BLACK AMERICANS AND SCHIZOPHRENIA: UNDERSTANDING RACIAL DISPARITIES IN FUNCTIONING

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ABSTRACT

Carrington C. Merritt: Black Americans and Schizophrenia: Understanding Racial Disparities in Functioning
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Black Americans are diagnosed with schizophrenia spectrum disorders at more than twice the rate of White individuals and experience significantly worse outcomes following the diagnostic event. Yet, little research to date has attempted to understand what specific factors contribute to worse functional outcomes among Black Americans with schizophrenia. The current study aims to broaden the current literature on such racial differences in functioning by using data from a double-blind, randomized treatment study to (1) examine baseline racial differences in established predictors of functioning (i.e., neurocognition, social cognition, and symptom severity); (2) investigate whether race moderates the strength of the relationship between these predictors and functioning at baseline; and (3) explore whether there are racial differences in the effectiveness of a novel psychopharmacological intervention of intranasal oxytocin in improving functioning among Black and White individuals with schizophrenia. Results revealed a significant difference in neurocognition at baseline as measured by the RBANS, with Black participants performing more poorly than White participants. No racial differences in measures of social cognition or symptom severity were observed. In addition, at baseline, race was found to moderate the relationship between PANSS-rated general symptoms and functioning measured by the SLOF but did not influence the relationship between other impact of oxytocin on functioning, social cognition, and symptom severity. Implications of

these findings and suggestions for future work aimed at understanding racial disparities in functioning among Black and White Americans with schizophrenia are discussed. Implications of these findings and suggestions for future work aimed at understanding racial disparities in functioning among Black and White Americans with schizophrenia are discussed.

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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 indices of functioning (Eack & Newhill, 2012). Given the systemic and structural inequality that disadvantages both Black individuals and individuals with mental illness (Lewis, Cogburn, & Williams, 2015 ; McGuire & Miranda, 2008 ; Merritt-Davis & Keshavan, 2006 ; D. R. Williams, Yan Yu, Jackson, & Anderson, 1997), it is understandable that Black individuals' experience with this disorder may differ from White individuals in several domains. Such racial disparities are evidenced by greater number hospitalizations (Eack & Newhill, 2012), higher rates of incarceration (Baillargeon, Binswanger, Penn, Williams, & Murray, 2009 ; Prince, Akincigil, & Bromet, 2007), homelessness (Folsom et al., 2005 ; Nagendra, Schooler, et al., 2018), and decreased employment rates (Rosenheck et al., 2006) for Black individuals with schizophrenia compared to White individuals with schizophrenia. Unfortunately, little research has attempted to understand what specific factors contribute to these poorer outcomes for Black individuals with schizophrenia. As such, the need for research in this area is long overdue.

Racial Differences in Predictors of Functioning

One way to better understand the factors contributing to these racial disparities is to examine factors that predict functional outcomes in this population. Numerous studies have shown that neurocognition, social cognition, and symptom severity are among the strongest predictors of 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). Additionally, a small number of studies have documented racial differences in these domains. Specifically, in two studies of nationally- representative samples of individuals with schizophrenia, Black individuals performed worse on neurocognitive assessment batteries compared to White individuals, even when controlling for patient 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 perhaps the most prevalent, with some suggesting higher prevalence rates of positive symptoms among Black individuals compared to Whites (Adebimpe, Klein, & Fried, 1981 ; Barrio et al., 2003 ; Chu, Sallach, Zakeria, & Klein, 1985 ; Nagendra, Schooler, et al., 2018), and others indicating more negative symptoms among White individuals compared to Blacks (Fabrega, Mezzich, & Ulrich, 1988). Taken together, these studies provide some evidence that racial disparities exist among important predictors of functioning in schizophrenia.

