaluating Connectomic Changes as Mechanisms for Symptom Expression and Functional Outcome

INTRODUCTION

Schizophrenia and other psychotic disorders are major mental illnesses associated with impaired functioning (Addington & Addington, 1999; Dickerson, Boronow, Ringel, & Parente, 1999), reduced well-being (Norman et al., 2000), and increased mortality (Brown, 1997; McGrath, Saha, Chant, & Welham, 2008), particularly in young patients (Patel et al., 2021). Identification of the psychosis prodrome has greatly furthered our understanding of the early stages and precursors to psychotic illnesses (Fusar-Poli et al., 2013). Despite recent advancements, there remains significant unexplained heterogeneity in outcomes among individuals identified as CHR (Addington et al., 2011; Schlosser et al., 2012). Beyond variability in diagnostic outcome, there is substantial variability in functional outcome in CHR individuals, and we are not yet able to predict who will function well and who will need additional support (Allswede et al., 2020). Approximately one-third of CHR individuals go on to develop a psychotic disorder (Fusar-Poli, 2012), one-third experience symptom remission, and one-third display persistent functional impairment (Addington et al., 2011; Schlosser et al., 2012). In addition, racial disparities in diagnosis and outcomes of serious mental illnesses remain a significant public health concern (McGuire & Miranda, 2008), and may contribute to the observed heterogeneity in outcome. However, the biopsychosocial mechanisms of the impact of racial disparities on symptom and functioning outcomes are not well understood.

Recent attempts at understanding heterogeneity have utilized data-driven clustering methods to describe subgroups within a population that are more homogenous. A study by Allswede et al. (2020) performed group-based multi-trajectory modeling on longitudinal

symptom and functioning data from the sample used here (NAPLS-2). They found three clinical trajectory groups: one with rapid and significant improvement in both functioning and attenuated psychosis symptoms (30% of the sample), one with limited improvement or worsening of functioning and symptoms (22%), and one with modest improvement in functioning or symptoms (49%). Integrating social risk factors and neurobiological mechanisms will improve our understanding of population heterogeneity and outcome prediction.

Previous investigations into neural predictors of outcome in CHR populations have largely focused on predictors of conversion to disorder (Anticevic et al., 2015; Cannon et al., 2015). However, some studies have found support for brain-based predictors of poor functional outcome in CHR populations, as well, including gray-matter volume (Koutsouleris et al., 2018), white matter integrity (Karlsgodt, Niendam, Bearden, & Cannon, 2009), and functional connectivity (Pelletier-Baldelli, Bernard, & Mittal, 2015). However, it is unknown how risk factors, like racial/ethnic discrimination, impact neurological predictors of functional and symptom outcome. A better understanding of the neurobiological effects of discrimination and how they are linked to the emergence of psychosis is crucial for prevention and intervention efforts to address disparities and outcome heterogeneity.

Functional dysconnectivity following discrimination offers a crucial neurobiological mechanism for understanding this risk factor. Experiences of acute social stress or defeat stimulate striatal dopamine release, with potential long-term effects on dopaminergic functioning if stressors are repeated or severe (Watt et al., 2014). Since striatal functional abnormalities are central to the pathophysiology of schizophrenia (McCutcheon, Abi-Dargham, & Howes, 2019; Zhang et al., 2019), exaggerated striatal abnormalities following discrimination may be a mechanism through which discrimination leads to worsening symptoms and conversion.

Alterations in striatal function are theorized to have downstream effects on large scale cortical brain network function (McCutcheon et al., 2019). Dysconnectivity between striatal regions and regions of the salience/ventral attention network (i.e., anterior insula, anterior cingulate cortex) has been found in individuals with schizophrenia and in individuals at risk for psychotic disorders when performing reward learning and salience attribution tasks (Gradin et al., 2013; Knolle et al., 2018). Abnormal salience network function and connectivity is believed to drive further dysconnectivity patterns in major brain networks in schizophrenia, particularly between the frontoparietal control network and default network (McCutcheon et al., 2019; Palaniyappan & Liddle, 2012) as coordination between task-positive and task-negative brain functions is disrupted (Palaniyappan & Liddle, 2012; Tu, Lee, Chen, Li, & Su, 2013; Woodward, Rogers, & Heckers, 2011). Further, exposure to acute stress in adolescence modulates the connectivity among the frontoparietal control network, salience/ventral attention network, and default network (Corr et al., 2022). In the Adolescent Brain and Cognitive Development study, experiences of bullying and peer victimization are linked to the development of subclinical psychotic experiences, mediated by default network connectivity (Saxena et al., 2024). This study will extend these recent findings with a focus on experiences of racial/ethnic discrimination as the focal social stressor.

Social stress and defeat are also associated with affective disturbance, including increased internalizing symptoms (Alvarez-Galvez & Rojas-Garcia, 2019), and poor cognitive functioning (Piccolo, Sbicigo, Grassi-Oliveira, & Fumagalli de Salles, 2014). Both internalizing (Deng et al., 2021; Deng, Grove, & Deldin, 2020) and neurocognitive (Seidman et al., 2016) difficulties are predictive of poor outcomes in CHR youth, suggesting a possible indirect path by which social stress and striatal function impact symptoms and functioning. Preclinical findings suggest social

defeat affects sociality (Zhang et al., 2016) and cognition (Jin et al., 2015; Von Frijtag et al., 2000) via alterations in DA signaling. We hypothesize that such DA alterations subsequently impact functional connectivity patterns, which predict symptom and functioning in early psychosis (Chopra et al., 2021; Rotarska-Jagiela et al., 2010). We therefore expect that functional connectivity effects following discrimination will impact symptom as well as social and role functioning in youth at risk for psychosis.

Hypotheses: 1) Experiences of racial/ethnic discrimination will be associated with poorer symptom and functioning outcomes in the full NAPLS-2 sample, which will be mediated by emotional and cognitive difficulties. 2) Functional connectivity alterations following discrimination uncovered in Study 2 will additionally mediate this relationship in the subgroup with available imaging data.

METHODS

Participants:

This study utilized data from the sample described in Study 2. Of the 764 CHR individuals who completed baseline assessments, 512 completed the six-month follow-up assessment. Several participants were missing key variable data from the baseline visit: reported discrimination (n = 79), parental education (n = 46), SIAS (n = 74), CDSS (n = 42), DSI (n = 128), ER-40 and PED (n = 108), TASIT (n = 100), RAD (n = 106), LNS, Mazes, and Fluency (n = 109), and SS (n = 110). Complete symptom and behavioral data were available for 367 CHR subjects. Complete functional connectivity and follow-up data were available for 190 individuals. Missing data was addressed in models below such that cases with partial data could contribute available information to model estimations.

Measures:

Prodromal symptoms were assessed by trained graduate student raters using the Structured Interview for Psychosis-Risk Syndromes (SIPS) and the Scale of Prodromal Symptoms (Miller et al., 2003). The SOPS contains 4 clinical subscales, each measuring symptom dimensions seen in psychosis spectrum populations: Positive symptoms, Negative symptoms, Disorganization, and General symptoms. The Positive SOPS contains 5 items: P1) Unusual Thought Content/Delusional Ideas, P2) Suspiciousness/Persecutory Ideas, P3) Grandiose Ideas, P4) Perceptual Abnormalities/Hallucinations, and P5) Disorganized Communications. The Negative SOPS contains 6 items: N1) Social Anhedonia, N2) Avolition, N3) Expression of Emotion, N4) Experience of Emotions and Self, N5) Ideational Richness, and N6) Occupational Functioning. Each item was rated on a scale from 0 (Absent) to 6 (Severe and Psychotic for Positive items or Extreme for Negative items). Conversion to full psychotic disorder was assessed using the SIPS and the Structured Clinical Interview for the DSM-4 (SCID). Other psychiatric diagnoses were made using the SCID. Functioning was assessed using the Global Functioning: Social and Role Scales (Cornblatt et al., 2007). Social and role functioning ratings are made following a semi-structed interview for current functioning, as well as the highest and lowest levels of functioning over the previous year. Current functioning levels were used in models predicting functioning.

Emotional dysregulation and reactivity were assessed via multiple scales sensitive to internalizing symptoms: the Calgary Depression Scale for Schizophrenia (CDSS, (Addington, Addington, & Maticka-Tyndale, 1993)), the Self-Report Anxiety Scale (SAS, (Zung, 1971)), the Social Interaction Anxiety Scale (SIAS, (Mattick & Clarke, 1998)), and the Daily Stress Inventory (DSI). The DSI offers scores for total number of stressful events reported and total stress experienced from these events. Total number of stressful events was used, and we

calculated an average stress score by dividing the total stress from the number of stressful events. Each measure was tested for skewness prior to entry into the models below. Scores on CDSS, SAS, SIAS, DSI-average stress and DSI-total events were all found to be moderately positively (coefficients of skewness = 1.053, 0.841, 0.541, 0.520, and 0.925, respectively). Mardia's test for multivariate skew and kurtosis revealed a high degree of multivariate skew (coefficient of skewness = 676.27, $p < .001$), but not kurtosis (coefficient of kurtosis = 0.13, $p = 0.9$). Transformation of each variable by taking the square root reduced positive univariate skewness (coefficients of skewness: CDSS = 0.119, SAS = 0.542, SIAS = -0.256, DSI-average stress = -0.208, DSI-total events = 0.007). Multivariate skewness was also reduced but remains significantly different from normal (skewness = 15.95, $p < .001$) and multivariate kurtosis becomes significantly different from normal (kurtosis = -14.27, $p < .001$). Transformed variables are used in further analyses, but the deviation from assumptions of normality is noted.

Social cognitive abilities were assessed via two emotion perception tasks: the Penn Emotion Recognition (ER-40, (Gur et al., 2002)) and the Penn Emotion Discrimination task (PED, (Erwin et al., 1992)). The ER-40 presents 40 static images of faces expressing one of four emotions: happiness, sadness, anger, fear, as well as a neutral expression. Participants are asked to select the emotion being expressed from a list of the five emotional states. Stimuli vary in the intensity of the expression and in gender and race of the models used. Total accuracy was used as the variable of interest. On the PED, participants are instructed to differentiate the intensity of the emotion expressed for two side-by-side photos of the same actor portraying the same emotion. Total accuracy was used as the variable of interest. Additional social cognition tasks were collected, including The Awareness of Social Inference Test (TASIT, (McDonald, Flanagan, Rollins, & Kinch, 2003)) and the Relationships Across Domains task (RAD, (Sergi et al., 2009)).

The TASIT assesses theory of mind by showing video clips of various social interactions and asking participants questions about the beliefs, intentions, and meaning of the speakers. On the RAD task, participants read vignettes representing different relationship models and answer questions about possible future interactions within the relationship. Total accuracy was used as the variable of interest for both TASIT and RAD. Each of the social cognition variables were found to be negatively skewed (coefficients of skewness: ER40 = -0.906, PED = -0.564, TASIT = -0.981, RAD = -0.583). Mardia's test revealed that these variables displayed significant multivariate skewness and kurtosis (skewness = 197.3, $p < .001$, kurtosis = -4.23, $p < .001$). Each variable was thus transformed by finding its square and then standardizing the squared variable. This transformation improved univariate skewness (coefficients of skewness: ER40 = -0.584, PED = 0.108, TASIT = -0.604, RAD = -0.166) and multivariate skewness and kurtosis (skewness = 59.37, $p < .001$; kurtosis = -1.12, $p = .26$). Transformed variables were used in following analyses, but continued violations of multivariate normality assumptions are noted.

Neurocognitive functioning was assessed using the MATRICS Consensus Cognitive Battery (MCCB, (Nuechterlein et al., 2008)), administered by trained graduate students. Neurocognitive measures relevant to this study are Spatial Span (SS) and Letter-Number Span (LNS), taken from the Wechsler Memory Scale, which measure working memory, and Category Fluency: Animal Naming and the Neuropsychological Assessment Battery: Mazes, each of which taps into aspects of executive functioning, such as monitoring and inhibition (Category Fluency) and planning and organization (Mazes). All neurocognitive measures were transformed into *T* scores, adjusting for age and sex, prior to analyses. Of note, adult and adolescent subjects were normed separately as the MCCB normative sample consisted of adult participants (Kern et al., 2008). Each of these variables was determined to be approximately symmetrically distributed

(coefficients of skewness: SS = -0.307, LNS = -0.292, Fluency = 0.120, Mazes = -0.206). Multivariate skewness and kurtosis were significantly different from a normal distribution (skewness = 13.23, $p < .001$; kurtosis = 3.02, $p = .003$). Data were not further transformed before being entered into following analyses.

Analytic Plan

To evaluate Hypothesis 1, the possible mediating roles of affective and social difficulties and neurocognitive abilities, path analyses were estimated using the *lavaan* package version 0.6-15 in R version 4.0.2. Initially, four latent variables were estimated: 1) an internalizing factor, estimated from CDSS, SAS, SIAS, and DSI scores, 2) a socioemotional factor, estimated from ER-40, PED, TASIT, and RAD accuracy, 3) a working memory factor, estimated from SS and LNS scores, and 4) an executive functioning model, estimated from Category Fluency and Mazes scores. These factors were evaluated using confirmatory factor analysis (CFA) and adjusted as indicated to better fit the data. Estimated factor models were tested against one another using a Chi-square goodness-of-fit test to determine the best fitting factor to use in analyses. Current social and role functioning were both entered as observed variables in the path models. Positive and Negative symptoms were also estimated as latent factors using the items from the SOPS. SOPS items were initially fit as continuous, rather than ordinal, variables. The Positive Symptom factor was initially estimated as a single factor, following previous analyses of the NAPLS2 dataset (Calkins et al., 2021). Three models were estimated for Negative symptoms: a single factor, a two-factor solution following a previous factor analysis of the SIPS/SOPS that separates N5 and N6 into a separate "Deteriorated Thought Process" factor (Tso et al., 2017), and a two-factor solution that mimics the two-factor structure of negative symptoms in schizophrenia (Avolition/Apathy and Diminished Expression) (Blanchard & Cohen, 2006; Strauss et al., 2018)

and previously reported in a CHR sample (Modinos et al., 2019). The Avolition/Apathy factor will be estimated from N1, N2, and N6 and Diminished Expression from N3, N4, and N5. These models were tested against each other to determine the one that best fits the data. Each of the latent factors were specified and evaluated within the full (CHR and TD) baseline sample, with path analyses utilizing the CHR sample and outcome variables measured at 6-month follow-up. All models containing continuous variables were estimated using maximum likelihood, and missing data was handled using maximum likelihood, such that available data could be used to estimate factor loadings and covariances. Models run with ordinal data were estimated using diagonal weighted least squares, with missing data excluded listwise.

See Figure 3.1 for a representation of a path model from discrimination to outcome group through these latent factors (Hypothesis 1). Discrimination status and all covariates will be entered into the model as observed variables.

For Hypothesis 2, functional connectivity alterations identified in Study 2 will be evaluated as additional mediators for the relationship between discrimination and outcome. Age significantly moderated the effect of discrimination on connectivity between the Frontoparietal (FPN) and Limbic networks, and quadratic age significantly moderated the connectivity between the FPN and Ventral Attention network (VAN). In these models, squared age and

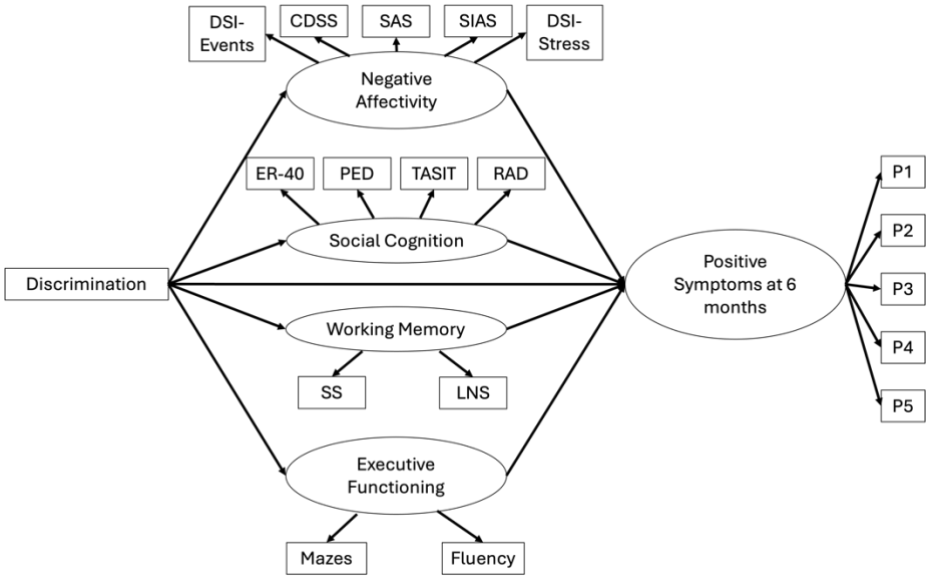


Figure 4.1 Proposed path model predicting positive symptoms at follow-up from perceived discrimination, via four simultaneous mediators. Covariates not pictured.

both age by discrimination interaction terms will additionally be entered as predictors of the mediators and outcome variables. Each model will be estimated in individuals reported no recent racial/ethnic discrimination and in individuals who did report discrimination. Selected paths will be tested between groups using Wald's test. Two path models will be estimated for each outcome variable: 1) with observed functional connectivity metrics as a simultaneous mediator of the association between discrimination and outcomes and 2) with functional connectivity as a sequential mediator, preceding mediators identified in analyses for Hypotheses 1. Prior to entry into path analyses, standardized correlation coefficients for the association between the Frontoparietal and Ventral Attention networks and between the Frontoparietal and Limbic networks were residualized on study site to reduce variability induced by different scanners across sites.

