



American Journal of Orthopsychiatry

Manuscript version of

Racial Disparities and Predictors of Functioning in Schizophrenia

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Funded by:

- National Institute of Mental Health
- US Department of Veterans Affairs, Office of Academic Affiliations

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Abstract

Black Americans are diagnosed with schizophrenia spectrum disorders at more than twice the rate of White individuals and experience significantly worse outcomes following diagnosis. Little research has examined specific factors that may contribute to worse functional outcomes among Black Americans diagnosed with schizophrenia. One approach to understanding why racial disparities emerge is to examine established predictors of functioning in this population: Neurocognition, social cognition, and symptom severity. The current study aims to broaden existing literature on racial differences within these domains by (1) examining racial differences in functioning and these established predictors of functioning (i.e., neurocognition, social, and symptom severity) and (2) investigating whether cognition and symptom domains similarly predict functioning between Black and White Americans with schizophrenia.

Sixty-six participants' baseline neurocognition, social cognition, symptom severity, and functioning were assessed. Black participants demonstrated lower neurocognition scores and higher levels of disorganized symptoms relative to White participants. No racial differences in functioning or social cognition were observed. Further, race did not moderate the relationship between any of these established predictors and functioning outcomes. The largely nonsignificant differences in known predictors of functioning highlight the need to further explore domains that may be more relevant for understanding racial disparities in schizophrenia. Considering that psychosocial treatments for schizophrenia spectrum disorders often focus on cognition, these results underscore the importance of identifying whether these domains or other treatment targets may be better in addressing racial disparities in functioning. Possible areas of exploration for future work (e.g., structural factors, racism-related stress) are discussed.

Public Policy Relevance

Black individuals are at greater risk for experiencing poorer functional outcomes once diagnosed with schizophrenia relative to White individuals. The findings of this study indicate a need to critically examine established predictors of functioning in schizophrenia (i.e., symptoms, social cognition, neurocognition) to better understand racial disparities in schizophrenia. This will importantly influence policy and treatment reform to better serve Black individuals suffering from schizophrenia spectrum disorders.

Keywords: Racial disparities, social cognition, neurocognition

Introduction

Black Americans are diagnosed with schizophrenia spectrum disorders at more than twice the rate of White individuals (Olbert, Nagendra, & Buck, 2018; Schwartz & Blankenship, 2014). After diagnosis, Black individuals fare worse than their White counterparts in various real-world outcomes (Eack & Newhill, 2012). Black Americans are also disproportionately exposed to various forms of racism such as interpersonal discrimination, reduced access to educational opportunities, and biased healthcare services (Lewis, Cogburn, & Williams, 2015; Maina, Belton, Ginzberg, Singh, & Johnson, 2018; D. R. Williams & Mohammed, 2013; S. A. Williams & Crockett, 2013). As such, it is understandable that Black individuals' experiences with schizophrenia may differ from White individuals in several domains because of these experiences. Evidence of these racial disparities in real-world outcomes among individuals with schizophrenia are demonstrated by greater number of hospitalizations (Eack & Newhill, 2012), higher rates of incarceration (Baillargeon, Binswanger, Penn, Williams, & Murray, 2009; Prince, Akincigil, & Bromet, 2007), higher rates of homelessness (Folsom et al., 2005; Nagendra, Schooler, et al., 2018), and lower employment rates (Rosenheck et al., 2006) for Black individuals compared to White counterparts. Such racial disparities are apparent in these realworld outcomes, yet it is unclear what specifically contributes to these disparities.

General functioning, which can refer to individuals' skills in social interactions, community living, occupational functioning, and daily living are strongly associated with the real-word outcomes mentioned above (Fett et al., 2011; Halverson, Orleans-Pobee, et al., 2019; Nagendra et al., 2020). Within the field of schizophrenia research, measures of functioning can encompass a variety of domains and constructs. For example, the Specific Levels of Functioning Scale (Schneider & Struening, 1983) is a commonly used rating scale in schizophrenia research that assesses real-world functioning within the domains of social, occupational, community, and general life skills (Harvey et al., 2011; Leifker, Patterson, Heaton, & Harvey, 2011). Of note, only two studies to date have explored differences in such measures of functioning between Black and White individuals with schizophrenia, with both showing no significant differences in this domain (Nagendra et al., 2020; Sabbag et al., 2015), suggesting a need for further investigation in this area.