Despite these initial studies documenting racial differences in predictors of functioning, work in this area is still quite limited. Indeed, a systematic review by Nagendra et al. (2020) found that among 474 studies on schizophrenia published between 2014-2016 in top psychiatric journals, only *nine percent* of these studies included primary analyses by race (i.e., investigated racial differences in primary outcomes of the study). Further, this review, along with its predecessors by Lewine et al. (1999) and Chakraborty and Steinhaur (2010), indicates that many schizophrenia studies treat racial differences as something to be controlled for (i.e., a nuisance

variable) rather than investigating them as meaningful differences to be addressed (Nagendra, Orleans-Pobee, et al., 2020). As such, further research focused on exploring meaningful racial disparities in domains related to functioning is certainly needed.

In addition to better understanding racial disparities in critical predictors of functioning, it may also be useful explore how the strength of the association between these predictors and functioning vary by race. Indeed, a few studies have offered preliminary evidence that race moderates the relationship between some of these predictors and functional outcomes in schizophrenia. For example, supplemental analyses from the Halverson et al. (2019) meta-analysis indicated that more racially diverse samples showed weaker relationships between neurocognition and functional outcomes. 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 functional outcomes. With the exception of these two studies, research investigating how race moderates the relationship between established predictors of functioning in schizophrenia is practically non-existent. Yet, the findings of Halverson et al. (2019) and Irani et al. (2012) crucially suggest that race may moderate the links between these predictors and functioning, thus indicating a need to investigate the strength of these predictors across racial lines. Importantly, an investigation of racial differences in these predictive relationships would contribute to the current literature by identifying more relevant treatment targets (i.e., factors that are better predictors of functioning for Black individuals) and offering further insight into the distinctive needs of this more vulnerable group.

Racial Differences in Treatment Effectiveness

In addition to examining predictors of functioning, another way to enhance understanding of racial disparities in schizophrenia is to examine racial differences in the effectiveness of interventions designed to improve functioning. Currently, a majority of studies investigating racial differences in treatment of schizophrenia are limited to describing differences in the *types of treatments* prescribed (Chien, 2008 ; Kreyenbuhl, Zito, Buchanan, Soeken, & Lehman, 2003 ; Kuno & Rothbard, 2002 ; Nagendra, Schooler, et al., 2018) or level of *treatment engagement* (Oluwoye et al., 2018). Indeed, only a few studies have examined differences in the actual *effectiveness* of treatments between Black and White individuals (Emsley et al., 2002). Thus, it is unclear whether existing treatments are actually helpful in improving racial disparities in functioning. Given that several treatments are designed to either target the predictors described above or directly intervene on functioning, examining racial differences in the effectiveness of such treatments may be useful in identifying interventions that are better suited for addressing racial disparities in schizophrenia.

One potential intervention worthy of investigating racial differences in effectiveness is a novel psychopharmacological intervention, intranasal oxytocin is a neuropeptide associated with a host of psychological effects in both animals and humans, including increased positive social behavior and antipsychotic-like outcomes (Macdonald & Macdonald, 2010 ; Pedersen et al., 2011). The focus on intranasal oxytocin in the present study is motivated by several factors. First, many interventions for schizophrenia aimed at improving functioning often do so through social skills training (Kurtz & Mueser, 2008 ; Mueser, Deavers, Penn, & Cassisi, 2013), and while such training can be effective in improving functioning, it is also a time-intensive intervention. On the other hand, acute intranasal oxytocin administration has been found to

increase oxytocin concentrations in the brain (Born et al., 2002) and is associated with improvements in domains targeted by social skills training such as increased in positive social behavior (e.g., interpersonal trust, eye gaze) and improved social cognition (Davis et al., 2014 ; Macdonald & Macdonald, 2010 ; Pedersen et al., 2011). As such, oxytocin may be a promising alternative intervention that targets social deficits to improve functioning while also reducing the need for time-intensive skills training. Notably, this is kind of intervention could be particularly useful for Black individuals given research suggesting less treatment engagement and higher attrition among Black patients in long-term psychosocial treatments (Maura & Weisman de Mamani, 2017 ; Oluwoye et al., 2018).