RESULTS

Model Specification

Negative Affectivity

Scores on the CDSS, SAS, SIAS, and both total number of stressful events and average stress from daily stressors were entered into a confirmatory factor analysis. The fit of the single factor model was adequate (CFI = 0.970, TLI = 0.940, RMSEA = 0.116, SRMR = 0.038). However, residual correlations suggested a possible two-factor solution would better fit the data. A two-factor model of Internalizing Symptoms (CDSS, SAS, and SIAS) and Stress (average stress and number of stressful events) was found to have good fit to the data (CFI = 0.991, TLI = 0.977, RMSEA = 0.071, SRMR = 0.019). A direct test of these models indicated that the two-factor model explained the data significantly better than the one-factor model (Chi-square

difference = 40.71, $p < .001$). The two factors were then entered separately into path analyses below.

Variable	Single Factor	Internalizing Factor	Stress Factor
CDSS	0.749	0.755	
SAS	0.868	0.869	
SIAS	0.807	0.813	
DSI-Average Stress	0.729		0.854
DSI – Total Events	0.505		0.566

Table 4.1. Factor loadings for negative affectivity variables in a single and two factor model. CDSS, Calgary Depression Scale for Schizophrenia; SAS, Self-Report Anxiety Scale; SIAS, Social Interaction Anxiety Scale; DSI, Daily Stress Inventory.

Social Cognition

Among ER-40 data, individuals with 50% accuracy or below were determined to be outliers. These 5 individuals were removed from analyses. ER-40, EDF, TASIT, and RAD scores were entered into a one-factor CFA. This model was shown to fit well (CFI = 0.990, TLI = 0.969, RMSEA = 0.055, SRMR = 0.016). A two-factor model was also estimated, separating the social perception (ER-40 and EDF) and social inference (TASIT and RAD) tasks. This two-factor model did not significantly improve the fit of the data (Chi-square difference = 0.792, $p = .374$), so a one-factor model was used in any following analyses.

Variable	Single factor model	Social Perception Factor	Social Inference Factor
ER40	0.339	0.358	
PED	0.491	0.526	
TASIT	0.733		0.733
RAD	0.739		0.742

Table 4.2. Factor loadings for social cognitive variables in a single and two factor model. ER40, Penn Emotion Recognition task; PED, Penn Emotion Discrimination task; TASIT, The Awareness of Social Inference Task; RAD, Relationships Across Domains task.

Working Memory and Executive Functioning

Following the model used in Study 1, a two-factor model of cognition, with Working Memory (observed variables: LNS and SS scores) and Executive Functioning (Mazes, Fluency) was initially estimated. Model fit was adequate (CFI = 0.966, TLI = 0.794, RMSEA = 0.166,

SRMR = 0.029). A single factor model was also estimated, but the single factor model fit the data significantly less well (Chi-square difference = 11.947, $p < .001$). The two-factor model was used in following analyses.

Variable	Single factor	Working Memory Factor	Executive Functioning Factor
SS	0.6889	0.699	
LNS	0.732	0.750	
Fluency	0.562		0.618
Mazes	0.539		0.593

Table 4.3. Factor loadings for neurocognition variables in a single and two factor model. SS, Spatial Span; LNS, Letter-Number Sequencing.

Outcomes

The CFA model with each Positive SOPS item entered into a single factor fit the data fairly well (CFI = 0.960, TLI = 0.920, RMSEA = 0.106, SRMR = 0.039). The dominant residual covariance was found between P3 – Grandiose Ideas and N5 – Disorganized Communication, so a two-factor model separating these items into a separate variable was estimated (CFI = 0.979, TLI = 0.948, RMSEA = 0.085, SRMR = 0.026). This two-factor model fit the data significantly better (Chi-square difference = 29.5, $p < .001$). Due to difficulty fitting the two-factor model in later analyses (see below), a CFA was also performed treating the Positive SOPS items as ordinal variables. The two-factor model of ordinal variables also fit the model well (CFI = 0.997, TLI = 0.992, RMSEA = 0.057, SRMR = 0.033).

Item	Single Factor	Factor 1 – Continuous	Factor 2 - Continuous	Factor 1 – Ordinal	Factor 2 – Ordinal
P1 – Unusual Thought Content	0.886	0.892		0.889	
P2 - Suspiciousness	0.689	0.685		0.702	
P3 – Grandiose Ideas	0.338		0.482		0.562
P4 – Perceptual Abnormalities	0.667	0.670		0.643	
P5 – Disorganized Communication	0.545		0.693		0.747

Table 4.4. Factor loadings for positive SOPS items in a single and two-factor model treated as continuous and a two-factor ordinal model.

Multiple CFAs were performed for the negative symptoms data, given empirical and theoretical work suggesting a two-factor structure to negative symptoms (Avolition-Apathy and Diminished Expression). First, a single-factor model was estimated, which fit the 6 Negative SOPS items adequately well (CFI = 0.889, TLI = 0.815, RMSEA = 0.147, SRMR = 0.051). Following an exploratory factor analysis performed on all SOPS items (Tso et al., 2017) items N1-N4 (Social Isolation, Avolition, Decreased Emotional Expression, and Decreased Experience of Emotion and Self) were placed into one factor, and items N5 and N6 (Decreased Ideational Richness and Deterioration of Role Functioning) were placed on a separate factor. This two-factor model did not improve upon the fit of the data (Chi-square difference = 1.352, $p = .245$). A two-factor model based on the theoretical structure of negative symptoms was estimated, with items N1, N2, and N6 as the Anhedonia/Apathy factor and N3, N4, and N5 as the Diminished Expression factor. This two-factor model was somewhat improved across fit indices (CFI = 0.931, TLI = 0.871, RMSEA = 0.123, SRMR = 0.046). This model is also significantly better fitting than the one factor model (Chi-square difference = 75.63, $p < .001$). This two-factor model was re-estimated with SOPS items entered as ordinal variables. This model also had fair fit to the data (CFI = 0.988, TLI = 0.977, RMSEA = 0.095, SRMR = 0.050).

Item	Single Factor	Model 1 – Negative Factor	Model 1 – Disorganization Factor	Model 2 – Avolition-Apathy	Model 2 – Diminished Expression
N1 – Social Anhedonia	0.663	0.661		0.624	
N2 – Avolition	0.790	0.790		0.847	
N3 – Expression of Emotion	0.601	0.600			0.693
N4 – Experience of Emotion and Self	0.610	0.608			0.689
N5 – Ideational Richness	0.428		0.415		0.459

N6 – Occupational Functioning	0.683		0.654	0.772	

Table 4.5. Factor loadings for negative SOPS items in a single and two factor model. Items treated as continuous.

Item Ordinal models	Single Factor	Model 2 – Avolition-Apathy	Model 2 – Diminished Expression
N1 – Social Anhedonia	0.701	0.715	
N2 – Avolition	0.830	0.851	
N3 – Expression of Emotion	0.709		0.769
N4 – Experience of Emotion and Self	0.683		0.740
N5 – Ideational Richness	0.501		0.532
N6 – Occupational Functioning	0.756	0.766	

Table 4.6. Factor loadings for negative SOPS items in a single and two factor model. Items treated ordinally.

Path Analyses

In the path model predicting the Positive SOPS factors from recent racial/ethnic discrimination through Internalizing Symptoms, Stress, Social Cognition, Working Memory, and Executive Functioning, the factor loadings for the second SOPS Positive factor were observed to be uneven (factor loadings: P3 = 6.010; P5 = 0.035). A new path model was estimated constraining the factor loadings to be equal between items P3 and P5. In this model, discrimination significantly predicted the Internalizing Symptoms (ß = 0.090, p = .042) and Stress latent variables (ß = 0.103, p = .025) above the effects of age, sex, racial/ethnic minority status, and parental education. Discrimination did not predict Social Cognition (ß = -0.041, p = .359), Working Memory (ß = 0.015, p = .747), or Executive Functioning factors (ß = 0.008, p = .881). Internalizing Symptoms predicted the first Positive factor at six-month follow-up above the effects of the covariates or other mediators (ß = 0.410, p = .021). No other mediator predicted the first Positive factor ($ß_{Stress}$ = -0.184, p = .278; $ß_{SC}$ = -0.092, p = .520; $ß_{WM}$ = -0.332, p = .284; $ß_{EF}$ = 0.515, p = .111). Total effect from discrimination to the first Positive factor is not significant (ß = 0.042, $CI_{95\%}$: [-0.309, 0.428]). No mediator significantly predicted the second

Positive factor above the effects of the covariates or other mediators ($ß_{IS}$ = -0.338, p = .197; $ß_{Stress}$ = 0.310, p = .235; $ß_{SC}$ = -0.312, p = .133; $ß_{WM}$ = 0.315, p = .432; $ß_{EF}$ = -0.154, p = .693). Total effect from discrimination to the second Positive factor is not significant (ß = 0.086, $CI_{95\%}$: [-0.104, 0.274]).

Path models were then estimated predicting both factors of Negative symptoms. Initial models were estimated while treating SOPS items continuously. Recent racial/ethnic discrimination predicted the Stress factor (ß = 0.107, p = .021). The Internalizing symptom factor predicted both Avolition-Apathy (ß = 0.520, p = .004) and Diminished Expression (ß = 0.632, p = .003) factors of SOPS Negative Symptoms. The Stress factor also negatively predicted Diminished Expression (ß = -0.424, p = .050). No other mediator predicted Avolition-Apathy ($ß_{Stress}$ = -0.210, p = .182; $ß_{SC}$ = -0.026, p = .842; $ß_{WM}$ = -0.165, p = .618; $ß_{EF}$ = 0.115, p = .651) or Diminished Expression ($ß_{SC}$ = -0.092, p = .555; $ß_{WM}$ = 0.126, p = .693; $ß_{EF}$ = -0.147, p = .631) above the effects of the covariates or other mediators. Total effect from discrimination to Anhedonia-Avolition is not significant (ß = 0.019, $CI_{95\%}$: [-0.167, 0.175]). The total effect of discrimination on Diminished Expression is not significant (ß = -0.077, $CI_{95\%}$: [-0.332, 0.166]). Indirect effects from recent racial/ethnic discrimination to Avolition-Apathy were nonsignificant ($ß_{Internalizing}$ = 0.068, $CI_{95\%}$: [-0.016, 0.224]; $ß_{Stress}$ = -0.037, $CI_{95\%}$: [-0.207, 0.022]; $ß_{SC}$ = 0.002, $CI_{95\%}$: [-0.035, 0.039]; $ß_{WM}$ = -0.006, $CI_{95\%}$: [-0.119, 0.068]; $ß_{EF}$ = -0.004, $CI_{95\%}$: [-0.124, 0.089]). The indirect effects from recent racial/ethnic discrimination to Avolition-Apathy were also nonsignificant ($ß_{Internalizing}$ = 0.111, $CI_{95\%}$: [-0.015, 0.410]; $ß_{Stress}$ = -0.100, $CI_{95\%}$: [-0.465, 0.009]; $ß_{SC}$ = 0.008, $CI_{95\%}$: [-0.056, 0.080]; $ß_{WM}$ = 0.006, $CI_{95\%}$: [-0.125, 0.208]; $ß_{EF}$ = 0.007, $CI_{95\%}$: [-0.160, 0.205]).

Separate path analyses were estimated predicting role functioning and social functioning at follow-up, with sex, age, racial/ethnic minority status, and maternal and paternal education level entered as covariates. Initial models for social and role functioning were estimated while treating functioning scores as continuous. The Internalizing symptom factor negatively predicted social functioning at follow-up (ß = -0.493, p = .003) and role functioning at follow-up (ß = -0.340, p = .024). No other hypothesized mediators significantly predicted social functioning ($ß_{Stress}$ = 0.283, p = .008; $ß_{SC}$ = 0.123, p = .339; $ß_{WM}$ = 0.393, p = .154; $ß_{EF}$ = -0.279, p = .284) or role functioning ($ß_{Stress}$ = 0.200, p = .253; $ß_{SC}$ = 0.139, p = .253; $ß_{WM}$ = 0.294, p = .237; $ß_{EF}$ = -0.137, p = .561) above the effect of the covariates and other potential mediators.

fcMRI models

To determine if the interaction effects of discrimination on the age and functional connectivity association patterns discovered in Study 2 may influence symptom and functioning outcomes for CHR youth, a series of multigroup path analyses were performed for each outcome model, with the binary discrimination variable representing the groupings. An initial model was estimated, allowing the two groups to vary freely for all model parameters. Separate models were then estimated, iteratively constraining paths of interest. Wald's test was used to estimate differences in the specified paths between the two groups. In the models predicting Positive symptom factors at follow-up, Wald's test revealed a significant difference between groups predicting the first Positive factor from age and age-squared through FPN-VAN connectivity (W = 14.20, p = .014). When testing paths individually, only the path from age-squared to FPN-VAN connectivity was significantly different between the two groups (W = 8.57, p = .003). The effect of group on the direct effects of age was significant, but the moderation of the effect of age-squared was nonsignificant (W_{age} = 4.50, p = .034; $W_{age\text{-}squared}$ = 1.88, p = .170). There was no

group difference in the path predicting the first Positive factor from FPN-VAN connectivity (W = 1.03, p = .310). The model testing group moderation of the paths predicting the second Positive factor through FPN-VAN connectivity was nonsignificant (W = 9.89, p = .079).

When evaluating group differences in the paths predicting positive symptoms from age and age-squared through FPN-Limbic connectivity, the omnibus test of all paths predicting the first Positive factor was significant (W = 14.79, p = .011). When testing paths individually, the paths from age and from age-squared to FPN-Limbic connectivity were significantly different between the two groups (W_{age} = 7.62, p = .006; $W_{age\text{-}squared}$ = 6.32, p = .012). There was no group difference in the path predicting the first Positive factor from FPN-Limbic connectivity (W = 1.68, p = .200). The omnibus test of all paths predicting the second Positive factor from age and age-squared through FPN-Limbic connectivity was also significant (W = 12.75, p = .026). However, this may have been driven by the moderation of racial/ethnic discrimination on age and age-squared associations with connectivity. The effects of group on the direct effects of age and age-squared were nonsignificant (W_{age} = 0.033, p = .855; $W_{age\text{-}squared}$ = 0.69, p = .408), and there was no group difference in the path predicting the second Positive factor from FPN-Limbic connectivity (W = 1.53, p = .217). Across these models, recent experiences of racial/ethnic discrimination did not moderate the effects of age or functional connectivity on positive psychotic symptoms.

In the models predicting Negative symptom factors at follow-up, Wald's test revealed that the group moderation of paths predicting Avolition-Apathy from age and age-squared through FPN-VAN connectivity was not significant (W = 9.06, p = .107). The model testing group moderation of the paths predicting Diminished Expression factor through FPN-VAN connectivity was significant (W = 11.68, p = .039). However, this may be driven by moderation effects of

recent racial/ethnic discrimination on the relationships between age and age-squared with connectivity, as the direct effects of age and age squared on Diminished Expression were not moderated by discrimination (W_{age} = 2.38, p = .123; $W_{age\text{-}squared}$ = 0.032, p = .857), nor was the relationship between FPN-VAN connectivity and Diminished Expression (W = 0.17, p = ,676).

When evaluating group differences in the paths predicting negative symptoms from age and age-squared through FPN-Limbic connectivity, the omnibus test of all paths predicting Avolition-Apathy was significant (W = 11.11, p = .015). When testing paths individually, the paths from age and from age-squared to FPN-Limbic connectivity were significantly moderated by discrimination group, as above (W_{age} = 9.00, p = .003; $W_{age\text{-}squared}$ = 7.00, p = .008). The group difference in the path predicting Avolition-Apathy from FPN-Limbic connectivity was nonsignificant (W = 3.24, p = .072).

The omnibus test of all paths predicting Diminished Expression from age and age-squared through FPN-Limbic connectivity was also significant (W = 13.25, p = .021). However, this may have been driven by the moderation of discrimination on age and age-squared associations with connectivity. The effects of group on the direct effects of age and age-squared on Diminished Expression were nonsignificant (W_{age} = 2.38, p = .123; $W_{age\text{-}squared}$ = 0.032, p = .857), and there was no group difference in the path predicting Diminished Expression from FPN-Limbic connectivity (W = 0.012, p = .913). Among CHR individuals, while recent racial/ethnic discrimination moderates the associations between age and frontoparietal connectivity, there is no moderation of indirect effects of age on negative symptoms through functional connectivity.