Established Predictors of Functioning in Schizophrenia

On the other hand, several studies have focused on exploring racial differences in established *predictors* of functioning. Neurocognition, social cognition, and symptom severity are separable constructs that strongly predict functioning in schizophrenia (Fervaha, Foussias, Agid, & Remington, 2014; Fett et al., 2011; Halverson, Orleans-Pobee, et al., 2019; Rabinowitz et al., 2012; Shamsi et al., 2011). Several studies have documented racial differences in these domains. For example, in two studies of nationally-representative samples of individuals with schizophrenia, Black individuals performed worse on neurocognitive assessment batteries compared to White individuals, even after controlling for education and other sociodemographic factors (Keefe et al., 2006; Nagendra, Schooler, et al., 2018). Black individuals also tend to perform worse on social cognitive assessments, particularly tasks evaluating emotion perception and theory of mind abilities (Brekke, Nakagami, Kee, & Green, 2005; Pinkham, Kelsven, Kouros, Harvey, & Penn, 2017). Studies demonstrating differences in symptom severity are most common, with results suggesting higher prevalence rates of positive symptoms among Black individuals compared to White individuals (Adebimpe, Klein, & Fried, 1981; Barrio et al., 2003; Chu, Sallach, Zakeria, & Klein, 1985; Nagendra, Schooler, et al., 2018), while other studies indicate more negative symptoms among White individuals compared to Black individuals

(Fabrega, Mezzich, & Ulrich, 1988). Taken together, these studies provide evidence that racial disparities exist among these established predictors of functioning in schizophrenia. However, little research has investigated whether these domains predict functioning similarly across race.

Race as a moderator of Predictive Relationships with Functioning

In addition to potential racial differences in predictors of functioning and actual measures of functioning, it may also be that there are differences in the strength of the predictive relationships between these predictors and measures of functioning. Consequently, there might be other predictors that are greater contributors to the observed differences in real-world outcomes between Black and White individuals with schizophrenia. Preliminary evidence, based on a small number of studies, suggests that race may moderate the relationship between some of these predictors and measures of functioning in schizophrenia. For example, supplemental analyses from a meta-analysis indicated that more racially diverse samples showed weaker relationships between neurocognition and measures of functioning (Halverson et al., 2019). In contrast, findings from a meta-analysis conducted by Irani et al. (2012) revealed that more racially homogenous samples (e.g., higher percentage of White individuals) had weaker associations between emotion perception -a domain of social cognition -and functioning. Apart from these two studies, research investigating whether cognition and symptom domains similarly predict functioning between Black and White Americans diagnosed with schizophrenia is practically non-existent. Thus, an investigation of racial differences in these predictive relationships could contribute to the current literature by potentially identifying more relevant treatment targets (i.e., factors that are better predictors of functioning for Black individuals), and in turn, promote better real-world outcomes among Black individuals with schizophrenia.

As such, the present study examined racial disparities in (1a) functioning and (1b) previously established predictors of functioning: Neurocognition, social cognition, and symptom severity between Black and White individuals diagnosed with schizophrenia. Additionally, as an exploratory aim, this study (2) investigates whether race moderates the strength of the relationship between these predictors and functioning. Based on prior work, it was hypothesized that significant racial differences would exist in predictors of functioning (i.e., neurocognition, social cognition, and symptoms) between Black and White individuals, but not in functioning outcomes. Specifically, it was expected that Black individuals would demonstrate worse performance on measures of neurocognition and social cognition compared to White individuals. It was also expected that racial differences would exist in symptom severity. However, the variety of symptom domains and mixed findings from the existing literature in this area precludes a directionality hypothesis of these differences. Regarding the second aim of this study, it was hypothesized that neurocognition, social cognition, and symptom severity would each independently predict functioning. Further, it was expected that the strength of the relationship between these predictors and functioning would be moderated by race, but due to the exploratory nature of this aim, no hypotheses regarding the direction of the moderation were made.