Further, oxytocin has also been linked with enhanced stress regulation (Grimm et al., 2014 ; Olff et al., 2013). Both psychosocial and biological responses to stress can have critical impacts on the pathogenesis and maintanence of psychosis (Anglin et al., 2021 ; Berger et al., 2018 ; Corcoran et al., 2003). Thus, researchers have suggested that oxytocin is a promising therapeutic intervention for alleviating psychiatric symptoms associated with dysregulated stress reactivity (Martins et al., 2020 ; Olff et al., 2013). Along these lines, race-related stress (i.e., experiences of racism and/or discrimination) is a unique stressor experienced by members of marginalized racial/ethnic groups, especially Black Americans (Brown, Mitchell, & Ailshire, 2020 ; Clark, Anderson, Clark, & Williams, 1999 ; Goosby, Cheadle, & Mitchell, 2018). It is possible that experiences of race-related stress may be contributing to differences in outcomes between Black and White Americans with schizophrenia given the links between stress and the maintenance of psychopathology (Anglin et al., 2021 ; Berger et al., 2018). As such, treatments that directly intervene on stress regulation may have particular importance for Black Americans with schizophrenia. Though this study is unable to directly explore the impact of oxytocin on

stress regulation, an exploration of racial differences in the effects of oxytocin may offer initial insight into whether interventions targeting biological mechanisms of stress reactivity might be especially useful for Black Americans with schizophrenia.

Finally, while some studies have found ameliorative effects of intranasal oxytocin such as reduced psychotic symptoms and improved social cognition and stress regulation (Davis et al., 2014 ; Gibson et al., 2014 ; Olff et al., 2013 ; Pedersen et al., 2011), other studies have found marginal or null effects (Halverson, Jarskog, Pedersen, & Penn, 2019 ; Jarskog et al., 2017 ; D. Williams & Bürkner, 2017), thus indicating some inconsistency of this intervention. Indeed, using the same data that will be analyzed in this current study, Jarskog et al., (2017) previously found limited effects of oxytocin in improving functioning and some factors associated with functioning (i.e., negative symptoms), yet no effect on other correlates of functioning (i.e., social cognition). These mixed findings, along with the lack of previous research on racial differences in the effects of this intervention, suggest the need to investigate whether the effects of intranasal oxytocin on functioning may vary as a result of race among individuals with schizophrenia.

Aims of the Present Study

The present study seeks to examine potential contributors to the observed racial disparities in functioning between Black and White individuals with schizophrenia. To do so, we aim to (1) assess baseline racial differences in established predictors of functioning, including neurocognition, social cognition, and symptom severity among Black and White individuals with schizophrenia; and (2) examine whether race moderates the strength of the relationship between these predictors and functioning; (3a) investigate whether there are racial differences in the effectiveness of a novel psychopharmacological intervention of intranasal oxytocin in improving functioning; and (3b) in investigate whether there are racial differences in the effectiveness

intranasal oxytocin in improving secondary outcomes associated with functioning, specifically social cognition and symptom severity.

Hypotheses

It is hypothesized that significant racial differences will exist in predictors of functioning in schizophrenia between Black and White participants. Specifically, it is expected that Black participants will demonstrate worse performance on measures of neurocognition and social cognition compared to White individuals. It also expected that racial differences will exist in symptom severity. However, given the variety in symptom domains and mixed findings in existing literature in this area, specific predictions about the directionality of these differences are difficult to make.

(a) It is hypothesized that neurocognition, social cognition, and symptom severity will each independently predict participants' level of functioning and (b) the strength of the predictive relationship between these factors and functioning will be moderated by participants' race. Of note, aim 2b will be exploratory as it is not possible to make empirically supported predictions about the direction of this moderation at the moment. No specific hypotheses are being made for aim 3a or 3b as these are exploratory objectives of this study designed to examine whether significant racial differences in treatment outcomes of intranasal oxytocin exist.

METHOD

Participants and Study Design

Data for this study comes from a larger double-blind, randomized treatment study conducted between June 2011 and September 2014, thus all data collection has been completed (NCT GOV Trial Number: NCT01394471). Primary findings of this treatment study 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; duration of illness was 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 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.