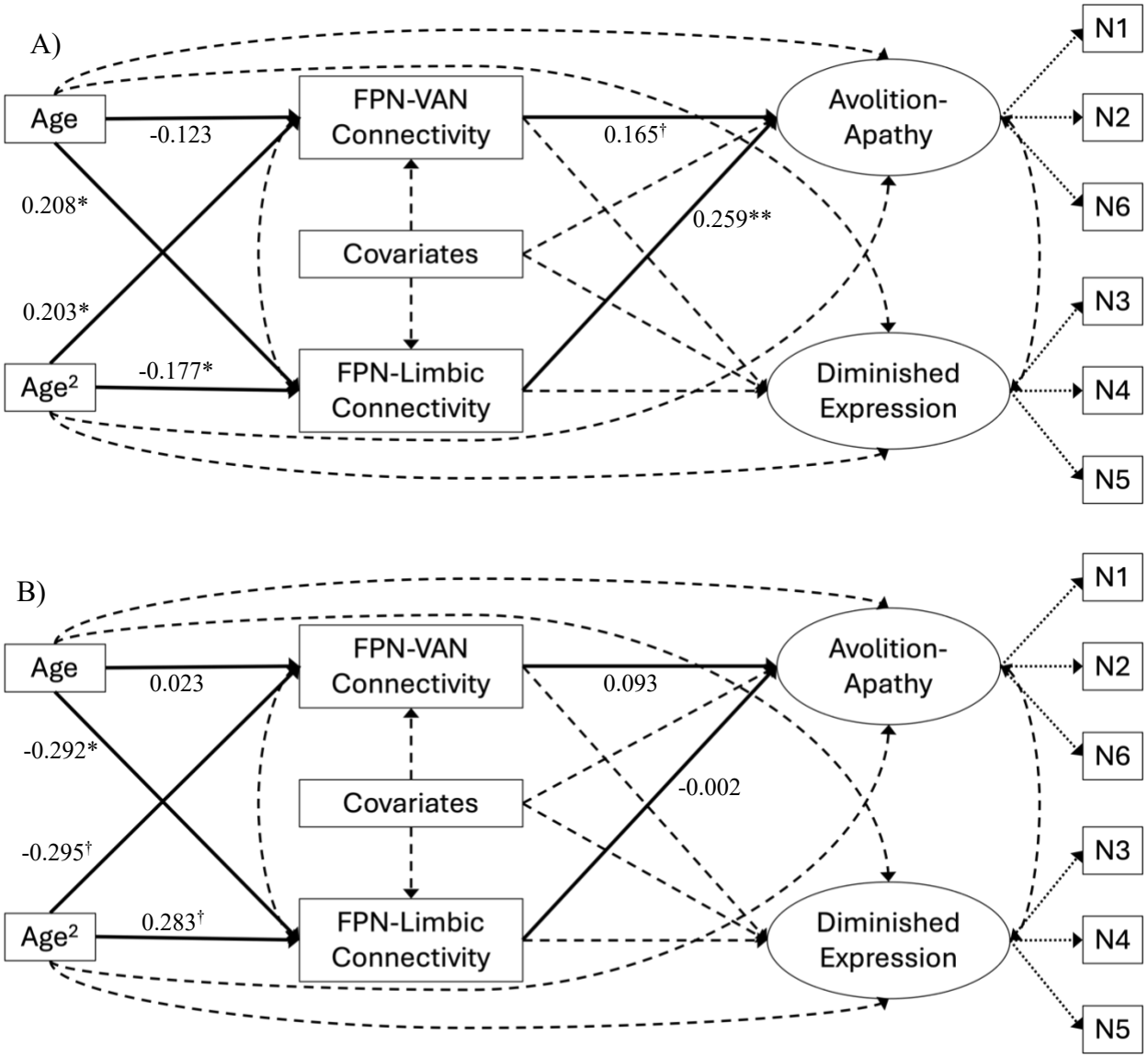


Figure 4.2. Illustration of the moderated mediation model predicting negative symptom factors from age through functional connectivity by reported discrimination. Solid lines indicate paths tested in an omnibus Wald test between groups. A) Path model with individuals reporting no discrimination. B) Path model with individuals reporting discrimination. Solid lines represent paths tested against between a freed parameter and constrained parameter model. Standardized regression coefficients when path is allowed to vary are reported; †, $p < .10$; *, $p < .05$; **, $p < 0.01$.

In the path models predicting social functioning symptoms, the omnibus Wald test comparing groups on paths predicting social functioning at six-month follow-up from age and

age-squared through FPN-VAN connectivity was significant (W = 13.87, p = .016). The effect of age on FPN-VAN connectivity did not differ by group (W = 0.901, p = .342), while the effect of age-squared on FPN-VAN connectivity was moderated by discrimination group (W = 8.66, p = .003). The effect of FPN-VAN connectivity was slightly, but not significantly different between groups (W = 3.66, p = .056). In the group reporting no discrimination, FPN-VAN connectivity slightly negatively predicted social functioning (β = -0.181, p = .023). In the group reporting recent racial/ethnic discrimination, FPN-VAN connectivity did not predict social functioning (β = .121, p = .382). There was no direct effect of age or age-squared in the group reporting no discrimination (β_{age} = -0.016, $CI_{95\%}$ = [-0.063, 0.027]; $\beta_{age\text{-}squared}$ = -0.001, $CI_{95\%}$ = [-0.009, 0.008]), or in the group reporting recent discrimination (β_{age} = -0.018, $CI_{95\%}$ = [-0.099, 0.056]; $\beta_{age\text{-}squared}$ = -0.006, $CI_{95\%}$ = [-0.016, 0.004]). The indirect effect of age-squared on social functioning through FPN-VAN connectivity was not significant in the group reported no discrimination (β = -0.003, $CI_{95\%}$ = [-0.007, 0.0002]), or in the group reporting discrimination (β = -0.001, $CI_{95\%}$ = [-0.007, 0.003]).

The omnibus Wald test comparing groups on paths predicting social functioning at six-month follow-up from age and age-squared through FPN-Limbic connectivity was significant (W = 14.49, p = .013). The effect of age on FPN-Limbic connectivity differed by group (W = 8.41, p = .004), as did the effect of age-squared on FPN-Limbic connectivity (W = 5.89, p = .015). The path predicting social functioning from FPN-Limbic connectivity differed significantly between groups (W = 3.88, p = .049). In the group reporting no discrimination, FPN-Limbic connectivity negatively predicted social functioning (β = -0.250, p = .001). In the group reporting recent racial/ethnic discrimination, FPN-Limbic connectivity did not predict social functioning (β = .031, p = .833). The indirect effect of age on social functioning through

FPN-Limbic connectivity was significant in the group reported no discrimination (β = -0.002, $CI_{95\%}$ = [-0.044, -0.003]), but was not significant in the group reporting recent discrimination (β = -0.003, $CI_{95\%}$ = [-0.004, 0.005]).

In the path models predicting role functioning symptoms, the omnibus Wald test on paths predicting role functioning at six-month follow-up through FPN-VAN connectivity was significant (W= 18.28, p = .003), indicating a difference between discrimination exposure groups. The effect of age on FPN-VAN connectivity did not differ by group (W = 0.76, p = .383), while the effect of age-squared on FPN-VAN connectivity did differ (W = 7.74, p = .005). The path predicting role functioning from FPN-VAN connectivity was moderated by group (W = 8.92, p = .003). In the group reporting no discrimination, FPN-VAN connectivity negatively predicted role functioning (β = -0.162, p = .050). In the group reporting recent racial/ethnic discrimination, FPN-VAN connectivity significantly predicted role functioning (β = .274, p = .024). The total effect of age on role functioning is significant in the group reporting recent discrimination (β = 0.078, $CI_{95\%}$ = [0.009, 0.153]), but was not significant in the group reporting no discrimination (β = 0.009, $CI_{95\%}$ = [-0.049, 0.069]). The total effect of age-squared on role functioning was not significant in either group ($\beta_{no\_discrimination}$ = 0.002, $CI_{95\%}$ = [-0.011, 0.014]; $\beta_{discrimination}$ = -0.007, $CI_{95\%}$ = [-0.019, 0.002]). The indirect effect of age on role functioning through FPN-VAN connectivity was not significant in either group ($\beta_{no\_discrimination}$ = 0.010, $CI_{95\%}$ = [-0.007, 0.036]; $\beta_{discrimination}$ = 0.002, $CI_{95\%}$ = [-0.038, 0.038]). The indirect effect of age-squared on role functioning through FPN-VAN connectivity was also not significant in either group ($\beta_{no\_discrimination}$ = -0.003, $CI_{95\%}$ = [-0.009, 0.001]; $\beta_{discrimination}$ = -0.003, $CI_{95\%}$ = [-0.012, 0.001]).

The omnibus Wald test on paths predicting role functioning at six-month follow-up through FPN-Limbic connectivity was significant (W= 16.05, p = .006). The effect of age on FPN-Limbic connectivity differed by group (W = 9.12, p = .003), as did the effect of age-squared on FPN-Limbic connectivity (W = 6.56, p = .010). The path predicting role functioning from FPN-Limbic connectivity differed significantly between groups (W = 5.39, p = .020). In the group reporting no discrimination, FPN-Limbic connectivity negatively predicted role functioning (β = -0.238, p = .003). In the group reporting recent racial/ethnic discrimination, FPN-Limbic connectivity did not predict social functioning (β = .053, p = .688). The indirect effect from age to role functioning through FPN-Limbic connectivity is significant in the group reporting no discrimination (β = -0.030, $CI_{95\%}$ = [-0.067, -0.006]), but not in the group reporting no discrimination (β = -0.005, $CI_{95\%}$ = [-0.049, 0.029]). Across models predicting functioning, there is a direct association between age and functioning outcomes among CHR individuals reporting no recent racial/ethnic discrimination. This effect is mediated by connectivity between the frontoparietal and limbic networks. Among CHR individuals reporting recent discrimination, no such direct or indirect effect was found, but connectivity between the frontoparietal and ventral attention networks was found to be positively predictive of role and social functioning outcomes.

Since no psychological variable significantly mediated the relationship between recent racial/ethnic discrimination and symptom or functioning outcomes, no serial mediation model was estimated.

DISCUSSION

This study was the first to integrate neurobiological mechanisms and psychological variables into a model of psychosis risk following discrimination. In a series of models

estimating subclinical psychosis symptoms as well as functioning outcome variables within a sample of individuals identified as being at clinical high risk for psychotic disorders, we detected failed to detect direct effects of recent racial/ethnic discrimination on symptom or functioning outcomes. We also did not find indirect effects of racial/ethnic discrimination on outcomes via a variety of putative affective and cognitive mechanisms.

When investigating the role of functional connectivity in the relationship between recent racial/ethnic discrimination and outcomes, several models were estimated to determine differences between individuals who did and did not report discrimination on the relationships among age, connectivity, and symptom and functional outcomes. Discrimination status did not impact the models predicting positive psychotic symptom factors, but there was significant moderation of the models estimating negative psychotic symptoms and both role and social functioning from age, through functional connectivity of the frontoparietal network.

While the test of moderation was not significant, among individuals identified as CHR who reported no recent experiences of racial/ethnic discrimination at baseline, adult participants, relative to early adolescent participants, tended to have a stronger degree of connectivity between their FPN and Limbic networks at baseline, which, in turn, led to more pronounced negative symptoms, specifically in the domain of Anhedonia/Avolition. For participants who did report recent racial/ethnic discrimination at baseline, relative to younger participants, adults identified at CHR demonstrated a lower degree of connectivity between the FPN and Limbic networks at baseline, but no relationship was detected between FPN-Limbic connectivity and Anhedonia-Avolition among these participants.

While individuals with schizophrenia generally display intact hedonic experience, prior work has shown that patients struggle with anticipation of pleasure and appropriate learning

related to pleasurable outcomes (Gard, Kring, Gard, Horan, & Green, 2007; Strauss & Gold, 2012). These processes are believed to involve prefrontal and limbic regions in order to recognize a reward, update reward valuation of a stimulus or event, and retrieve that reward valuation in order to direct appropriate behavior (i.e., effort toward a reward, engaging in a pleasurable activity) (Dowd & Barch, 2012; Liang, Wu, Hanxiaoran, Greenshaw, & Li, 2022; Wang et al., 2015). Reward learning and other hedonic processes develop during adolescence, along with internetwork connectivity (Davidow et al., 2016; Galván, 2010; Walker et al., 2017). Abnormal development of fronto-limbic circuitry during adolescence may contribute to worsened negative symptoms among individuals identified as at risk for a psychotic disorder. Individuals at risk for a psychotic disorder who report recent racial/ethnic discrimination display a distinct age-related pattern of FPN-Limbic network connectivity, as connectivity in these individuals appears to decrease with age. Further, since FPN-Limbic connectivity is not associated with Avolition-Anhedonia in this group, the above relationship among age, functional connectivity, and negative symptoms and/or hedonics does not seem to hold among individuals who endorse discrimination.

While the hedonic processes of anhedonia as a negative symptom of psychosis are believed to be distinct from the hedonics of anhedonia in mood disorders, the experience of anhedonia is a transdiagnostic symptom that is present in psychotic disorders, depressive disorders, and post-traumatic stress disorder (American Psychiatric Association, 2013). Additionally, mood disorders and PTSD are highly comorbid with each other (O'Donnell, Creamer, & Pattison, 2004) and psychotic disorders (Buckley, Miller, Lehrer, & Castle, 2009; Shevlin, Dorahy, & Adamson, 2007). Further, experiences of racial discrimination have been linked to development of both major depressive disorder (Hudson, Neighbors, Geronimus, &

Jackson, 2016; Noh & Kaspar, 2003) and PTSD (Bird et al., 2021; Kirkinis, Pieterse, Martin, Agiliga, & Brownell, 2021). Although FPN-Limbic network connectivity was not found to mediate the association between discrimination and Avolition-Anhedonia, it is possible that this may be a transdiagnostic mechanism contributing to anhedonia and avolition across disorder categories.

Similarly to the results of models predicting Negative symptoms, for individuals at CHR reported no recent discrimination, FPN-Limbic network connectivity increased with age and was associated with poorer social and role functioning at follow-up. This pattern of results is consistent with the model predicting negative symptoms as increased negative symptoms are associated with and predictive of poor functioning outcomes (Strassnig et al., 2015; Ventura et al., 2015). In individuals who reported discrimination, FPN-Limbic connectivity was not associated with social or role functioning outcomes. Alternatively, FPN-VAN connectivity was positively associated with social and role functioning among those reporting discrimination, across age. Connectivity between the frontoparietal and ventral attention networks appears to serve as a protective factor among individuals at risk for psychosis who report discrimination. While the directionality of this connection is unknown, a stronger relationship between these two networks may facilitate task orientation, which is believed to be a role of the VAN and impaired in individuals with schizophrenia (Menon & Uddin, 2010; Palaniyappan & Liddle, 2012; Sridharan, Levitin, & Menon, 2008). Alternatively, increased connectivity between FPN-VAN networks may represent top-down regulation of VAN activity. Aberrant salience attribution due to dysfunction of the salience network is theorized to contribute to the emergence of certain psychotic symptoms like auditory hallucinations (Mallikarjun et al., 2018; Palaniyappan & Liddle, 2012). Ventral attention and frontoparietal regions are also believed to be involved in

automatic and effortful regulation of emotion (Bertocci et al., 2023; Morawetz et al., 2020), so FPN-VAN connectivity may be related to adaptive coping strategies that are protective against factors contributing to poor functioning among individuals who have experienced discrimination. This offers a potential focus for further research developing interventions and prevention efforts for individuals exposed to racism and other forms of discriminatory stress.

Despite uncovering the role of FPN-Limbic and FPN-VAN connectivity in predicting outcomes among CHR with and without experiences of discrimination, we failed to find supporting evidence for our hypotheses that social cognitive and neurocognitive variables would mediate the relationship between discrimination and outcomes or our hypothesis that internalizing symptoms and stress would mediate the effect of discrimination on negative symptoms and functioning outcomes. Some limitations of the current study may have contributed to the lack of evidence for these hypotheses. As previously discussed, the measure of discrimination utilized in this study does not capture the form an act of discrimination takes, the frequency of discriminatory experiences, or the perceived impact of such experiences (e.g., loss of a job or educational opportunity, physical injury, ostracism). Therefore, the variability in experiences and the potential effect of form or frequency of discrimination on mediator variables and outcomes are lost. Similarly, while this study focused on the effects of racial/ethnic discrimination, report of other types of discrimination (i.e., based on gender, sexual orientation, etc.) was collected. Individuals who have experienced multiple marginalization may be at greater risk for poor outcomes (Seng, Lopez, Sperlich, Hamama, & Meldrum, 2012) and likely demonstrate compounded impacts on affective and cognitive disturbances as well as symptom and functioning outcomes.

Although outcome data was collected at follow-up, reported discrimination and all

mediator data, including functional connectivity scans, were collected at the baseline visit. Therefore, there is no clear temporal precedence of the predictor variable (experiences of discrimination) and the mediator variables. Therefore, alternative interpretations of the path models are possible. For example, individuals reporting higher levels of stress may be more likely to endorse an experience of discrimination. Additionally, since no measure of discrimination was captured at the six-month follow-up, experiences of discrimination following the baseline visit, which may have impacted symptom and outcome variables, were unaccounted for.

These results may help better prevention and early intervention efforts for vulnerable ethnic and racial minority youth. For example, cognitive-behavioral therapy (CBT) has been shown to affect cortico-striatal functional connectivity in a fashion associated with improved treatment outcomes in a variety of disorders (Linden, 2006; Roffman, Marci, Glick, Dougherty, & Rauch, 2005). Therefore, CBT may be effective in normalizing functional connectivity patterns seen in youth at risk for psychosis. Further, a variety of psychotropic medications have been shown to have effects on striatal functional connectivity (Linden, 2006; Sarpal et al., 2015), which may then be investigated as treatments for reducing negative effects of discrimination.

This study extends previous research on outcomes for CHR youth by modeling predictors not just for symptom outcomes or conversion to full disorder but also social and functional outcomes. Although heterogeneity in functional outcomes have been described in the past (Allswede et al., 2020) few studies have investigated how social and neurobiological risk factors and mechanisms contribute to functional trajectory and outcome. An additional strength of this study is the focus on developmental effects of discrimination and connectome organization. Because psychotic disorders are viewed as neurodevelopmental in nature (Patel et al., 2021),

understanding the interacting role of social stressors, like discrimination, and brain development is crucial for efforts of early identification and prevention for vulnerable populations.