Methods

Participants and Study Design

This study is a secondary data analysis of a double-blind, randomized controlled trial (RCT) conducted between June 2011 and September 2014 (NCT GOV Trial Number: NCT01394471). Primary RCT findings are detailed in Jarskog et al. (2017). Additional exploratory outcomes are also detailed in Halverson et al. (2019). Eligibility criteria included:

18–65 years of age; diagnosed with schizophrenia or schizoaffective disorder as determined by the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (SCID-IV; DSM-IV; American Psychiatric Association); duration of illness greater than one year; clinically stable outpatient status and receiving antipsychotic medication with no change in antipsychotic agents or dose for one month prior to study entry; concomitant medications were permitted (except as noted in exclusion criteria) if doses were unchanged for one month prior to entry. Women of childbearing potential had to use an acceptable method of birth-control. Additionally, to ensure baseline deficits in social functioning, participants had to score below 24 on Reading the Mind in the Eyes Test, a measure of theory of mind and emotion recognition (a score below 24 is 0.5 standard deviations below the mean in a large normative sample) or score greater than or equal to three on two or more of the following Positive and Negative Syndrome Scale (PANSS) items: suspiciousness/persecution, hostility, passive/apathetic social withdrawal, uncooperativeness, active social avoidance.

Exclusion criteria were as follows: Manic or hypomanic episode within the past two years for individuals with schizoaffective disorder; alcohol or substance abuse or dependence in the past three months (except caffeine or nicotine); simulant or chronic glucocorticoid use; unstable serious medical illness; major surgery/trauma in the past four months; pregnancy, childbirth in the past six months, or breast-feeding in the past three months; <fifth grade reading level on the Wide Range Achievement Test (WRAT).

While a total of 68 individuals were included in the initial study of Jarskog et al. (2017), the current study included 66 individuals (31 Black; 48 male), since two participants included in the original study identified as a race other than White or Black. All participants had a diagnosis of schizophrenia or schizoaffective disorder and identified as either non-Hispanic White or non-

Hispanic Black. Participants completed screening, baseline, and assessment visits at six and 12 weeks. Participants were randomized to twice-daily intranasal oxytocin or placebo stratified by sex and total PANSS score (see Figure 1 CONSORT diagram); However, only baseline data was analyzed in the current study. All participants provided written informed consent to participate in this study. All subjects participated voluntarily and received compensation for their time. The Biomedical Institutional Review Board of the University of North Carolina at Chapel Hill approved the procedures of this study (IRB #11-0259). For a comprehensive description of study methods and participant inclusion/exclusion criteria, see Jarskog et al. (2017).

Measures

Symptom Severity

Symptom severity was assessed with the Positive and Negative Syndrome Scale (PANSS). It is a 30-item interview-based measure conducted by a trained rater that assesses positive and negative symptoms of schizophrenia, as well as general psychopathology (Kay, Fiszbein, & Opler, 1987). The PANSS is subdivided into distinct subscales using the five-factor model (van der Gaag et al., 2006): Positive symptoms, negative symptoms, excitement, disorganized symptoms, and emotional distress symptoms. PANSS rater reliability was established through a training process in which research assistants were trained by the lead project coordinator until they reached 80% agreement on practice interviews. Additionally, the lead study coordinator would occasionally observe newer raters during study sessions with participants to ensure consistency in how the PANSS interview was conducted.

Neurocognition

Neurocognition was assessed using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, Tierney, Mohr, & Chase, 1998). The RBANS consists of 12 subtests that yield five index scores: Immediate Memory,

Visuospatial/Constructional, Language, Attention, and Delayed Memory. Index scores were age adjusted and standardized such that the normal mean was equal to 100 with a SD of 15, based on a normative sample (Randolph et al., 1998). Index scores were combined to form a total score, a summary measure of RBANS performance.

Social Cognition

Social cognition was assessed using both skills-based and bias-oriented tasks. Skillsbased tasks measure coordinated processing and assessment of external social situations, including correct interpretation of social situations, and thus have right or wrong answers. In contrast, bias-oriented tasks have no right or wrong answers, but rather assess individuals' automatic interpretation of imagined interpresonal scenarios and examine patterns of interpretations to identify social cognitive biases (Buck, Pinkham, Harvey, & Penn, 2016).