Further, to ensure participants were functioning at a deficit level relative to a normative sample on primary outcome measures, participants had to score below a 24 on Reading the Mind in the Eyes Test (a theory of mind task; see below for details about this measure). This cutoff score was selected because a score below 24 is 0.5 standard deviation (SD) below the mean in a large normative sample. If participants scored above this cutoff on the Eyes Test, then they had to have a score of three or greater on the Positive and Negative Syndrome Scale (PANSS) items:

suspiciousness/persecution, hostility, passive/apathetic social withdrawal, uncooperativeness, active social avoidance in order to be eligible. All subjects provided written informed consent.

Exclusion criteria were as follows: Manic or hypomanic episode within the past 2 years for subjects with schizoaffective disorder; alcohol or substance abuse or dependence in the past 3 months (except caffeine or nicotine); simulant or chronic glucocorticoid use; unstable serious medical illness; major surgery/trauma in the past 4 months; pregnancy, childbirth in the past 6 months, or breast-feeding in the past 3 months; <5th 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), as two participants identified as a race other than White or Black. All participants had a diagnosis of schizophrenia or schizoaffective disorder. 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 CONSORT diagram adapted from Jarskog et al. (2017).

Intervention

Participants remained on their pre-study medications and doses over the course of the study. Intranasal study drug was self-administered twice daily (before breakfast and before dinner) for 12 weeks. Participants were trained on how to administer the spray prior to baseline and administration was also observed for accuracy at 2 and 6 weeks. Each dose consisted of six 0.1 mL insufflations (alternating every 30 seconds between the left and right nostril); each dose was approximately 24 international units of oxytocin (Syntocinon Spray, Novartis) or placebo

(containing all ingredients in Syntocinon Spray except oxytocin). This dose was selected based on efficacy in previous pilot studies (Gibson et al., 2014; Pedersen et al., 2011). Bottles containing study drug (50 mL solution) were weighed before dispensing to subjects and upon return. Bottle weights and a daily medication diary were used to assess drug adherence.

Measures

Symptom Severity

Symptom severity was assessed via the Positive and Negative Syndrome Scale (PANSS), a thirty-item measure of positive and negative symptoms of schizophrenia (Kay, Fiszbein, & Opler, 1987). Items were scored by a trained assessor on a scale from 1 (asymptomatic) to 7 (extremely symptomatic) via structured clinical interview and behavioral observations. Severity of symptoms was thus indexed by total scores for Positive, Negative, and General Symptom Subscales. The PANSS was administered at baseline, six, and 12 weeks.

Neurocognition

Neurocognition was assessed using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). The RBANS consists of 12 subtests that were used to calculate 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 an SD of 15, based on a normative sample (Randolph, Tierney, Mohr, & Chase, 1998). The index scores were combined to form the total score, a summary measure of RBANS performance. This battery has demonstrated solid psychometric properties for testing neurocognitive abilities of individuals with schizophrenia (Chianetta, Lefebvre, LeBlanc, & Grignon, 2008). The RBANS was administered at baseline and 12 weeks.

Social Cognition

Social cognition was assessed using a variety of measures that included both skills-based tasks and bias-oriented tasks. Skills-based tasks measure coordinated processing and assessment of external social situations. Further, skills-based tasks assess correct interpretation of such 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 interpersonal scenarios and examine patterns in such interpretations to identify social cognitive biases (Buck, Pinkham, Harvey, & Penn, 2016). Social cognitive assessments were conducted at baseline, six, and 12 weeks.

Skills-Based SC 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 one by one on a computer. Participants are asked to select the most fitting mental state from four possible options that are listed on the screen along with the eye image (i.e., "irritated", "joking", "flirtatious", "pensive"). Of note, all images are eyes of White faces. Performance is indexed by the total number correct. Possible scores range from 0-36. Comprehensive evaluation of the reliability and validity of this task has demonstrated sound psychometric properties, and it is considered a gold-standard measure of social cognition in schizophrenia (Browne et al., 2016 ; Pinkham et al., 2014 ; Pinkham, Harvey, & Penn, 2018).