CHAPTER 5 | GENERAL DISCUSSION

This dissertation was executed to investigate the impact of experiencing discrimination on account of one's race or ethnic background and the links between these experiences and risk for psychotic disorders. To do so, three studies were performed to evaluate the effects of discriminatory experiences on affect, social cognition, and neurocognition, as well as functional brain connectivity, in order to integrate psychological and neurobiological models of stress. Across two samples representing a broad spectrum of subclinical psychosis, these psychological and neurobiological effects were leveraged to predict subclinical psychotic symptoms and functioning for at-risk individuals. Further, the age-ranges of these samples covered the adolescent and young adult periods of development, allowing insight into stages and processes of development that may be particularly vulnerable to the effects of significant stressors like discrimination.

In Study 1, distinct mechanisms linking discrimination to positive and negative subclinical psychotic symptoms were described. Among generally healthy, young adult college students, experiences of discrimination predicted higher levels of both positive psychotic-like experiences (PLEs) and negative PLEs. The association between discrimination and positive PLEs was mediated by self-reported difficulties with behavioral and emotional regulation. Conversely, the effect of discrimination on negative PLEs was mediated through depressive symptoms and self-reported cognitive concerns. These set of findings highlighted the effect of discriminatory stress on predicting both positive and negative subclinical symptoms, but via subtly distinct mechanisms. Further insights were gained into how certain features of discriminatory experiences affect the impact on subclinical symptoms. Experiences of multiple minoritization (i.e., discrimination on the basis of multiple held identities) predicted positive, but

not negative PLEs, while experiencing multiple forms of discrimination was associated with both positive and negative PLEs.

Following models of social defeat and functional dysconnectivity in the pathophysiology of psychotic disorder, Study 2 evaluated the effect of experiences of racial/ethnic discrimination on functional connectivity of the striatum and between large-scale cortical networks. This study, along with Study 3, utilized a community help-seeking sample of adolescents and young adults identified as being at clinical high risk (CHR) for developing a psychotic disorder as well as typically developing (TD) individuals. The analyses in Study 2 did not offer direct support for the social defeat model as an adequate theory for psychosis risk following discrimination, as striatal connectivity was not associated with experiences of discrimination in youth at risk for developing a psychotic disorder or in typically developing youth and young adults, although the internetwork connectivity patterns we detect may be downstream effects of altered dopamine signaling, which requires further study. When considering developmental stage, interesting patterns emerged, providing evidence for the impact of discrimination on brain functioning. Overall, age-related effects echoed existing models of functional connectome development during adolescence (Menon & Uddin, 2010), as connectivity between the striatum and cortical networks was negatively associated with age, and internetwork connectivity was also generally negatively associated with age, as cortical networks tend to become more segregated and specialized as they mature into adulthood (Ernst et al., 2015; Grayson & Fair, 2017). Experiences of discrimination were then found to moderate these age-related connectivity patterns for two pairs of networks. For individuals identified as CHR, connectivity between the frontoparietal network and the ventral attention network was associated with age in a quadratic pattern, decreasing in strength through adolescence into adulthood, then becoming stronger through the

third decade of life. For CHR subjects who did report recent racial/ethnic discrimination, the opposite age-related pattern was observed: connectivity between these networks increased through adolescence before decreasing in strength into young adulthood. Dysconnectivity between the ventral attention network and frontoparietal network has been implicated in aberrant salience models of psychosis (Howes & Nour, 2016; Palaniyappan & Liddle, 2012), but this is the first study to link experiences of discrimination to such patterns. Additionally, connectivity between the frontoparietal network and the limbic network was observed to increase in strength with age from early adolescence to adulthood among individuals at risk for psychosis reporting no racial/ethnic discrimination. Among the CHR youth who did report racial/ethnic discrimination, internetwork connectivity between the frontoparietal and limbic networks was negatively associated with age. Frontoparietal and cortical limbic regions are associated with dopamine-mediated hedonic processes such as representation of reward, reward updating, and control of reward-motivated behavior (Berridge & Kringelbach, 2015; Ferenczi et al., 2016; Sescousse, Redouté, & Dreher, 2010). Structural and functional abnormalities in these regions have been observed across the psychosis spectrum (Kirschner et al., 2021) and are associated with negative symptomatology (Kirschner et al., 2021; Lacerda et al., 2007; Shukla et al., 2019). Functional connectivity patterns for these regions have also been implicated in treatment response for major depressive disorder (Downar et al., 2014), which offers transdiagnostic implications for the effect of discrimination on frontoparietal-limbic connectivity, moderated by age.

The goal of Study 3 was to integrate the model of psychological mechanisms from Study 1 with the neurobiological effects noted in Study 2. Several differences were noted between Studies 1 and 3. Chiefly, Study 3 utilized the same sample as Study 2, which included CHR and

TD youth and young adults. Additionally, mediator and outcome variables were estimated as latent factors containing at least two items or measures, opposed to singular measures in Study 1. In Study 3, Internalizing Symptoms and Stress factors were predictive of the positive symptom factor containing unusual ideation, suspiciousness, and hallucination items. Internalizing Symptoms were also predictive of both negative symptom factors at follow-up and Stress was predictive of the Diminished Expression factor of negative symptoms at follow-up. In Study 1, depressive symptoms positively predicted positive symptoms which was replicated in Study 3. While the CAPE does include items probing for grandiose ideation, which is captures in the second positive factor in Study 3, effects of the model on those items were not estimated in Study 1. No Stress measure was entered as a mediator in Study 1, but the Behavioral Regulation Index of the BRIEF does include items relevant to emotional control and coping skills, which may partially tap into stress. Further, perceived stress, particularly chronic stress, impairs subjective and observed regulatory capabilities (Blair, 2010), so there may be some relationship between these two mediators. Study 3 found no impact of working memory or executive functioning on any symptom or functioning outcome, above the effects of the other mediators. In Study 3, cognition was assessed via a neurocognitive battery, while in Study 1, participants self-reported on their executive functioning difficulties, which likely introduces bias due to self-esteem and insight. Further, college students in a competitive university setting are likely cognitively high functioning and have a biased sample upon which to draw comparisons between their cognitive abilities and those of people around them.

In Study 3, moderated mediation effects were estimated to determine the possible role of age-related trajectories of functional connectivity, altered by experiences of discrimination, on symptom and functioning outcomes. For individuals reporting no recent discrimination,

frontoparietal-limbic connectivity was shown to mediate the relationship between age and both social and role functioning. These effects were not seen in the sample who reported discrimination. Instead, we found that frontoparietal-ventral attention connectivity mediated the relationship between age and role functioning for CHR individuals reporting discrimination. Since this effect was not found in those reporting no discrimination, it may represent a possible compensatory strategy in response to stressors like discrimination. These results open various lines of inquiry into other factors that may mitigate connectivity patterns associated with poorer outcomes as well as those that may support patterns associated with better outcomes.

Taken together, these studies represent the first effort to integrate psychological and neurobiological mechanisms to better understand the impact of discrimination on psychosis risk. Across studies, discrimination is associated, directly or indirectly, with more severe subclinical positive and negative psychotic symptoms and social and role functioning outcomes. Since a large proportion of at-risk individuals are observed to maintain poor functioning and residual symptoms or develop other psychological disorders, even if they do not convert to psychosis, better understanding of the mechanisms that underlie risk factors for symptom development and functioning outcomes is crucial for developing and implementing interventions that can reduce suffering and improve quality of life among vulnerable populations. A variety of pharmaceutical and psychological interventions have been shown to improve mood symptoms and executive functioning difficulties, which may moderate downstream psychotic symptoms and functioning difficulties. Additionally, interventions like mindfulness-based stress reduction have been shown to impact functional connectivity patterns among the ventral attention/salience, frontoparietal, and default networks (Boyd, Lanius, & McKinnon), so similar interventions may be levied to alleviate connectivity patterns associated with poor outcomes. Finally, while such interventions

will be crucial for interrupting the negative effects of discrimination on an individual level, systemic efforts to reduce racism and discrimination are necessary to prevent further harm to vulnerable minoritized communities and address disparities in psychotic illness diagnosis and care.

REFERENCES

Aas, M., Navari, S., Gibbs, A., Mondelli, V., Fisher, H. L., Morgan, C., . . . Zanelli, J. (2012). Is there a link between childhood trauma, cognition, and amygdala and hippocampus volume in first-episode psychosis? *Schizophrenia research, 137*(1-3), 73-79.

Addington, D., Addington, J., & Maticka-Tyndale, E. (1993). Assessing depression in schizophrenia: the Calgary Depression Scale. *The British Journal of Psychiatry, 163*(S22), 39-44.

Addington, J., & Addington, D. (1999). Neurocognitive and social functioning in schizophrenia. *Schizophrenia Bulletin, 25*(1), 173-182.

Addington, J., Cornblatt, B. A., Cadenhead, K. S., Cannon, T. D., McGlashan, T. H., Perkins, D. O., . . . Woods, S. W. (2011). At clinical high risk for psychosis: outcome for nonconverters. *American Journal of Psychiatry, 168*(8), 800-805.

Addington, J., Liu, L., Buchy, L., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., . . . McGlashan, T. H. (2015). North American Prodrome Longitudinal Study (NAPLS 2): The Prodromal Symptoms. *J Nerv Ment Dis, 203*(5), 328-335. doi:10.1097/nmd.0000000000000290

Agnew-Blais, J., & Seidman, L. J. (2013). Neurocognition in youth and young adults under age 30 at familial risk for schizophrenia: a quantitative and qualitative review. *Cognitive neuropsychiatry, 18*(1-2), 44-82.

Akdeniz, C., Tost, H., Streit, F., Haddad, L., Wüst, S., Schäfer, A., . . . Meyer-Lindenberg, A. (2014). Neuroimaging evidence for a role of neural social stress processing in ethnic minority-associated environmental risk. *JAMA Psychiatry, 71*(6), 672-680. doi:10.1001/jamapsychiatry.2014.35

Akdeniz, C., Tost, H., Streit, F., Haddad, L., Wüst, S., Schäfer, A., . . . Meyer-Lindenberg, A. (2014). Neuroimaging evidence for a role of neural social stress processing in ethnic minority–associated environmental risk. *JAMA Psychiatry, 71*(6), 672-680.

Akinhanmi, M. O., Biernacka, J. M., Strakowski, S. M., McElroy, S. L., Balls Berry, J. E., Merikangas, K. R., . . . LeBoyer, M. (2018). Racial disparities in bipolar disorder treatment and research: a call to action. *Bipolar disorders, 20*(6), 506-514.

Alisic, E., Zalta, A. K., Van Wesel, F., Larsen, S. E., Hafstad, G. S., Hassanpour, K., & Smid, G. E. (2014). Rates of post-traumatic stress disorder in trauma-exposed children and adolescents: meta-analysis. *The British Journal of Psychiatry, 204*(5), 335-340.

Allswede, D. M., Addington, J., Bearden, C. E., Cadenhead, K. S., Cornblatt, B. A., Mathalon, D. H., . . . Tsuang, M. T. (2020). Characterizing covariant trajectories of individuals at clinical high risk for psychosis across symptomatic and functional domains. *American Journal of Psychiatry, 177*(2), 164-171.

Alvarez-Galvez, J., & Rojas-Garcia, A. (2019). Measuring the impact of multiple discrimination on depression in Europe. *BMC public health, 19*(1), 1-11.

American Psychiatric Association, D., & Association, A. P. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (Vol. 5): American psychiatric association Washington, DC.

Amiot, C. E., De la Sablonniere, R., Terry, D. J., & Smith, J. R. (2007). Integration of social identities in the self: Toward a cognitive-developmental model. *Personality and social psychology review, 11*(4), 364-388.

Anglin, D. M. (2023a). Racism and social determinants of psychosis. *Annual review of clinical psychology, 19*.

Anglin, D. M. (2023b). Racism and social determinants of psychosis. *Annual review of clinical psychology, 19*, 277-302.

Anglin, D. M., Ereshefsky, S., Klaunig, M. J., Bridgwater, M. A., Niendam, T. A., Ellman, L. M., . . . Musket, C. W. (2021). From Womb to Neighborhood: A Racial Analysis of Social Determinants of Psychosis in the United States. *American journal of Psychiatry*, appi. ajp. 2020.20071091.

Anglin, D. M., Lighty, Q., Greenspoon, M., & Ellman, L. M. (2014). Racial discrimination is associated with distressing subthreshold positive psychotic symptoms among US urban ethnic minority young adults. *Soc Psychiatry Psychiatr Epidemiol, 49*(10), 1545-1555. doi:10.1007/s00127-014-0870-8

Anglin, D. M., & Lui, F. (2023). Racial microaggressions and major discriminatory events explain ethnoracial differences in psychotic experiences. *Schizophrenia research, 253*, 5-13.

Anglin, D. M., Lui, F., Espinosa, A., Tikhonov, A., & Ellman, L. (2018). Ethnic identity, racial discrimination and attenuated psychotic symptoms in an urban population of emerging adults. *Early Interv Psychiatry, 12*(3), 380-390. doi:10.1111/eip.12314

Anticevic, A., Haut, K., Murray, J. D., Repovs, G., Yang, G. J., Diehl, C., . . . Goodyear, B. (2015). Association of thalamic dysconnectivity and conversion to psychosis in youth and young adults at elevated clinical risk. *JAMA Psychiatry, 72*(9), 882-891.

Anticevic, A., Haut, K., Murray, J. D., Repovs, G., Yang, G. J., Diehl, C., . . . Cannon, T. D. (2015). Association of Thalamic Dysconnectivity and Conversion to Psychosis in Youth and Young Adults at Elevated Clinical Risk. *JAMA Psychiatry, 72*(9), 882-891. doi:10.1001/jamapsychiatry.2015.0566

Auerbach, R. P., Admon, R., & Pizzagalli, D. A. (2014). Adolescent depression: stress and reward dysfunction. *Harvard review of psychiatry, 22*(3), 139.

Ayduk, O., Mendoza-Denton, R., Mischel, W., Downey, G., Peake, P. K., & Rodriguez, M. (2000). Regulating the interpersonal self: strategic self-regulation for coping with rejection sensitivity. *Journal of personality and social psychology, 79*(5), 776.

Baams, L., Grossman, A. H., & Russell, S. T. (2015). Minority stress and mechanisms of risk for depression and suicidal ideation among lesbian, gay, and bisexual youth. *Developmental psychology, 51*(5), 688.

Badcock, J. C., Paulik, G., & Maybery, M. T. (2011). The role of emotion regulation in auditory hallucinations. *Psychiatry research, 185*(3), 303-308.

Barch, D. M., & Ceaser, A. (2012). Cognition in schizophrenia: core psychological and neural mechanisms. *Trends Cogn Sci, 16*(1), 27-34. doi:10.3389/fnbeh.2016.00149

Barch, D. M., & Sheffield, J. M. (2017). Cognitive control in schizophrenia: Psychological and neural mechanisms.

Barnett, J. H., McDougall, F., Xu, M. K., Croudace, T. J., Richards, M., & Jones, P. B. (2012). Childhood cognitive function and adult psychopathology: associations with psychotic and non-psychotic symptoms in the general population. *The British Journal of Psychiatry, 201*(2), 124-130.

Berger, M., & Sarnyai, Z. (2015). "More than skin deep": stress neurobiology and mental health consequences of racial discrimination. *Stress, 18*(1), 1-10. doi:10.3109/10253890.2014.989204

Berjot, S., & Gillet, N. (2011). Stress and coping with discrimination and stigmatization. *Frontiers in psychology, 2*, 33.

Berridge, K. C., & Kringelbach, M. L. (2015). Pleasure systems in the brain. *Neuron, 86*(3), 646-664.

Bertocci, M. A., Afriyie-Agyemang, Y., Rozovsky, R., Iyengar, S., Stiffler, R., Aslam, H. A., . . . Phillips, M. L. (2023). Altered patterns of central executive, default mode and salience network activity and connectivity are associated with current and future depression risk in two independent young adult samples. *Molecular psychiatry, 28*(3), 1046-1056.

Bird, C. M., Webb, E. K., Schramm, A. T., Torres, L., Larson, C., & deRoon-Cassini, T. A. (2021). Racial discrimination is associated with acute posttraumatic stress symptoms and predicts future posttraumatic stress disorder symptom severity in trauma-exposed Black adults in the United States. *Journal of Traumatic Stress, 34*(5), 995-1004.

Blair, C. (2010). Stress and the development of self-regulation in context. *Child Development Perspectives, 4*(3), 181-188.

Blakemore, S.-J., & Robbins, T. W. (2012). Decision-making in the adolescent brain. *Nature neuroscience, 15*(9), 1184-1191.

Blanchard, J. J., & Cohen, A. S. (2006). The structure of negative symptoms within schizophrenia: implications for assessment. *Schizophrenia bulletin, 32*(2), 238-245.

Blanchard, J. J., Mueser, K. T., & Bellack, A. S. (1998). Anhedonia, positive and negative affect, and social functioning in schizophrenia. *Schizophr Bull, 24*(3), 413-424. doi:10.1093/oxfordjournals.schbul.a033336

Booth, A. L., Leigh, A., & Varganova, E. (2012). Does ethnic discrimination vary across minority groups? Evidence from a field experiment. *Oxford Bulletin of Economics and Statistics, 74*(4), 547-573.