Skills-Based Social Cognition Measures.

The Eyes Task. The Reading the Mind in the Eyes Task (Eyes Task, Baron-Cohen et al., 2001) is a measure of theory of mind that requires participants to rapidly determine the mental state of another individual based solely on the eye regions of 36 different faces. Participants are asked to select the most fitting mental state from four possible options that are listed on the screen along with each eye image. Of note, all images are eyes of White faces. Performance is indexed by the total number correct (range 0-36).

ER-40. The Penn Emotion Recognition Task (ER-40; Kohler et al., 2003) assesses emotion perception abilities. Participants must correctly identify the emotional expression (Happy, Sad, Anger, Fear, or No Emotion) displayed for 40 different colored photos of faces

balanced for age, sex, and race. Performance is indexed by the total number of correctly identified emotions (range 0-40),

IPT-15. The Interpersonal Perception Task (IPT-15; Costanzo & Archer, 1989) is a measure of social perception processes. The measure consists of 15 video clips of common social interactions between 1-4 persons of diverse age, race, and gender. Each video clip is followed by a multiple choice question about the status of persons in the video (e.g., "who won the game?"), the accuracy of statements made about persons in the video (e.g., "which was the truth: the first or the second statement?"), or the level of intimacy between the persons in the video (e.g., how long have two in the video been dating, two weeks or two years?"). Performance was indexed via total number of accurate responses (range 0-15).

Bias-oriented Measures.

AIHQ. The Ambiguous Intentions Hostility Questionnaire (Combs, Penn, Wicher, & Waldheter, 2007) includes five second-person vignettes describing negative social situations with ambiguous causes (e.g., "you are walking by a group of young people who laugh as you pass by"). After reading the vignettes, participants are asked to rate the following on Likert scales: the intentionality of the other's action, how angry it would make the participant feel, and how much he or she would blame the other. Responses to each item are averaged across scenarios and summed to create an overall 'blame score.' Total scores range from three to 16 with higher scores indicating greater blame bias.

Trustworthiness Task. The Trustworthiness Task (Adolphs, Tranel, & Damasio, 1998) is an assessment of participants' immediate social judgements about the trustworthiness of a range of people from diverse gender and ethnic backgrounds presented via photographs. Participants rate trustworthiness of each individual presented on a scale of -3 (strongly distrust) to 3 (strongly trust). Scores range from -126 to 126, with lower scores indicating greater distrust bias.

Functioning

SLOF. Social functioning was assessed using the Specific Levels of Functioning Scale (SLOF; Schneider & Struening, 1983). This measure assesses functioning of individuals across multiple domains. The SLOF is a 30-item, five-point scale assessing a participant's behavior and functioning in four areas: interpersonal relationships, social acceptability, community activities, and work skills. Functioning was indexed by participants' total scores on two separate scales: self-report (SLOF-P) and informant-report (SLOF-I; e.g., parent, spouse/partner, caseworker). Scores ranged from 30 - 150 with higher scores indicating better functioning.

Statistical Analysis

Aim 1: Racial Differences in Predictors of Functioning

To assess baseline racial differences in functioning and predictors of functioning (i.e., neurocognition, social cognition, and symptom severity), univariate analyses of covariance (ANCOVA) and multivariate analyses of variance (MANOVA) were used. ANCOVAs with education as a covariate were used for all analyses involving functioning and cognition variables given established associations between education and cognitive ability, and functioning (McGurk & Meltzer, 2000; Ritchie, Bates, & Deary, 2015). Education was not included as a covariate for symptom severity analyses, as associations between education and symptoms have not been well-established in the literature.

To assess differences in functioning, two separate one-way ANCOVAs were conducted to compare differences in the SLOF-P and SLOF-I by race while covarying for education. Similarly, a one-way ANCOVA was conducted to compare differences in RBANS scores by race while covarying for education. To assess differences in social cognition, a composite score for skills-based social cognition tasks was created by calculating *z*-scores for each task and computing the mean for the Eyes, ER-40, and IPT (Nagendra, Twery, et al., 2018). For these three measures, the average ICC was .69, with confidence intervals between .50 and .79, p < .0001. ICCs between the social cognition bias-oriented tasks revealed no correlation between the AIHQ and Trustworthiness tasks, thus a bias-oriented composite was not computed, and these measures were analyzed separately. The skills-based composite score was entered into a one-way ANCOVA to assess differences in social cognition skills-based tasks by race, covarying for education. The AIHQ and Trustworthiness Task were also separately entered into a one-way ANCOVA covarying for education. Finally, to assess racial differences in symptom severity a MANOVA was conducted with the PANSS 5-factor subscales (positive, negative, disorganized, excited, and emotional distress symptoms) as the dependent variables and racial group as the independent variable. This analysis followed up with post hoc analyses adjusting for multiple comparisons via Bonferroni correction.

Aim 2: Race as a Moderator of Functioning

First, to examine the relationship between our predictors and functioning capacity, multiple linear regressions were conducted with all neurocognition, social cognition, and symptom variables entered simultaneously into the model as predictors and functioning measures entered as outcome variables. To explore whether race moderates the relationships between baseline predictors of functioning (i.e., social cognition, neurocognition, and symptoms) and baseline measures of functioning, a series of hierarchal regressions were conducted. For these regressions, each cognition or symptom variable (e.g., AIHQ) and racial grouping variable were entered first. Next, the interaction term of predictor and race (e.g., AIHQxRace) was then added to the model to assess whether moderation occurred. These analyses included the full sample where applicable, however, due to some missing data for the functioning measures, sample size varies for some analyses (see table notes for report of sample size for each analysis).

Results

Sociodemographic Characteristics

Independent samples *t*-tests and chi-squares were used to analyze racial differences among demographic and symptom variables as summarized in **Table 1**. There was a significant difference in years of education between White and Black participants, with White individuals (M = 13.66, SD = 1.99) completing more years of education compared to Black individuals (M =12.24, SD = 1.61, p < .05). Given existing research demonstrating associations between education and outcomes of interest (i.e., neurocognition and social cognition), education was entered as a covariate in subsequent analyses in which neurocognition or social cognition were outcomes.

Racial Differences in Functioning and Predictors of Functioning

There were no statistically significant differences between White and Black participants on either the SLOF-P (F(1, 51) = 4.07, p < .10, partial $\eta^2 = .07$) or SLOF-I (F(1, 32) = 3.56, p < .10, partial $\eta^2 = .10$). However, there was a statistical trend whereby Black participants had higher scores on both scales, indicating greater reported functioning.

White and Black participants significantly differed in scores on the RBANS after covarying for education, F(1, 55) = 12.38, p < .001, partial $\eta^2 = .19$, with White participants scoring higher than Black participants. There were no significant differences between racial groups in skills-based social cognition when controlling for education, p > .10. Regarding the social cognitive bias measures, there were no significant correlations between the AIHQ and Trustworthiness tasks, thus a bias-oriented composite was not computed, and these measures were analyzed separately. There were no significant differences between Black and White participants on the AIHQ nor Trustworthiness Task (ps > .10).

Regarding racial differences in symptom severity, there was a statistically significant difference between Black and White participants on the combined PANSS subscales, F(5, 56) = 2.4, p < .05; Wilk's $\Lambda = 8.2$; partial $\eta^2 = .18$. Post-hoc analyses revealed that on average, Black participants had higher scores of disorganized symptoms compared to White participants, F(1, 60) = 4.29, p < .05; partial $\eta^2 = .07$, but did not significantly differ from White participants on any other subscales or in total scores. See **Table 2** for a summary of racial group differences in functioning, cognition, and symptom variables, including a full report of adjusted means and standard errors.

Race as a Moderator of Functioning

A multiple regression was conducted to predict functioning as measured by the SLOF-P from the RBANS, AIHQ, Trustworthiness Task, SC skills composite, and total PANSS scores across the entire sample. The overall model was statistically significant, F(5, 51) = 3.83, p < .005, adj. $R^2 = .20$. Of note, the PANSS total score was the only predictor that significantly contributed to the model (B = -.38, p < .005). This indicates that there was a negative linear relationship between scores on the PANSS and the SLOF-P such that lower ratings of symptoms predicted higher functioning. The AIHQ and SC skills composite trended toward significance (B = -.55, p < .10, B = 3.7, p < .10 respectively), indicating that lower scores on the AIHQ and social cognitive skills tasks were associated with higher functioning. Neither the RBANS nor Trustworthiness Task scores contributed significantly to the model (all ps > .05). A second multiple regression was conducted with the SLOF-I as the outcome variable. The overall model

was not significant, F(5, 33) = 1.50, p > .05, adj. $R^2 = .06$. See **Table 3** and **Table 4** for full report of multiple regression analyses.