Bora, E., & Murray, R. M. (2014). Meta-analysis of cognitive deficits in ultra-high risk to

psychosis and first-episode psychosis: do the cognitive deficits progress over, or after, the onset of psychosis? *Schizophrenia bulletin, 40*(4), 744-755.

Bourque, F., van der Ven, E., & Malla, A. (2011). A meta-analysis of the risk for psychotic disorders among first-and second-generation immigrants. *Psychological medicine, 41*(5), 897.

Boyd, J. E., Lanius, R. A., & McKinnon, M. C. (2018). Mindfulness-based treatments for posttraumatic stress disorder: a review of the treatment literature and neurobiological evidence. *Journal of Psychiatry and Neuroscience, 43*(1), 7-25.

Broudy, R., Brondolo, E., Coakley, V., Brady, N., Cassells, A., Tobin, J. N., & Sweeney, M. (2007). Perceived ethnic discrimination in relation to daily moods and negative social interactions. *Journal of behavioral medicine, 30*, 31-43.

Brown, S. (1997). Excess mortality of schizophrenia: a meta-analysis. *The British Journal of Psychiatry, 171*(6), 502-508.

Buckley, P. F., Miller, B. J., Lehrer, D. S., & Castle, D. J. (2009). Psychiatric comorbidities and schizophrenia. *Schizophrenia bulletin, 35*(2), 383-402.

Calabrese, S. K., Meyer, I. H., Overstreet, N. M., Haile, R., & Hansen, N. B. (2015). Exploring discrimination and mental health disparities faced by Black sexual minority women using a minority stress framework. *Psychology of women quarterly, 39*(3), 287-304.

Calkins, M. E., Woods, S. W., Bearden, C. E., Liu, L., Moore, T. M., Cadenhead, K. S., . . . Perkins, D. O. (2021). Concordance and factor structure of subthreshold positive symptoms in youth at clinical high risk for psychosis. *Schizophrenia research, 227*, 72-77.

Camara, E., Rodriguez-Fornells, A., Ye, Z., & Münte, T. F. (2009). Reward networks in the

brain as captured by connectivity measures. *Frontiers in neuroscience, 3*, 875.

Cannon, T. D., Cadenhead, K., Cornblatt, B., Woods, S. W., Addington, J., Walker, E., . . . McGlashan, T. (2008). Prediction of psychosis in youth at high clinical risk: a multisite longitudinal study in North America. *Archives of general psychiatry, 65*(1), 28-37.

Cannon, T. D., Chung, Y., He, G., Sun, D., Jacobson, A., van Erp, T. G., . . . Cadenhead, K. (2015). Progressive reduction in cortical thickness as psychosis develops: a multisite longitudinal neuroimaging study of youth at elevated clinical risk. *Biological psychiatry, 77*(2), 147-157.

Cannon, T. D., Van Erp, T. G., Bearden, C. E., Loewy, R., Thompson, P., Toga, A. W., . . . Tsuang, M. T. (2003). Early and late neurodevelopmental influences in the prodrome to schizophrenia: contributions of genes, environment, and their interactions. *Schizophrenia bulletin, 29*(4), 653-669.

Cannon, T. D., Yu, C., Addington, J., Bearden, C. E., Cadenhead, K. S., Cornblatt, B. A., . . . McGlashan, T. H. (2016). An individualized risk calculator for research in prodromal psychosis. *American Journal of Psychiatry, 173*(10), 980-988.

Carter, R. T. (2007). Racism and psychological and emotional injury: Recognizing and assessing race-based traumatic stress. *The Counseling Psychologist, 35*(1), 13-105.

Chakraborty, A., McKenzie, K., & King, M. (2009). Discrimination, ethnicity and psychosis—a qualitative study. *Ethnicity and Inequalities in Health and Social Care*.

Chapman, L. J., Chapman, J. P., Kwapil, T. R., Eckblad, M., & Zinser, M. C. (1994). Putatively psychosis-prone subjects 10 years later. *Journal of abnormal psychology, 103*(2), 171.

Chopra, S., Francey, S. M., O'Donoghue, B., Sabaroedin, K., Arnatkeviciute, A., Cropley, V., . . . Tahtalian, S. (2021). Functional connectivity in antipsychotic-treated and antipsychotic-

naive patients with first-episode psychosis and low risk of self-harm or aggression: a secondary analysis of a randomized clinical trial. *JAMA Psychiatry, 78*(9), 994-1004.

Clark, T. T., Salas-Wright, C. P., Vaughn, M. G., & Whitfield, K. E. (2015). Everyday discrimination and mood and substance use disorders: A latent profile analysis with African Americans and Caribbean Blacks. *Addictive behaviors, 40*, 119-125.

Cloutier, M., Aigbogun, M. S., Guerin, A., Nitulescu, R., Ramanakumar, A. V., Kamat, S. A., . . . Wu, E. (2016). The Economic Burden of Schizophrenia in the United States in 2013. *J Clin Psychiatry*, *77*(6), 764-771. doi:10.4088/JCP.15m10278

Cohen, M., Heller, A., & Ranganath, C. (2005). Functional connectivity with anterior cingulate and orbitofrontal cortices during decision-making. *Cognitive Brain Research, 23*(1), 61-70.

Collins, M. A., Chung, Y., Addington, J., Bearden, C. E., Cadenhead, K. S., Cornblatt, B. A., . . . Seidman, L. J. (2021). Discriminatory experiences predict neuroanatomical changes and anxiety among healthy individuals and those at clinical high risk for psychosis. *NeuroImage: Clinical, 31*, 102757.

Cornblatt, B. A., Auther, A. M., Niendam, T., Smith, C. W., Zinberg, J., Bearden, C. E., & Cannon, T. D. (2007). Preliminary findings for two new measures of social and role functioning in the prodromal phase of schizophrenia. *Schizophr Bull, 33*(3), 688-702.

Corr, R., Glier, S., Bizzell, J., Pelletier-Baldelli, A., Campbell, A., Killian-Farrell, C., & Belger, A. (2022). Triple network functional connectivity during acute stress in adolescents and the influence of polyvictimization. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 7*(9), 867-875.

Crisp, A. H., Gelder, M. G., Rix, S., Meltzer, H. I., & Rowlands, O. J. (2000). Stigmatisation of

people with mental illnesses. *The British Journal of Psychiatry, 177*(1), 4-7.

Davidow, J. Y., Foerde, K., Galván, A., & Shohamy, D. (2016). An upside to reward sensitivity: the hippocampus supports enhanced reinforcement learning in adolescence. *Neuron, 92*(1), 93-99.

Dean, D. J., & Mittal, V. A. (2015). Spontaneous parkinsonisms and striatal impairment in neuroleptic free youth at ultrahigh risk for psychosis. *NPJ schizophrenia, 1*(1), 1-6.

Deng, W., Addington, J., Bearden, C. E., Cadenhead, K. S., Cornblatt, B. A., Mathalon, D. H., . . . Tsuang, M. T. (2021). Depression Predicts Global Functional Outcomes in Individuals at Clinical High Risk for Psychosis. *Psychiatric Research and Clinical Practice, 3*(4), 163-171.

Deng, W. Y., Grove, T., & Deldin, P. (2020). Anxiety Mediates the Relationship between Psychotic-Like Experiences and Social Functioning in the General Population. *Psychopathology, 53*(2), 95-102.

DeRosse, P., & Karlsgodt, K. H. (2015). Examining the psychosis continuum. *Current behavioral neuroscience reports, 2*(2), 80-89.

Devoe, D., Lu, L., Cannon, T., Cadenhead, K., Cornblatt, B., McGlashan, T., . . . Woods, S. (2021). Persistent negative symptoms in youth at clinical high risk for psychosis: a longitudinal study. *Schizophrenia research, 227*, 28-37.

DeVylder, J. E., Cogburn, C., Oh, H. Y., Anglin, D., Smith, M. E., Sharpe, T., . . . Link, B. (2017). Psychotic experiences in the context of police victimization: Data from the survey of police–public encounters. *Schizophrenia bulletin, 43*(5), 993-1001.

DeVylder, J. E., Oh, H., Nam, B., Sharpe, T. L., Lehmann, M., & Link, B. G. (2017). Prevalence, demographic variation and psychological correlates of exposure to police

victimisation in four US cities. *Epidemiology and psychiatric sciences, 26*(5), 466-477.

DeVylder, J. E., Oh, H. Y., Yang, L. H., Cabassa, L. J., Chen, F.-p., & Lukens, E. P. (2013). Acculturative stress and psychotic-like experiences among Asian and Latino immigrants to the United States. *Schizophrenia research, 150*(1), 223-228.

Diamond, A. (2013). Executive functions. *Annual review of psychology, 64*, 135-168.

Dickerson, F., Boronow, J. J., Ringel, N., & Parente, F. (1999). Social functioning and neurocognitive deficits in outpatients with schizophrenia: a 2-year follow-up. *Schizophr Res, 37*(1), 13-20. doi:10.1016/s0920-9964(98)00134-0

Dong, D., Wang, Y., Chang, X., Luo, C., & Yao, D. (2018). Dysfunction of large-scale brain networks in schizophrenia: a meta-analysis of resting-state functional connectivity. *Schizophrenia bulletin, 44*(1), 168-181.

Dowd, E. C., & Barch, D. M. (2012). Pavlovian reward prediction and receipt in schizophrenia: relationship to anhedonia. *PLoS One, 7*(5), e35622.

Downar, J., Geraci, J., Salomons, T. V., Dunlop, K., Wheeler, S., McAndrews, M. P., . . . Kennedy, S. H. (2014). Anhedonia and reward-circuit connectivity distinguish nonresponders from responders to dorsomedial prefrontal repetitive transcranial magnetic stimulation in major depression. *Biological Psychiatry, 76*(3), 176-185.

Duggirala, S. X., Schwartze, M., Pinheiro, A. P., & Kotz, S. A. (2020). Interaction of emotion and cognitive control along the psychosis continuum: A critical review. *International Journal of Psychophysiology, 147*, 156-175.

Duman, R. S., & Monteggia, L. M. (2006). A neurotrophic model for stress-related mood disorders. *Biological Psychiatry, 59*(12), 1116-1127.

Dykxhoorn, J., Lewis, G., Hollander, A.-C., Kirkbride, J. B., & Dalman, C. (2020). Association

of neighbourhood migrant density and risk of non-affective psychosis: a national, longitudinal cohort study. *The Lancet Psychiatry, 7*(4), 327-336.

English, D., Rendina, H. J., & Parsons, J. T. (2018). The effects of intersecting stigma: A longitudinal examination of minority stress, mental health, and substance use among Black, Latino, and multiracial gay and bisexual men. *Psychology of violence, 8*(6), 669.

Ered, A., Gibson, L. E., Maxwell, S. D., Cooper, S., & Ellman, L. M. (2017). Coping as a mediator of stress and psychotic-like experiences. *European Psychiatry, 43*, 9-13.

Ernst, M., Torrisi, S., Balderston, N., Grillon, C., & Hale, E. A. (2015). fMRI functional connectivity applied to adolescent neurodevelopment. *Annual review of clinical psychology, 11*, 361-377.

Ernst, M., Torrisi, S., Balderston, N., Grillon, C., & Hale, E. A. (2015). fMRI functional connectivity applied to adolescent neurodevelopment. *Annu Rev Clin Psychol, 11*, 361-377. doi:10.1146/annurev-clinpsy-032814-112753

Erwin, R. J., Gur, R. C., Gur, R. E., Skolnick, B., Mawhinney-Hee, M., & Smailis, J. (1992). Facial emotion discrimination: I. Task construction and behavioral findings in normal subjects. *Psychiatry research, 42*(3), 231-240.

Fani, N., Carter, S. E., Harnett, N. G., Ressler, K. J., & Bradley, B. (2021). Association of racial discrimination with neural response to threat in Black women in the US exposed to trauma. *JAMA Psychiatry, 78*(9), 1005-1012.

Ferenczi, E. A., Zalocusky, K. A., Liston, C., Grosenick, L., Warden, M. R., Amatya, D., . . . Ramakrishnan, C. (2016). Prefrontal cortical regulation of brainwide circuit dynamics and reward-related behavior. *Science, 351*(6268), aac9698.

French, S. E., Seidman, E., Allen, L., & Aber, J. L. (2006). The development of ethnic identity

during adolescence. *Developmental psychology, 42*(1), 1.

Friedman, N. P., & Robbins, T. W. (2022). The role of prefrontal cortex in cognitive control and executive function. *Neuropsychopharmacology, 47*(1), 72-89.

Friston, K. J. (1998). The disconnection hypothesis. *Schizophr Res, 30*(2), 115-125. doi:10.1016/s0920-9964(97)00140-0

Frodl, T., & O'Keane, V. (2013). How does the brain deal with cumulative stress? A review with focus on developmental stress, HPA axis function and hippocampal structure in humans. *Neurobiology of disease, 52*, 24-37.

Fusar-Poli, P. (2012). Prodromal psychosis: diagnosis and treatment. *Curr Pharm Des, 18*(4), 337. doi:10.2174/138161212799316154

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., . . . Yung, A. (2013). The psychosis high-risk state: a comprehensive state-of-the-art review. *JAMA Psychiatry, 70*(1), 107-120.

Fusar-Poli, P., Deste, G., Smieskova, R., Barlati, S., Yung, A. R., Howes, O., . . . Borgwardt, S. (2012). Cognitive functioning in prodromal psychosis: a meta-analysis. *Archives of general psychiatry, 69*(6), 562-571.

Gabard-Durnam, L. J., Flannery, J., Goff, B., Gee, D. G., Humphreys, K. L., Telzer, E., . . . Tottenham, N. (2014). The development of human amygdala functional connectivity at rest from 4 to 23 years: a cross-sectional study. *Neuroimage, 95*, 193-207.

Galván, A. (2010). Adolescent development of the reward system. *Frontiers in human neuroscience, 4*, 1018.

Gard, D. E., Kring, A. M., Gard, M. G., Horan, W. P., & Green, M. F. (2007). Anhedonia in schizophrenia: distinctions between anticipatory and consummatory pleasure. *Schizophr*

Res, 93(1-3), 253-260. doi:10.1016/j.schres.2007.03.008

Garety, P. A., Kuipers, E., Fowler, D., Freeman, D., & Bebbington, P. (2001). A cognitive model of the positive symptoms of psychosis. *Psychological medicine, 31*(2), 189-195.

Gee, D. G., Humphreys, K. L., Flannery, J., Goff, B., Telzer, E. H., Shapiro, M., . . . Tottenham, N. (2013). A developmental shift from positive to negative connectivity in human amygdala–prefrontal circuitry. *Journal of Neuroscience, 33*(10), 4584-4593.

Gee, D. G., Karlsgodt, K. H., van Erp, T. G., Bearden, C. E., Lieberman, M. D., Belger, A., . . . Constable, T. (2012). Altered age-related trajectories of amygdala-prefrontal circuitry in adolescents at clinical high risk for psychosis: a preliminary study. *Schizophrenia research, 134*(1), 1-9.

Gevonden, M., Booij, J., van den Brink, W., Heijtel, D., van Os, J., & Selten, J. P. (2014). Increased release of dopamine in the striata of young adults with hearing impairment and its relevance for the social defeat hypothesis of schizophrenia. *JAMA Psychiatry, 71*(12), 1364-1372. doi:10.1001/jamapsychiatry.2014.1325

Gioia, G. A., Isquith, P. K., Guy, S. C., & Kenworthy, L. (2000). Test review behavior rating inventory of executive function. *Child Neuropsychology, 6*(3), 235-238.

Girotti, M., Adler, S. M., Bulin, S. E., Fucich, E. A., Paredes, D., & Morilak, D. A. (2018). Prefrontal cortex executive processes affected by stress in health and disease. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 85*, 161-179.

Gold, J. M., Waltz, J. A., Prentice, K. J., Morris, S. E., & Heerey, E. A. (2008). Reward processing in schizophrenia: a deficit in the representation of value. *Schizophrenia bulletin, 34*(5), 835-847.

Golden, S. A., Covington III, H. E., Berton, O., & Russo, S. J. (2011). A standardized protocol

for repeated social defeat stress in mice. *Nature protocols, 6*(8), 1183.

Goldman-Rakic, P. S. (1994). Working memory dysfunction in schizophrenia.

Goosby, B. J., Cheadle, J. E., & Mitchell, C. (2018). Stress-related biosocial mechanisms of discrimination and African American health inequities. *Annual Review of Sociology, 44*, 319-340.

Gradin, V. B., Waiter, G., O'Connor, A., Romaniuk, L., Stickle, C., Matthews, K., . . . Steele, J. D. (2013). Salience network-midbrain dysconnectivity and blunted reward signals in schizophrenia. *Psychiatry Research: Neuroimaging, 211*(2), 104-111.

Grayson, D. S., & Fair, D. A. (2017). Development of large-scale functional networks from birth to adulthood: A guide to the neuroimaging literature. *Neuroimage, 160*, 15-31.

Greene, D. J., Laumann, T. O., Dubis, J. W., Ihnen, S. K., Neta, M., Power, J. D., . . . Schlaggar, B. L. (2014). Developmental changes in the organization of functional connections between the basal ganglia and cerebral cortex. *Journal of Neuroscience, 34*(17), 5842-5854.