Though there were no significant main effects on functioning for most of our predictor variables, hierarchal multiple regressions were still conducted to explore the potential moderating effect of race on each cognition/symptom variable in predicting functioning. Results of these analyses revealed that race did not significantly moderate the effect of neurocognition, social cognition, or symptom severity on functioning as measured by the SLOF-P or SLOF-I, all ps > .05. However, the moderation effect of race on PANSS total symptoms predicting SLOF-I scores trended toward significance, F(3, 36) = 3.50, p < .10, $\Delta R^2 = .08$, adj. $R^2 = .16$. Specifically, there was a significant negative linear relationship between PANSS symptoms and functioning as measured by the SLOF-I among White individuals, such that lower ratings of symptoms predicted higher functioning, (b = ..61, SE = ..21, p < ..005); however, this relationship did not exist among Black individuals (b = .02, SE = ..25, p > ..05). See **Table 5** and **Table 6** for full report of these moderation analyses.

Discussion

This secondary analysis of baseline data from an RCT examined (1) racial differences in measures of functioning and established predictors of functioning (i.e., neurocognition, social cognition, and symptom severity); and (2) explored whether race moderated the strength of the relationship between these predictors and functioning. Regarding the first aim of this study, the hypothesis that significant racial differences would exist in established predictors of functioning between Black and White individuals was partially supported. Black individuals demonstrated lower neurocognitive performance relative to White individuals, even when covarying for education. The present findings replicate previous studies showing that Black individuals with

schizophrenia demonstrate lower scores on measures of neurocognition relative to White individuals (Keefe et al., 2006; Nagendra et al., 2020; Nagendra, Schooler, et al., 2018). Findings also replicate a robust body of research in nonclinical populations demonstrating similar trends of racial disparities in cognitive assessments; these previous studies highlight that disparities may be due to bias in assessment instruments (Berry, Clark, & McClure, 2011) and structural factors like income inequality (Zahodne, Manly, Smith, Seeman, & Lachman, 2017), rather than reflect true differences in cognitive ability.

Regarding symptom severity, Black participants were rated as having higher disorganized symptoms as measured by the PANSS. This finding complements previous work by Nagendra et al. (2018), which found that Black individuals with first-episode psychosis reported higher levels of disorganized symptoms relative to White individuals. Since the current sample comprised of individuals in a more chronic course of illness, the replication of Nagendra et al.'s (2018) finding suggests that this finding may be present across illness duration. No significant differences were observed among any other symptom subscales, despite previous findings showing racial differences in this domain. One potential reason for this discrepancy may be that prior studies have utilized different methods of assessing symptom severity. For example, some studies utilized item level analysis of PANSS items (Barrio et al., 2003; Monette, Lysaker, & Minor, 2021), rather than the five-factor model. Another explanation for discrepant findings may be the inclusion criteria restricting individuals in this study to being clinically stable, as previous studies have examined racial differences in symptoms within inpatient samples with more severe symptomatology (Adebimpe et al., 1981; Chu et al., 1985). Therefore, the present findings may primarily apply to clinically stable individuals with chronic schizophrenia.

Unlike with neurocognition and symptom severity, there were no statistically significant racial differences in functioning nor social cognition. While prior studies have found no racial differences in functioning (Nagendra et al., 2020; Sabbag et al., 2015), it is interesting to note that there was a trend-level difference demonstrating higher scores on the SLOF (both participant and informant-rated scales) among Black participants. The difference in scores on the informantrated SLOF may be related to differences in the nature of relationships between the participant and informant between Black and White participants. Specifically, White participants were more likely to have informants that were parents or romantic partners, while Black participants had a greater variety of informants that included parents, but also staff and service providers from community care settings, who may have different perceptions of functioning relative to close family members¹. The finding of trend-level racial differences on the participant-rated SLOF also aligns with findings from a recent study in which Black individuals with psychotic disorders self-reported less stigma and greater recovery relative to White individuals (Nagendra et al., 2022). However, this finding was only trending toward statistical significance, thus we make these interpretations cautiously. It is also possible that the eligibility criteria for this study that required participants to be at a clinically stable outpatient status may have limited the range of functioning the study sample; thus, it may be difficult to make generalizable conclusions about racial differences in this domain among non-stable, outpatient populations.

The lack of significant differences in social cognition contrasts with previous studies demonstrating racial differences in this domain among individuals with schizophrenia (Brekke et al., 2005; Monette et al., 2021; Pinkham et al., 2017). One reason for these null findings may again be related to the inclusion criteria and clinical characteristics required for eligibility for this study. A primary aim of the original RCT was to assess the effects of intranasal oxytocin on ¹For White participants, 84% of informants for the informant-rated SLOF were close family members (i.e., parents, partners, siblings), while only 46% of the informants for Black participants were close family members.

social cognition. As a result, individuals randomized to the study were required to either demonstrate impairment on social cognitive measures (i.e., score below a 24 on the Eyes Task – 0.5 standard deviation below the mean in a large normative sample) or they had to score three or greater on two of the following PANSS items: suspiciousness/persecution, hostility, passive/apathetic social withdrawal, uncooperativeness, and active social avoidance. Moreover, all participants were required to be clinically stable, with no recent changes to their antipsychotic medications. As such, this study selected for participants who were clinically stable and performed at relatively similar levels of impairment on social cognitive measures. These inclusion criteria may have subsequently reduced variation across racial groups and contributed to null results.

Regarding the second, exploratory aim of this study, it was hypothesized that (a) neurocognition, social cognition, and symptom severity would each independently predict participants' level of functioning and (b) the strength of the predictive relationship between these domains and functioning would be moderated by participants' race. Only the PANSS significantly predicted functioning, specifically for the participant-rated SLOF, with lower symptoms predicting higher functioning. However, the moderating effect of race only trended toward significance. In other words, for White individuals, lower ratings of symptoms predicted higher functioning did not exist among Black individuals.

This trend level finding suggests that the relationship between symptoms and functioning may operate differently between Black and White individuals. However, race did not moderate the relationship between any of the cognition variables and functioning outcomes. As such, perhaps the predictive relationship between these cognitive domains and functioning may be comparable among Black and White individuals with schizophrenia. Still, before this interpretation can be fully considered, it is important to note that the null results of these moderation analyses may have been due to issues with power. According to a power analysis conducted in G*Power (Faul, Erdfelder, Lang, & Buchner, 2007), a sample size of 395 participants would be required to be sufficiently powered (i.e., .80) to detect a small effect size using the moderation analyses employed in this study. Our sample size was significantly below this number given that this was a secondary data analysis study, and thus was underpowered. Because it is unlikely that a single study would be able to recruit a sample of this size with this specific population, an important follow up to the exploratory analyses in this study may be to combine multiple datasets that include symptom (and cognition) variables collected from Black and White individuals diagnosed with schizophrenia. With a larger sample size, future work may be able to make more substantive conclusions about whether these domains predict functioning similarly across racial lines.

Moreover, social cognition and neurocognition were not significantly predictive of functioning in the current sample. However, the predictive relationship between the AIHQ and SLOF-P, and SC skills composite and SLOF-P were trending toward statistical significance, with both having a negative linear relationship. The negative relationship between the AIHQ and SLOF-P is expected, as lower hostility bias is likely to allow for better functioning, especially in social contexts. However, the negative relationship between social cognition skills and the SLOF-P is less intuitive, as previous studies have shown that greater social cognitive abilities are predictive of better functioning in schizophrenia (Halverson et al. 2019; Fett et al. 2011). This somewhat paradoxical finding could possibly be an effect of the SLOF-P being a self-report measure in which participants may have rated their <u>perceived</u> level of functioning rather than <u>objective</u> ability. Consistent with this interpretation, those with greater social cognitive ability

may be more likely to discern and compare others' functioning abilities to their own (Swencionis and Fiske 2014), and thus may have been more likely to perceive themselves as lower functioning relative to other individuals. Of course, these findings were only trend-level, so this interpretation is speculative at best.