Gu, S., Satterthwaite, T. D., Medaglia, J. D., Yang, M., Gur, R. E., Gur, R. C., & Bassett, D. S. (2015). Emergence of system roles in normative neurodevelopment. *Proc Natl Acad Sci U S A, 112*(44), 13681-13686. doi:10.1016/j.neuroimage.2017.01.079

Gur, R. C., Sara, R., Hagendoorn, M., Marom, O., Hughett, P., Macy, L., . . . Gur, R. E. (2002). A method for obtaining 3-dimensional facial expressions and its standardization for use in neurocognitive studies. *J Neurosci Methods, 115*(2), 137-143. doi:10.1016/s0165-0270(02)00006-7

Hackett, R. A., Ronaldson, A., Bhui, K., Steptoe, A., & Jackson, S. E. (2020). Racial discrimination and health: a prospective study of ethnic minorities in the United

Kingdom. *BMC public health, 20*(1), 1-13.

Harikumar, A., Solovyeva, K. P., Misiura, M., Iraji, A., Plis, S. M., Pearlson, G. D., . . . Calhoun, V. D. (2023). Revisiting Functional Dysconnectivity: A Review of Three Model Frameworks in Schizophrenia. *Current Neurology and Neuroscience Reports, 23*(12), 937-946.

Harter, S. (1990). Processes underlying adolescent self-concept formation.

Hermans, E. J., Henckens, M. J., Joëls, M., & Fernández, G. (2014). Dynamic adaptation of large-scale brain networks in response to acute stressors. *Trends in neurosciences, 37*(6), 304-314.

Herringa, R. J., Burghy, C. A., Stodola, D. E., Fox, M. E., Davidson, R. J., & Essex, M. J. (2016). Enhanced prefrontal-amygdala connectivity following childhood adversity as a protective mechanism against internalizing in adolescence. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 1*(4), 326-334.

Hobson, J. M., Moody, M. D., Sorge, R. E., & Goodin, B. R. (2022). The neurobiology of social stress resulting from Racism: Implications for pain disparities among racialized minorities. *Neurobiology of Pain, 12*, 100101.

Hofmann, W., Schmeichel, B. J., & Baddeley, A. D. (2012). Executive functions and self-regulation. *Trends in cognitive sciences, 16*(3), 174-180.

Honey, G. D., Pomarol-Clotet, E., Corlett, P. R., Honey, R. A., Mckenna, P. J., Bullmore, E. T., & Fletcher, P. C. (2005). Functional dysconnectivity in schizophrenia associated with attentional modulation of motor function. *Brain, 128*(11), 2597-2611.

Hooker, C. I., Tully, L. M., Verosky, S. C., Fisher, M., Holland, C., & Vinogradov, S. (2011). Can I trust you? Negative affective priming influences social judgments in schizophrenia.

Journal of abnormal psychology, 120(1), 98.

Horga, G., Cassidy, C. M., Xu, X., Moore, H., Slifstein, M., Van Snellenberg, J. X., & Abi-Dargham, A. (2016). Dopamine-related disruption of functional topography of striatal connections in unmedicated patients with schizophrenia. *JAMA Psychiatry, 73*(8), 862-870.

Horne, C. M., Sahni, A., Pang, S. W., Vanes, L. D., Szentgyorgyi, T., Averbeck, B., . . . Shergill, S. S. (2022). The role of cognitive control in the positive symptoms of psychosis. *NeuroImage: Clinical, 34*, 103004.

Howes, O. D., & Kapur, S. (2009). The dopamine hypothesis of schizophrenia: version III--the final common pathway. *Schizophr Bull, 35*(3), 549-562.

Howes, O. D., McCutcheon, R., Owen, M. J., & Murray, R. M. (2017). The Role of Genes, Stress, and Dopamine in the Development of Schizophrenia. *Biol Psychiatry, 81*(1), 9-20. doi:10.1016/j.biopsych.2016.07.014

Howes, O. D., & Nour, M. M. (2016). Dopamine and the aberrant salience hypothesis of schizophrenia. *World Psychiatry, 15*(1), 3.

Hubl, D., Schultze-Lutter, F., Hauf, M., Dierks, T., Federspiel, A., Kaess, M., . . . Kindler, J. (2018). Striatal cerebral blood flow, executive functioning, and fronto-striatal functional connectivity in clinical high risk for psychosis. *Schizophr Res, 201*, 231-236. doi:10.1016/j.schres.2018.06.018

Hudson, D. L., Neighbors, H. W., Geronimus, A. T., & Jackson, J. S. (2016). Racial discrimination, john henryism, and depression among African Americans. *Journal of Black psychology, 42*(3), 221-243.

Hur, J. W., Choi, S.-H., Yun, J.-Y., Chon, M.-W., & Kwon, J. S. (2015). Parental socioeconomic

status and prognosis in individuals with ultra-high risk for psychosis: A 2-year follow-up study. *Schizophrenia research, 168*(1-2), 56-61.

Jacobs, G. R., Ameis, S. H., Ji, J. L., Viviano, J. D., Dickie, E. W., Wheeler, A. L., . . . Voineskos, A. N. (2019). Developmentally divergent sexual dimorphism in the cortico-striatal-thalamic-cortical psychosis risk pathway. *Neuropsychopharmacology, 44*(9), 1649-1658.

Jalbrzikowski, M., Murty, V. P., Tervo-Clemmens, B., Foran, W., & Luna, B. (2019). Age-associated deviations of amygdala functional connectivity in youths with psychosis spectrum disorders: relevance to psychotic symptoms. *American Journal of Psychiatry, 176*(3), 196-207.

Janssen, I., Hanssen, M., Bak, M., Bijl, R., De Graaf, R., Vollebergh, W., . . . Van Os, J. (2003). Discrimination and delusional ideation. *The British Journal of Psychiatry, 182*(1), 71-76.

Jin, H.-M., Muna, S. S., Bagalkot, T., Cui, Y., Yadav, B., & Chung, Y.-C. (2015). The effects of social defeat on behavior and dopaminergic markers in mice. *Neuroscience, 288*, 167-177.

Karlsgodt, K. H., Jacobson, S. C., Seal, M., & Fusar-Poli, P. (2012). The relationship of developmental changes in white matter to the onset of psychosis. *Current pharmaceutical design, 18*(4), 422-433.

Karlsgodt, K. H., Jacobson, S. C., Seal, M., & Fusar-Poli, P. (2012). The relationship of developmental changes in white matter to the onset of psychosis. *Curr Pharm Des, 18*(4), 422-433.

Karlsgodt, K. H., Niendam, T. A., Bearden, C. E., & Cannon, T. D. (2009). White matter integrity and prediction of social and role functioning in subjects at ultra-high risk for

psychosis. *Biol Psychiatry, 66*(6), 562-569. doi:10.1016/j.biopsych.2009.03.013

Kelleher, I., Wigman, J. T., Harley, M., O'Hanlon, E., Coughlan, H., Rawdon, C., . . . Cannon, M. (2015). Psychotic experiences in the population: association with functioning and mental distress. *Schizophrenia research, 165*(1), 9-14.

Kern, R. S., Nuechterlein, K. H., Green, M. F., Baade, L. E., Fenton, W. S., Gold, J. M., . . . Seidman, L. J. (2008). The MATRICS Consensus Cognitive Battery, part 2: co-norming and standardization. *American journal of Psychiatry, 165*(2), 214-220.

Kerns, J. G., Nuechterlein, K. H., Braver, T. S., & Barch, D. M. (2008). Executive functioning component mechanisms and schizophrenia. *Biological Psychiatry, 64*(1), 26-33.

Kessler, R. C., Mickelson, K. D., & Williams, D. R. (1999). The prevalence, distribution, and mental health correlates of perceived discrimination in the United States. *Journal of health and social behavior*, 208-230.

King, K. M., McLaughlin, K. A., Silk, J., & Monahan, K. C. (2018). Peer effects on self-regulation in adolescence depend on the nature and quality of the peer interaction. *Development and psychopathology, 30*(4), 1389-1401.

Kirkbride, J. B., Hameed, Y., Ioannidis, K., Ankireddypalli, G., Crane, C. M., Nasir, M., . . . Espandian, A. (2017). Ethnic minority status, age-at-immigration and psychosis risk in rural environments: evidence from the SEPEA study. *Schizophrenia Bulletin, 43*(6), 1251-1261.

Kirkinis, K., Pieterse, A. L., Martin, C., Agiliga, A., & Brownell, A. (2021). Racism, racial discrimination, and trauma: A systematic review of the social science literature. *Ethnicity & Health, 26*(3), 392-412.

Kirschner, M., Schmidt, A., Hodzic-Santor, B., Burrer, A., Manoliu, A., Zeighami, Y., . . .

Habermeyer, B. (2021). Orbitofrontal-striatal structural alterations linked to negative symptoms at different stages of the schizophrenia spectrum. *Schizophrenia bulletin, 47*(3), 849-863.

Klein, K., & Boals, A. (2001). The relationship of life event stress and working memory capacity. *Applied Cognitive Psychology: The Official Journal of the Society for Applied Research in Memory and Cognition, 15*(5), 565-579.

Klippel, A., Myin-Germeys, I., Chavez-Baldini, U., Preacher, K. J., Kempton, M., Valmaggia, L., . . . Hubbard, K. (2017). Modeling the interplay between psychological processes and adverse, stressful contexts and experiences in pathways to psychosis: an experience sampling study. *Schizophrenia Bulletin, 43*(2), 302-315.

Klippel, A., Myin-Germeys, I., Chavez-Baldini, U., Preacher, K. J., Kempton, M., Valmaggia, L., . . . Reininghaus, U. (2017). Modeling the Interplay Between Psychological Processes and Adverse, Stressful Contexts and Experiences in Pathways to Psychosis: An Experience Sampling Study. *Schizophr Bull, 43*(2), 302-315. doi:10.1093/schbul/sbw185

Knolle, F., Ermakova, A. O., Justicia, A., Fletcher, P. C., Bunzeck, N., Düzel, E., & Murray, G. K. (2018). Brain responses to different types of salience in antipsychotic naïve first episode psychosis: An fMRI study. *Translational psychiatry, 8*(1), 196.

Ko, J. H., Ptito, A., Monchi, O., Cho, S. S., Van Eimeren, T., Pellecchia, G., . . . Strafella, A. P. (2009). Increased dopamine release in the right anterior cingulate cortex during the performance of a sorting task: a [11C] FLB 457 PET study. *Neuroimage, 46*(2), 516-521.

Koutsouleris, N., Kambeitz-Ilankovic, L., Ruhrmann, S., Rosen, M., Ruef, A., Dwyer, D. B., . . . Haidl, T. (2018). Prediction models of functional outcomes for individuals in the clinical high-risk state for psychosis or with recent-onset depression: a multimodal, multisite

machine learning analysis. *JAMA Psychiatry, 75*(11), 1156-1172.

Krabbendam, L., Myin-Germeys, I., Hanssen, M., de Graaf, R., Vollebergh, W., Bak, M., & van Os, J. (2005). Development of depressed mood predicts onset of psychotic disorder in individuals who report hallucinatory experiences. *British Journal of Clinical Psychology, 44*(1), 113-125.

Kwapil, T. R. (1998). Social anhedonia as a predictor of the development of schizophrenia-spectrum disorders. *J Abnorm Psychol, 107*(4), 558-565. doi:10.1037//0021-843x.107.4.558

Kwapil, T. R., Miller, M. B., Zinser, M. C., Chapman, J., & Chapman, L. J. (1997). Magical ideation and social anhedonia as predictors of psychosis proneness: a partial replication. *Journal of abnormal psychology, 106*(3), 491.

Lacerda, A. L., Hardan, A. Y., Yorbik, O., Vemulapalli, M., Prasad, K. M., & Keshavan, M. S. (2007). Morphology of the orbitofrontal cortex in first-episode schizophrenia: relationship with negative symptomatology. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 31*(2), 510-516.

Larøi, F., Luhrmann, T. M., Bell, V., Christian Jr, W. A., Deshpande, S., Fernyhough, C., . . . Woods, A. (2014). Culture and hallucinations: overview and future directions. *Schizophrenia bulletin, 40*(Suppl_4), S213-S220.

Lebel, C., Walker, L., Leemans, A., Phillips, L., & Beaulieu, C. (2008). Microstructural maturation of the human brain from childhood to adulthood. *Neuroimage, 40*(3), 1044-1055. doi:10.1016/j.neuroimage.2007.12.053

Li, S., Hu, N., Zhang, W., Tao, B., Dai, J., Gong, Y., . . . Lui, S. (2019). Dysconnectivity of multiple brain networks in schizophrenia: a meta-analysis of resting-state functional

connectivity. *Frontiers in Psychiatry, 10*, 482.

Liang, S., Wu, Y., Hanxiaoran, L., Greenshaw, A. J., & Li, T. (2022). Anhedonia in depression and schizophrenia: brain reward and aversion circuits. *Neuropsychiatric disease and treatment, 18*, 1385.

Linden, D. E. J. (2006). How psychotherapy changes the brain–the contribution of functional neuroimaging. *Molecular psychiatry, 11*(6), 528-538.

Linscott, R., & Van Os, J. (2013a). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychological medicine, 43*(6), 1133.

Linscott, R., & Van Os, J. (2013b). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychological medicine, 43*(6), 1133-1149.

Liston, C., McEwen, B. S., & Casey, B. (2009). Psychosocial stress reversibly disrupts prefrontal processing and attentional control. *Proceedings of the National Academy of Sciences, 106*(3), 912-917.

Liu, Y., Liang, M., Zhou, Y., He, Y., Hao, Y., Song, M., . . . Jiang, T. (2008). Disrupted small-world networks in schizophrenia. *Brain, 131*(Pt 4), 945-961. doi:10.1093/brain/awn018

Livingston, N. A., Berke, D. S., Ruben, M. A., Matza, A. R., & Shipherd, J. C. (2019). Experiences of trauma, discrimination, microaggressions, and minority stress among trauma-exposed LGBT veterans: Unexpected findings and unresolved service gaps. *Psychological Trauma: Theory, Research, Practice, and Policy, 11*(7), 695.

Livingston, N. A., Flentje, A., Brennan, J., Mereish, E. H., Reed, O., & Cochran, B. N. (2020). Real-time associations between discrimination and anxious and depressed mood among sexual and gender minorities: The moderating effects of lifetime victimization and identity concealment. *Psychology of sexual orientation and gender diversity, 7*(2), 132.

Lynall, M. E., Bassett, D. S., Kerwin, R., McKenna, P. J., Kitzbichler, M., Muller, U., & Bullmore, E. (2010). Functional connectivity and brain networks in schizophrenia. *J Neurosci, 30*(28), 9477-9487. doi:10.2174/138161212799316073

Makowski, C., Lepage, M., & Evans, A. C. (2019). Head motion: the dirty little secret of neuroimaging in psychiatry. *Journal of psychiatry & neuroscience: JPN, 44*(1), 62.

Mallikarjun, P. K., Lalousis, P. A., Dunne, T. F., Heinze, K., Reniers, R. L., Broome, M. R., . . . Upthegrove, R. (2018). Aberrant salience network functional connectivity in auditory verbal hallucinations: a first episode psychosis sample. *Translational psychiatry, 8*(1), 69.

Marcus, D. S., Harms, M. P., Snyder, A. Z., Jenkinson, M., Wilson, J. A., Glasser, M. F., . . . Ramaratnam, M. (2013). Human Connectome Project informatics: quality control, database services, and data visualization. *Neuroimage, 80*, 202-219.

Marenco, S., & Weinberger, D. R. (2000). The neurodevelopmental hypothesis of schizophrenia: following a trail of evidence from cradle to grave. *Development and psychopathology, 12*(3), 501-527.

Masucci, M. D., Lister, A., Corcoran, C. M., Brucato, G., & Girgis, R. R. (2018). Motor dysfunction as a risk factor for conversion to psychosis independent of medication use in a psychosis-risk cohort. *The Journal of nervous and mental disease, 206*(5), 356-361.

Matthews, M., Bondi, C., Torres, G., & Moghaddam, B. (2013). Reduced presynaptic dopamine activity in adolescent dorsal striatum. *Neuropsychopharmacology, 38*(7), 1344-1351.

Mattick, R. P., & Clarke, J. C. (1998). Development and validation of measures of social phobia scrutiny fear and social interaction anxiety. *Behaviour research and therapy, 36*(4), 455-470.

Maxwell, S. E., & Cole, D. A. (2007). Bias in cross-sectional analyses of longitudinal mediation. *Psychological methods, 12*(1), 23.

Maynard, T. M., Sikich, L., Lieberman, J. A., & LaMantia, A.-S. (2001). Neural development, cell-cell signaling, and the "two-hit" hypothesis of schizophrenia. *Schizophrenia Bulletin, 27*(3), 457-476.

Mayo, D., Corey, S., Kelly, L. H., Yohannes, S., Youngquist, A. L., Stuart, B. K., . . . Loewy, R. L. (2017). The role of trauma and stressful life events among individuals at clinical high risk for psychosis: A review. *Frontiers in Psychiatry, 8*, 247326.

McCutcheon, R. A., Abi-Dargham, A., & Howes, O. D. (2019). Schizophrenia, Dopamine and the Striatum: From Biology to Symptoms. *Trends Neurosci, 42*(3), 205-220.

McCutcheon, R. A., Nour, M. M., Dahoun, T., Jauhar, S., Pepper, F., Expert, P., . . . Mehta, M. A. (2019). Mesolimbic dopamine function is related to salience network connectivity: an integrative positron emission tomography and magnetic resonance study. *Biological Psychiatry, 85*(5), 368-378.

McCutcheon, R. A., Nour, M. M., Dahoun, T., Jauhar, S., Pepper, F., Expert, P., . . . Howes, O. D. (2019). Mesolimbic Dopamine Function Is Related to Salience Network Connectivity: An Integrative Positron Emission Tomography and Magnetic Resonance Study. *Biol Psychiatry, 85*(5), 368-378.

McDonald, S., Flanagan, S., Rollins, J., & Kinch, J. (2003). TASIT: A new clinical tool for assessing social perception after traumatic brain injury. *J Head Trauma Rehabil, 18*(3),

219-238. doi:10.1097/00001199-200305000-00001

McEwen, B. S. (2003). Mood disorders and allostatic load. *Biological Psychiatry, 54*(3), 200-207.

McGarrity, L. A., Huebner, D. M., Smith, T. W., & Suchy, Y. (2020). Minority stress, emotion regulation, and executive function: An experimental investigation of gay and lesbian adults. *Personality and Social Psychology Bulletin, 46*(3), 365-376.

McGrath, J., Saha, S., Chant, D., & Welham, J. (2008). Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidemiologic reviews, 30*(1), 67-76.

McGuire, T. G., & Miranda, J. (2008). New evidence regarding racial and ethnic disparities in mental health: Policy implications. *Health Affairs, 27*(2), 393-403.

Meador-Woodruff, J. H., Damask, S. P., Wang, J., Haroutunian, V., Davis, K. L., & Watson, S. J. (1996). Dopamine receptor mRNA expression in human striatum and neocortex. *Neuropsychopharmacology, 15*(1), 17-29.

Mennigen, E., & Bearden, C. E. (2020). Psychosis risk and development: What do we know from population-based studies? *Biological Psychiatry, 88*(4), 315-325.

Menon, V. (2013). Developmental pathways to functional brain networks: emerging principles. *Trends Cogn Sci, 17*(12), 627-640. doi:10.1016/j.tics.2013.09.015

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: a network model of insula function. *Brain structure and function, 214*, 655-667.

Merz, E. C., Wiltshire, C. A., & Noble, K. G. (2019). Socioeconomic inequality and the developing brain: Spotlight on language and executive function. *Child Development Perspectives, 13*(1), 15-20.

Michaels, T. I., Carrión, R. E., Addington, J., Bearden, C. E., Cadenhead, K. S., Cannon, T. D., .

. . Perkins, D. O. (2023). Ethnoracial discrimination and the development of suspiciousness symptoms in individuals at clinical high-risk for psychosis. *Schizophrenia research, 254*, 125-132.

Miller, T. J., McGlashan, T. H., Rosen, J. L., Cadenhead, K., Cannon, T., Ventura, J., . . . Woods, S. W. (2003). Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. *Schizophr Bull, 29*(4), 703-715. doi:10.1093/oxfordjournals.schbul.a007040

Mittal, V. A., Jalbrzikowski, M., Daley, M., Roman, C., Bearden, C. E., & Cannon, T. D. (2011). Abnormal movements are associated with poor psychosocial functioning in adolescents at high risk for psychosis. *Schizophrenia research, 130*(1-3), 164-169.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive psychology, 41*(1), 49-100.

Mizrahi, R., Addington, J., Rusjan, P. M., Suridjan, I., Ng, A., Boileau, I., . . . Wilson, A. A. (2012). Increased stress-induced dopamine release in psychosis. *Biological Psychiatry, 71*(6), 561-567.

Modinos, G., Kempton, M. J., Tognin, S., Calem, M., Porffy, L., Antoniades, M., . . . Group, E.-G. H. R. S. (2019). Association of Adverse Outcomes With Emotion Processing and Its Neural Substrate in Individuals at Clinical High Risk for Psychosis. *JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2019.3501

Mollon, J., David, A. S., Morgan, C., Frissa, S., Glahn, D., Pilecka, I., . . . Reichenberg, A. (2016). Psychotic experiences and neuropsychological functioning in a population-based

sample. *JAMA Psychiatry, 73*(2), 129-138.

Morawetz, C., Riedel, M. C., Salo, T., Berboth, S., Eickhoff, S. B., Laird, A. R., & Kohn, N. (2020). Multiple large-scale neural networks underlying emotion regulation. *Neuroscience & Biobehavioral Reviews, 116*, 382-395.

Morgan, C., Fearon, P., Lappin, J., Heslin, M., Donoghue, K., Lomas, B., . . . Dazzan, P. (2017). Ethnicity and long-term course and outcome of psychotic disorders in a UK sample: the ÆSOP-10 study. *Br J Psychiatry, 211*(2), 88-94. doi:10.5498/wjp.v4.i4.133

Morgan, C., & Fisher, H. (2007). Environment and schizophrenia: environmental factors in schizophrenia: childhood trauma—a critical review. *Schizophrenia Bulletin, 33*(1), 3-10.

Moritz, S., Birkner, C., Kloss, M., Jahn, H., Hand, I., Haasen, C., & Krausz, M. (2002). Executive functioning in obsessive–compulsive disorder, unipolar depression, and schizophrenia. *Archives of Clinical Neuropsychology, 17*(5), 477-483.

Moriya, J., & Takahashi, Y. (2013). Depression and interpersonal stress: The mediating role of emotion regulation. *Motivation and Emotion, 37*(3), 600-608.

Mow, J. L., Gandhi, A., & Fulford, D. (2020). Imaging the "social brain" in schizophrenia: A systematic review of neuroimaging studies of social reward and punishment. *Neuroscience & Biobehavioral Reviews*.

Muraven, M., & Baumeister, R. F. (2000). Self-regulation and depletion of limited resources: Does self-control resemble a muscle? *Psychological bulletin, 126*(2), 247.

Myin-Germeys, I., van Os, J., Schwartz, J. E., Stone, A. A., & Delespaul, P. A. (2001). Emotional reactivity to daily life stress in psychosis. *Archives of general psychiatry, 58*(12), 1137-1144.

Nawijn, L., van Zuiden, M., Frijling, J. L., Koch, S. B., Veltman, D. J., & Olff, M. (2015).

Reward functioning in PTSD: a systematic review exploring the mechanisms underlying anhedonia. *Neuroscience & Biobehavioral Reviews, 51*, 189-204.

Neighbors, H. W., Jackson, J. S., Campbell, L., & Williams, D. (1989). The influence of racial factors on psychiatric diagnosis: A review and suggestions for research. *Community Mental Health Journal, 25*, 301-311.

Nima, A. A., Rosenberg, P., Archer, T., & Garcia, D. (2013). Anxiety, affect, self-esteem, and stress: mediation and moderation effects on depression. *PLoS One, 8*(9), e73265.

Noh, S., & Kaspar, V. (2003). Perceived discrimination and depression: Moderating effects of coping, acculturation, and ethnic support. *American journal of public health, 93*(2), 232-238.

Norman, R. M., Malla, A. K., McLean, T., Voruganti, L. P. N., Cortese, L., McIntosh, E., . . . Rickwood, A. (2000). The relationship of symptoms and level of functioning in schizophrenia to general wellbeing and the Quality of Life Scale. *Acta Psychiatrica Scandinavica, 102*(4), 303-309.

Novick, A. M., Forster, G. L., Tejani-Butt, S. M., & Watt, M. J. (2011). Adolescent social defeat alters markers of adult dopaminergic function. *Brain Res Bull, 86*(1-2), 123-128.

Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., Cohen, J. D., . . . Gold, J. M. (2008). The MATRICS Consensus Cognitive Battery, part 1: test selection, reliability, and validity. *American journal of Psychiatry, 165*(2), 203-213.

O'Donnell, M. L., Creamer, M., & Pattison, P. (2004). Posttraumatic stress disorder and depression following trauma: understanding comorbidity. *American journal of Psychiatry, 161*(8), 1390-1396.

Oh, H., Cogburn, C. D., Anglin, D., Lukens, E., & DeVylder, J. (2016). Major discriminatory

events and risk for psychotic experiences among Black Americans. *American journal of orthopsychiatry, 86*(3), 277.

Oluwoye, O., Davis, B., Kuhney, F. S., & Anglin, D. M. (2021). Systematic review of pathways to care in the US for Black individuals with early psychosis. *NPJ schizophrenia, 7*(1), 1-10.

Oluwoye, O., Stiles, B., Monroe-DeVita, M., Chwastiak, L., McClellan, J. M., Dyck, D., . . . McDonell, M. G. (2018). Racial-ethnic disparities in first-episode psychosis treatment outcomes from the RAISE-ETP study. *Psychiatric Services, 69*(11), 1138-1145.

Oswald, L. M., Wand, G. S., Kuwabara, H., Wong, D. F., Zhu, S., & Brasic, J. R. (2014). History of childhood adversity is positively associated with ventral striatal dopamine responses to amphetamine. *Psychopharmacology (Berl), 231*(12), 2417-2433.

Pachankis, J. E., Rendina, H. J., Restar, A., Ventuneac, A., Grov, C., & Parsons, J. T. (2015). A minority stress—emotion regulation model of sexual compulsivity among highly sexually active gay and bisexual men. *Health Psychology, 34*(8), 829.

Palaniyappan, L., & Liddle, P. F. (2012). Does the salience network play a cardinal role in psychosis? An emerging hypothesis of insular dysfunction. *J Psychiatry Neurosci, 37*(1), 17-27. doi:10.1503/jpn.100176

Pascoe, E. A., & Smart Richman, L. (2009). Perceived discrimination and health: a meta-analytic review. *Psychological bulletin, 135*(4), 531.

Patel, P. K., Leathem, L. D., Currin, D. L., & Karlsgodt, K. H. (2021). Adolescent Neurodevelopment and Vulnerability to Psychosis. *Biological Psychiatry, 89*(2), 184-193. doi:10.1016/j.biopsych.2020.06.028

Pearce, J., Rafiq, S., Simpson, J., & Varese, F. (2019). Perceived discrimination and psychosis: a

systematic review of the literature. *Soc Psychiatry Psychiatr Epidemiol, 54*(9), 1023-1044. doi:10.1007/s00127-019-01729-3

Pelletier-Baldelli, A., Bernard, J. A., & Mittal, V. A. (2015). Intrinsic functional connectivity in salience and default mode networks and aberrant social processes in youth at ultra-high risk for psychosis. *PloS one, 10*(8), e0134936.

Pettersson-Yeo, W., Allen, P., Benetti, S., McGuire, P., & Mechelli, A. (2011). Dysconnectivity in schizophrenia: where are we now? *Neuroscience & Biobehavioral Reviews, 35*(5), 1110-1124.

Phillips, L. J., Francey, S. M., Edwards, J., & McMurray, N. (2007). Stress and psychosis: towards the development of new models of investigation. *Clinical psychology review, 27*(3), 307-317.

Phillips, L. J., Yung, A. R., & McGorry, P. D. (2000). Identification of young people at risk of psychosis: validation of Personal Assessment and Crisis Evaluation Clinic intake criteria. *Australian and New Zealand Journal of Psychiatry, 34*, S164-S169.

Phinney, J. S. (1989). Stages of ethnic identity development in minority group adolescents. *The Journal of Early Adolescence, 9*(1-2), 34-49.

Piccolo, L. d. R., Sbicigo, J. B., Grassi-Oliveira, R., & Fumagalli de Salles, J. (2014). Do socioeconomic status and stress reactivity really impact neurocognitive performance? *Psychology & Neuroscience, 7*(4), 567.

Pignatelli, M., & Bonci, A. (2015). Role of dopamine neurons in reward and aversion: a synaptic plasticity perspective. *Neuron, 86*(5), 1145-1157.

Pizzagalli, D. A., Iosifescu, D., Hallett, L. A., Ratner, K. G., & Fava, M. (2008). Reduced hedonic capacity in major depressive disorder: evidence from a probabilistic reward task.

Journal of psychiatric research, 43(1), 76-87.

Plieger, T., & Reuter, M. (2020). Stress & executive functioning: A review considering moderating factors. *Neurobiology of Learning and Memory, 173*, 107254.

Porter, J. N., Roy, A. K., Benson, B., Carlisi, C., Collins, P. F., Leibenluft, E., . . . Ernst, M. (2015). Age-related changes in the intrinsic functional connectivity of the human ventral vs. dorsal striatum from childhood to middle age. *Developmental cognitive neuroscience, 11*, 83-95.

Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *Neuroimage, 59*(3), 2142-2154.

Pruessner, J. C., Champagne, F., Meaney, M. J., & Dagher, A. (2004). Dopamine release in response to a psychological stress in humans and its relationship to early life maternal care: a positron emission tomography study using [11C] raclopride. *Journal of Neuroscience, 24*(11), 2825-2831.

Quidé, Y., Morris, R. W., Shepherd, A. M., Rowland, J. E., & Green, M. J. (2013). Task-related fronto-striatal functional connectivity during working memory performance in schizophrenia. *Schizophr Res, 150*(2-3), 468-475. doi:10.1016/j.schres.2013.08.009

Read, J., Fosse, R., Moskowitz, A., & Perry, B. (2014). The traumagenic neurodevelopmental model of psychosis revisited. *Neuropsychiatry, 4*(1), 65-79.

Read, J., Perry, B. D., Moskowitz, A., & Connolly, J. (2001). The contribution of early traumatic events to schizophrenia in some patients: a traumagenic neurodevelopmental model. *Psychiatry, 64*(4), 319-345. doi:10.1521/psyc.64.4.319.18602

Read, J., van Os, J., Morrison, A. P., & Ross, C. A. (2005). Childhood trauma, psychosis and

schizophrenia: a literature review with theoretical and clinical implications. *Acta Psychiatrica Scandinavica, 112*(5), 330-350.

Riehle, M., & Lincoln, T. M. (2017). Social consequences of subclinical negative symptoms: An EMG study of facial expressions within a social interaction. *Journal of behavior therapy and experimental psychiatry, 55*, 90-98.

Rodriguez, J. M., Karlamangla, A. S., Gruenewald, T. L., Miller-Martinez, D., Merkin, S. S., & Seeman, T. E. (2019). Social stratification and allostatic load: shapes of health differences in the MIDUS study in the United States. *Journal of biosocial science, 51*(5), 627-644.

Roffman, J. L., Marci, C. D., Glick, D. M., Dougherty, D. D., & Rauch, S. L. (2005). Neuroimaging and the functional neuroanatomy of psychotherapy. *Psychological medicine, 35*(10), 1385-1398.

Romeo, R. D. (2010). Adolescence: a central event in shaping stress reactivity. *Dev Psychobiol, 52*(3), 244-253. doi:10.1002/dev.20437

Rotarska-Jagiela, A., van de Ven, V., Oertel-Knöchel, V., Uhlhaas, P. J., Vogeley, K., & Linden, D. E. (2010). Resting-state functional network correlates of psychotic symptoms in schizophrenia. *Schizophrenia research, 117*(1), 21-30.

Saleem, M. M., Stowkowy, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., McGlashan, T. H., . . . Walker, E. F. (2014). Perceived discrimination in those at clinical high risk for psychosis. *Early intervention in psychiatry, 8*(1), 77-81.

Salehinejad, M. A., Ghanavati, E., Rashid, M. H. A., & Nitsche, M. A. (2021). Hot and cold executive functions in the brain: A prefrontal-cingular network. *Brain and Neuroscience Advances, 5*, 23982128211007769.

Sandi, C. (2013). Stress and cognition. *Wiley Interdisciplinary Reviews: Cognitive Science, 4*(3), 245-261.

Sarpal, D. K., Robinson, D. G., Lencz, T., Argyelan, M., Ikuta, T., Karlsgodt, K., . . . Malhotra, A. K. (2015). Antipsychotic treatment and functional connectivity of the striatum in first-episode schizophrenia. *JAMA Psychiatry, 72*(1), 5-13. doi:10.1001/jamapsychiatry.2014.1734

Sato, J. R., Salum, G. A., Gadelha, A., Vieira, G., Zugman, A., Picon, F. A., . . . Moura, L. M. (2015). Decreased centrality of subcortical regions during the transition to adolescence: a functional connectivity study. *Neuroimage, 104*, 44-51.

Satterthwaite, T. D., Wolf, D. H., Loughead, J., Ruparel, K., Elliott, M. A., Hakonarson, H., . . . Gur, R. E. (2012). Impact of in-scanner head motion on multiple measures of functional connectivity: relevance for studies of neurodevelopment in youth. *Neuroimage, 60*(1), 623-632.

Saxena, A., Liu, S., Handley, E. D., & Dodell-Feder, D. (2024). Social victimization, default mode network connectivity, and psychotic-like experiences in adolescents. *Schizophrenia research, 264*, 462-470.

Schlosser, D. A., Jacobson, S., Chen, Q., Sugar, C. A., Niendam, T. A., Li, G., . . . Cannon, T. D. (2012). Recovery from an at-risk state: clinical and functional outcomes of putatively prodromal youth who do not develop psychosis. *Schizophr Bull, 38*(6), 1225-1233. doi:10.1176/appi.ajp.2011.10081191

Schneider, K. (1959). *Clinical psychopathology*: Grune & Stratton.

Schoofs, D., Preuß, D., & Wolf, O. T. (2008). Psychosocial stress induces working memory impairments in an n-back paradigm. *Psychoneuroendocrinology, 33*(5), 643-653.

Schulze, B., & Angermeyer, M. C. (2003). Subjective experiences of stigma. A focus group study of schizophrenic patients, their relatives and mental health professionals. *Social science & medicine, 56*(2), 299-312.