In terms of the null findings for all other cognition variables predicting functioning, differences in the measurement of cognition may explain why the present study results contrast with prior work. For example, neurocognition was assessed using a summary score on the RBANS, rather than looking at the individual domains that make up the battery (e.g., immediate memory, attention, language). To reduce Type 1 errors associated with multiple comparisons, the current study opted to utilize summary or composite scores when applicable, rather than conducting analyses at the level of individual domains. However, there may be advantages of exploring specific domains, as prior studies found that specific domains of neurocognition are linked to functioning as measured by the SLOF (Halverson, Orleans-Pobee, et al., 2019). Similarly, the use of a social cognition composite may have obscured relationships between social cognition domains and measures of functioning. As such, exploring the moderating effect of race in the relationship between cognition and functioning in a sample where these domains are significantly related is an important next step for this research.

In addition to further investigating whether established predictors of functioning (i.e., cognition and symptom severity) predict functioning similarly for both Black and White individuals, future research should identify additional domains that may be important to explaining racial differences in functional outcomes in schizophrenia. Indeed, it is possible that presentation of symptoms and cognitive performance may be negatively impacted by racism experienced by Black individuals. For example, greater experiences of interpersonal racism are

associated with more severe psychotic symptoms (Anglin et al., 2021; Oh, Yang, Anglin, & DeVykler, 2014). There is a robust literature establishing the role of stress exposure in the etiology of schizophrenia (Corcoran et al., 2003; Norman & Malla, 1993; Walker, Kestler, Bollini, & Hochman, 2004), as well as the negative relationship between exposure to stress and functioning among individuals with schizophrenia (Berger et al., 2018; Buonocore et al., 2019; Yanos & Moos, 2007). Additionally, Black individuals, as well as other racial/ethnic minority groups, may be more susceptible to experiencing stress relative to White peers due to interpersonal and systemic racism (Berger & Sarnyai, 2015; Brown, Mitchell, & Ailshire, 2020; Clark, Anderson, Clark, & Williams, 1999). Moreover, lack of investment in education in Black neighborhoods may impact performance on cognitive assessments. As such, cognitive performance and symptom severity may be weaker predictors of functioning relative to other, less explored factors (e.g., structural factors, stress associated with experiencing racism), for Black Americans diagnosed with schizophrenia.

Limitations

The current study had several limitations. First, this study utilized a subset of data from a larger RCT examining the effects of daily intranasal oxytocin on treatment outcomes in individuals with schizophrenia; this RCT was one of the largest oxytocin trials in schizophrenia when it was conducted, however, the study was not adequately powered for all outcomes (Jarskog et al., 2017). By extension, this secondary analysis was similarly underpowered given that it utilized a subset of individuals identifying as either Black or White, and the sample was also split roughly in half to analyze group differences by race. Likewise, a smaller percentage of our participants had an informant complete the SLOF-I (relative to the self-report, SLOF-P), which may have influenced the pattern of predictor variables across our outcome variables.

Moreover, because this study was not conducted with the intent to investigate racial differences in the domains explored in the present study, other relevant variables that may explain observed differences were not included (e.g., nuanced measure of SES, assessment of racism-related stress), limiting the ability to conduct a more definitive investigation of mechanisms contributing to racial disparities in functional outcomes in schizophrenia. Relatedly, the neurocognitive, social cognitive, and symptom measures used in this study need cross-cultural validation, thus complicating interpretations of any differences between races, as they may be related to cultural differences or bias in measurement.

Conclusion

Despite these limitations, the present study adds to the nascent work in this area by highlighting the need to further examine whether widely studied domains like cognition and symptom severity comparably predict functioning between Black and White individuals with schizophrenia. Additionally, future work should explore additional domains that explain racial disparities in functioning in individuals with schizophrenia. Research along these lines will be a critical steppingstone to address the long-standing inequities experienced by Black Americans with schizophrenia and may offer insight into more effective intervention and treatment targets for this underserved population.

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