Schwartz, R. C., & Blankenship, D. M. (2014). Racial disparities in psychotic disorder diagnosis: A review of empirical literature. *World journal of psychiatry, 4*(4), 133.

Schwartz, R. C., & Blankenship, D. M. (2014). Racial disparities in psychotic disorder diagnosis: A review of empirical literature. *World J Psychiatry, 4*(4), 133-140.

Sebastian, C., Burnett, S., & Blakemore, S.-J. (2008). Development of the self-concept during adolescence. *Trends in cognitive sciences, 12*(11), 441-446.

Seidman, L. J., Shapiro, D. I., Stone, W. S., Woodberry, K. A., Ronzio, A., Cornblatt, B. A., . . . Cannon, T. D. (2016). Association of neurocognition with transition to psychosis: baseline functioning in the second phase of the North American Prodrome Longitudinal Study. *JAMA Psychiatry, 73*(12), 1239-1248.

Selemon, L., & Zecevic, N. (2015). Schizophrenia: a tale of two critical periods for prefrontal cortical development. *Translational psychiatry, 5*(8), e623-e623.

Selten, J. P., van der Ven, E., Rutten, B. P., & Cantor-Graae, E. (2013). The social defeat hypothesis of schizophrenia: an update. *Schizophr Bull, 39*(6), 1180-1186. doi:10.1093/schbul/sbt134

Seng, J. S., Lopez, W. D., Sperlich, M., Hamama, L., & Meldrum, C. D. R. (2012). Marginalized identities, discrimination burden, and mental health: Empirical exploration of an interpersonal-level approach to modeling intersectionality. *Social science & medicine, 75*(12), 2437-2445.

Sergi, M. J., Fiske, A. P., Horan, W. P., Kern, R. S., Kee, K. S., Subotnik, K. L., . . . Green, M.

F. (2009). Development of a measure of relationship perception in schizophrenia. *Psychiatry research, 166*(1), 54-62.

Sescousse, G., Redouté, J., & Dreher, J.-C. (2010). The architecture of reward value coding in the human orbitofrontal cortex. *Journal of Neuroscience, 30*(39), 13095-13104.

Shaw, P., Kabani, N. J., Lerch, J. P., Eckstrand, K., Lenroot, R., Gogtay, N., . . . Rapoport, J. L. (2008). Neurodevelopmental trajectories of the human cerebral cortex. *Journal of Neuroscience, 28*(14), 3586-3594.

Sheffield, J. M., Karcher, N. R., & Barch, D. M. (2018). Cognitive deficits in psychotic disorders: a lifespan perspective. *Neuropsychology review, 28*, 509-533.

Shevlin, M., Dorahy D Clin Psych, P. D., Martin J, & Adamson, G. (2007). Trauma and psychosis: an analysis of the National Comorbidity Survey. *American journal of Psychiatry, 164*(1), 166-169.

Shukla, D. K., Chiappelli, J. J., Sampath, H., Kochunov, P., Hare, S. M., Wisner, K., . . . Hong, L. E. (2019). Aberrant frontostriatal connectivity in negative symptoms of schizophrenia. *Schizophrenia bulletin, 45*(5), 1051-1059.

Shurman, B., Horan, W. P., & Nuechterlein, K. H. (2005). Schizophrenia patients demonstrate a distinctive pattern of decision-making impairment on the Iowa Gambling Task. *Schizophrenia research, 72*(2-3), 215-224.

Simpson, E. H., Kellendonk, C., & Kandel, E. (2010). A possible role for the striatum in the pathogenesis of the cognitive symptoms of schizophrenia. *Neuron, 65*(5), 585-596. doi:10.1016/j.schres.2014.09.022

Sinclair, D., Purves-Tyson, T. D., Allen, K. M., & Weickert, C. S. (2014). Impacts of stress and sex hormones on dopamine neurotransmission in the adolescent brain.

Psychopharmacology, 231(8), 1581-1599. doi:10.1007/s00213-013-3415-z

Sowislo, J. F., & Orth, U. (2013). Does low self-esteem predict depression and anxiety? A meta-analysis of longitudinal studies. *Psychological bulletin, 139*(1), 213.

Sridharan, D., Levitin, D. J., & Menon, V. (2008). A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. *Proceedings of the National Academy of Sciences, 105*(34), 12569-12574.

Staines, L., Healy, C., Coughlan, H., Clarke, M., Kelleher, I., Cotter, D., & Cannon, M. (2022). Psychotic experiences in the general population, a review; definition, risk factors, outcomes and interventions. *Psychological medicine*, 1-12.

Stefanis, N., Hanssen, M., Smirnis, N., Avramopoulos, D., Evdokimidis, I., Verdoux, H., . . . van Osl, J. (2002). Evidence that three dimensions of psychosis have a distribution in the general population. *European Psychiatry*(17), 61.

Stowkowy, J., Liu, L., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., McGlashan, T. H., . . . Addington, J. (2016). Early traumatic experiences, perceived discrimination and conversion to psychosis in those at clinical high risk for psychosis. *Soc Psychiatry Psychiatr Epidemiol, 51*(4), 497-503. doi:10.1007/s00127-016-1182-y

Strassnig, M. T., Raykov, T., O'Gorman, C., Bowie, C. R., Sabbag, S., Durand, D., . . . Harvey, P. D. (2015). Determinants of different aspects of everyday outcome in schizophrenia: the roles of negative symptoms, cognition, and functional capacity. *Schizophrenia research, 165*(1), 76-82.

Strauss, G. P., & Cohen, A. S. (2017). A transdiagnostic review of negative symptom phenomenology and etiology. *Schizophrenia bulletin, 43*(4), 712-719.

Strauss, G. P., Frank, M. J., Waltz, J. A., Kasanova, Z., Herbener, E. S., & Gold, J. M. (2011).

Deficits in positive reinforcement learning and uncertainty-driven exploration are associated with distinct aspects of negative symptoms in schizophrenia. *Biological Psychiatry, 69*(5), 424-431.

Strauss, G. P., & Gold, J. M. (2012). A new perspective on anhedonia in schizophrenia. *American journal of Psychiatry, 169*(4), 364-373.

Strauss, G. P., Nuñez, A., Ahmed, A. O., Barchard, K. A., Granholm, E., Kirkpatrick, B., . . . Allen, D. N. (2018). The latent structure of negative symptoms in schizophrenia. *JAMA Psychiatry, 75*(12), 1271-1279.

Strauss, G. P., Waltz, J. A., & Gold, J. M. (2014). A review of reward processing and motivational impairment in schizophrenia. *Schizophrenia bulletin, 40*(Suppl_2), S107-S116.

Sullivan, S. A., Kounali, D., Cannon, M., David, A. S., Fletcher, P. C., Holmans, P., . . . Zammit, S. (2020). A Population-Based Cohort Study Examining the Incidence and Impact of Psychotic Experiences From Childhood to Adulthood, and Prediction of Psychotic Disorder. *Am J Psychiatry, 177*(4), 308-317. doi:10.1176/appi.ajp.2019.19060654

Takahashi, H., Koeda, M., Oda, K., Matsuda, T., Matsushima, E., Matsuura, M., . . . Okubo, Y. (2004). An fMRI study of differential neural response to affective pictures in schizophrenia. *Neuroimage, 22*(3), 1247-1254.

Taylor, S. E., & Stanton, A. L. (2007). Coping resources, coping processes, and mental health. *Annu. Rev. Clin. Psychol., 3*, 377-401.

Thoroughgood, C. N., Sawyer, K. B., & Webster, J. R. (2017). What lies beneath: How paranoid cognition explains the relations between transgender employees' perceptions of discrimination at work and their job attitudes and wellbeing. *Journal of Vocational*

Behavior, 103, 99-112.

Tidey, J. W., & Miczek, K. A. (1996). Social defeat stress selectively alters mesocorticolimbic dopamine release: an in vivo microdialysis study. *Brain research, 721*(1-2), 140-149.

Tso, I. F., Taylor, S. F., Grove, T. B., Niendam, T., Adelsheim, S., Auther, A., . . . Ragland, J. D. (2017). Factor analysis of the S cale of P rodromal S ymptoms: data from the E arly D etection and I ntervention for the P revention of P sychosis P rogram. *Early intervention in psychiatry, 11*(1), 14-22.

Tu, P.-C., Lee, Y.-C., Chen, Y.-S., Li, C.-T., & Su, T.-P. (2013). Schizophrenia and the brain's control network: aberrant within-and between-network connectivity of the frontoparietal network in schizophrenia. *Schizophrenia research, 147*(2-3), 339-347.

Tu, P. C., Hsieh, J. C., Li, C. T., Bai, Y. M., & Su, T. P. (2012). Cortico-striatal disconnection within the cingulo-opercular network in schizophrenia revealed by intrinsic functional connectivity analysis: a resting fMRI study. *Neuroimage, 59*(1), 238-247. doi:10.1016/j.neuroimage.2011.07.086

Tully, L. M., & Niendam, T. A. (2014). Beyond “cold” cognition: exploring cognitive control of emotion as a risk factor for psychosis. *Current behavioral neuroscience reports, 1*, 170-181.

Van Der Ven, E., & Selten, J.-P. (2018). Migrant and ethnic minority status as risk indicators for schizophrenia: new findings. *Current opinion in psychiatry, 31*(3), 231-236.

van der Ven, E., Susser, E., Dixon, L. B., Olfson, M., & Gilmer, T. P. (2020). Racial-Ethnic Differences in Service Use Patterns Among Young, Commercially Insured Individuals With Recent-Onset Psychosis. *Psychiatr Serv, 71*(5), 433-439. doi:10.1176/appi.ps.201900301

van Harmelen, A.-L., van Tol, M.-J., Demenescu, L. R., van der Wee, N. J., Veltman, D. J., Aleman, A., . . . Elzinga, B. M. (2013). Enhanced amygdala reactivity to emotional faces in adults reporting childhood emotional maltreatment. *Social cognitive and affective neuroscience, 8*(4), 362-369.

van Marle, H. J., Hermans, E. J., Qin, S., & Fernández, G. (2009). From specificity to sensitivity: how acute stress affects amygdala processing of biologically salient stimuli. *Biological Psychiatry, 66*(7), 649-655.

Van Marle, H. J., Hermans, E. J., Qin, S., & Fernández, G. (2010). Enhanced resting-state connectivity of amygdala in the immediate aftermath of acute psychological stress. *Neuroimage, 53*(1), 348-354.

Van Os, J., Hanssen, M., Bijl, R. V., & Ravelli, A. (2000). Strauss (1969) revisited: a psychosis continuum in the general population? *Schizophrenia research, 45*(1-2), 11-20.

Veling, W., Susser, E., van Os, J., Mackenbach, J. P., Selten, J. P., & Hoek, H. W. (2008). Ethnic density of neighborhoods and incidence of psychotic disorders among immigrants. *Am J Psychiatry, 165*(1), 66-73. doi:10.1176/appi.ajp.2007.07030423

Velligan, D., & Bow-Thomas, C. (1999). *Executive function in schizophrenia.* Paper presented at the Seminars in clinical neuropsychiatry.

Ventura, J., Subotnik, K. L., Gitlin, M. J., Gretchen-Doorly, D., Ered, A., Villa, K. F., . . . Nuechterlein, K. H. (2015). Negative symptoms and functioning during the first year after a recent onset of schizophrenia and 8 years later. *Schizophrenia research, 161*(2-3), 407-413.

Vijayakumar, N., Cheng, T. W., & Pfeifer, J. H. (2017). Neural correlates of social exclusion across ages: A coordinate-based meta-analysis of functional MRI studies. *Neuroimage,*

153, 359-368. doi:10.1016/j.neuroimage.2017.02.050

Von Frijtag, J. C., Reijmers, L. G., Van der Harst, J. E., Leus, I. E., Van den Bos, R., & Spruijt, B. M. (2000). Defeat followed by individual housing results in long-term impaired reward- and cognition-related behaviours in rats. *Behav Brain Res, 117*(1-2), 137-146. doi:10.1016/s0166-4328(00)00300-4

Wahlstrom, D., White, T., & Luciana, M. (2010). Neurobehavioral evidence for changes in dopamine system activity during adolescence. *Neuroscience & Biobehavioral Reviews, 34*(5), 631-648.

Walker, D. M., Bell, M. R., Flores, C., Gulley, J. M., Willing, J., & Paul, M. J. (2017). Adolescence and reward: making sense of neural and behavioral changes amid the chaos. *Journal of Neuroscience, 37*(45), 10855-10866.

Walker, E., Kestler, L., Bollini, A., & Hochman, K. M. (2004). Schizophrenia: etiology and course. *Annu Rev Psychol, 55*, 401-430. doi:10.1146/annurev.psych.55.090902.141950

Walther, S., Stegmayer, K., Federspiel, A., Bohlhalter, S., Wiest, R., & Viher, P. V. (2017). Aberrant hyperconnectivity in the motor system at rest is linked to motor abnormalities in schizophrenia spectrum disorders. *Schizophrenia bulletin, 43*(5), 982-992.

Wang, J., Huang, J., Yang, X.-h., Lui, S. S., Cheung, E. F., & Chan, R. C. (2015). Anhedonia in schizophrenia: Deficits in both motivation and hedonic capacity. *Schizophrenia research, 168*(1-2), 465-474.

Watt, M. J., Roberts, C. L., Scholl, J. L., Meyer, D. L., Miiller, L. C., Barr, J. L., . . . Forster, G. L. (2014). Decreased prefrontal cortex dopamine activity following adolescent social defeat in male rats: role of dopamine D2 receptors. *Psychopharmacology (Berl), 231*(8), 1627-1636. doi:10.1007/s00213-013-3353-9

Watt, M. J., Roberts, C. L., Scholl, J. L., Meyer, D. L., Miiller, L. C., Barr, J. L., . . . Forster, G. L. (2014). Decreased prefrontal cortex dopamine activity following adolescent social defeat in male rats: role of dopamine D 2 receptors. *Psychopharmacology, 231*, 1627-1636.

Webb, E. K., Bird, C. M., deRoon-Cassini, T. A., Weis, C. N., Huggins, A. A., Fitzgerald, J. M., . . . Torres, L. (2022). Racial discrimination and resting-state functional connectivity of salience network nodes in trauma-exposed Black adults in the United States. *JAMA network open*, *5*(1), e2144759-e2144759.

Werner, S., Malaspina, D., & Rabinowitz, J. (2007). Socioeconomic status at birth is associated with risk of schizophrenia: population-based multilevel study. *Schizophrenia Bulletin, 33*(6), 1373-1378.

Whaley, A. L. (1998). Cross-cultural perspective on paranoia: A focus on the Black American experience. *Psychiatric Quarterly, 69*, 325-343.

Whaley, A. L. (2001). Cultural mistrust: An important psychological construct for diagnosis and treatment of African Americans. *Professional Psychology: Research and Practice, 32*(6), 555.

Whitfield-Gabrieli, S., Thermenos, H. W., Milanovic, S., Tsuang, M. T., Faraone, S. V., McCarley, R. W., . . . LaViolette, P. (2009). Hyperactivity and hyperconnectivity of the default network in schizophrenia and in first-degree relatives of persons with schizophrenia. *Proceedings of the National Academy of Sciences*, *106*(4), 1279-1284.

Williams, D. R., Yu, Y., Jackson, J. S., & Anderson, N. B. (1997). Racial differences in physical and mental health: Socio-economic status, stress and discrimination. *Journal of health psychology*, *2*(3), 335-351.

Williams, S. M., & Goldman-Rakic, P. (1998). Widespread origin of the primate mesofrontal dopamine system. *Cerebral cortex (New York, NY: 1991), 8*(4), 321-345.

Woodward, N. D., Rogers, B., & Heckers, S. (2011). Functional resting-state networks are differentially affected in schizophrenia. *Schizophrenia research*, *130*(1-3), 86-93.

Yang, T.-C., & Chen, D. (2018). A multi-group path analysis of the relationship between perceived racial discrimination and self-rated stress: how does it vary across racial/ethnic groups? *Ethnicity & Health*, *23*(3), 249-275.

Yeo, B. T., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead, M., . . . Polimeni, J. R. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of neurophysiology*.

Yuan, L., Ma, X., Li, D., Li, Z., Ouyang, L., Fan, L., . . . He, Y. (2022). Abnormal Brain Network Interaction Associated With Positive Symptoms in Drug-Naive Patients With First-Episode Schizophrenia. *Frontiers in Psychiatry*, *13*, 870709.

Zelazo, P. D., & Carlson, S. M. (2012). Hot and cool executive function in childhood and adolescence: Development and plasticity. *Child Development Perspectives*, *6*(4), 354-360.

Zhang, B., Lin, P., Wang, X., Öngür, D., Ji, X., Situ, W., . . . Wang, X. (2019). Altered Functional Connectivity of Striatum Based on the Integrated Connectivity Model in First-Episode Schizophrenia. *Front Psychiatry*, *10*, 756. doi:10.3389/fpsyt.2019.00756

Zhang, F., Yuan, S., Shao, F., & Wang, W. (2016). Adolescent Social Defeat Induced Alterations in Social Behavior and Cognitive Flexibility in Adult Mice: Effects of Developmental Stage and Social Condition. *Front Behav Neurosci*, *10*, 149. doi:10.3389/fnbeh.2016.00149

Zung, W. W. (1971). A rating instrument for anxiety disorders. *Psychosomatics: Journal of Consultation and Liaison Psychiatry*.