***ER-40*.** The Penn Emotion Recognition Task (ER-40; Kohler et al., 2003) assesses emotion perception abilities. Participants must correctly identify what type of emotional expression (Happy, Sad, Anger, Fear, or No Emotion) is being displayed for 40 different colored photos of faces that are balanced for age, sex, and race. For each emotion, 4 of the pictures are

high intensity and 4 are low intensity. Performance is indexed by the total number of correctly identified emotions, with possible scores ranging from 0 to 40. The ER-40 is also considered a gold-standard measure of social cognition in schizophrenia with sound psychometric properties (Browne et al., 2016 ; Pinkham et al., 2014, 2018).

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 groups. 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; thus, scores could range from 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 scenario and summed to create an overall 'blame score.' Total scores range from 3 to 16 with higher scores indicating greater blame. Based on psychometric analysis, this tasks has been supported as a gold-standard for measuring social cognitive biases in schizophrenia (Buck et al., 2016).

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 bias toward distrusting others. Based on psychometric analysis, this tasks has also been supported as a gold-standard for measuring social cognitive biases in schizophrenia (Buck et al., 2016).

Functioning

Social functioning will be assessed using two different assessments, which were administered at baseline and 12 weeks.

SLOF. The Specific Levels of Functioning Scale (SLOF; Harvey et al., 2011) assesses functioning of individuals across multiple domains. The SLOF is a 30-item, five point, informant and self-rated scale of a participant's behavior and functioning in four areas: interpersonal relationships (e.g., initiating, accepting, and maintaining social contacts, effective communication), social acceptability (e.g., verbal and physical abuse, repetitive behaviors), participation in community activities (e.g., shopping, using the telephone, paying bills, use of leisure time, public transportation), and work skills (e.g., employable skills, punctuality, level of supervision needed). Performance was indexed by participant's total scores as rated by themselves and their informant on the 30-item scale.

SSPA. The Social Skills Performance Assessment (SSPA; Patterson et al., 2001) assesses competence in social functioning via roleplays. Due to the aims of the original study (Jarskog et al., 2017), only a modified version of the SSPA was administered to participants. Specifically, the modified SSPA consists of two 90-second roleplays. The first roleplay is an

unstructured conversation in which the research confederate plays the role of a new neighbor with whom the subject is instructed to strike up a conversation. In the second roleplay, the research confederate plays an upset friend with whom the subject is instructed to attempt to console. The roleplays are recorded and later rated on the following factors: Verbal social skill (e.g., content, clarity, fluency, asks questions), nonverbal social skill (e.g., gaze, involvement, meshing, appropriate affect, flat affect), and global social skill (e.g., social anxiety and overall social skill). Raters were trained to reliability by first watching several roleplays (from a previous study that used the same assessment) together with an advanced doctoral student, discussing their ratings and coming to a consensus. They then rated 20 role-plays on their own and reliability was calculated. Once they attained acceptable reliability (ICCs N 0.6), they were permitted to rate the roleplays from this study. Interrater reliability was calculated on the ratings of the first 39 videos of the schizophrenia sample completed by the coders; ICCs for all items were above 0.7 with the exception of Appropriate Affect (0.654). As such, performance was indexed via total ratings on each factor, which ranged from 1 to 5. Higher ratings indicate better social competence.

Statistical Analysis

Aim 1: Racial Differences in Predictors of Functioning

To assess baseline racial differences in predictors of functioning: neurocognition, social cognition, and symptom severity, univariate analyses of covariance (ANCOVA) and multivariate analyses of variance (MANOVA) were used. Specifically, for assessing differences in neurocognition, a one-way ANCOVA was conducted to compare differences in RBANS scores by race while controlling 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 interval 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 skill-based composite score was entered into a one-way ANCOVA to assess differences in social cognition skills-based tasks by race, controlling for education. The AIHQ and Trustworthiness Task were also separately entered into a one-way ANCOVA controlling for education. Finally, to assess racial differences in symptom severity a MANOVA was conducted with Positive, Negative, and General Symptom Subscales of the PANSS 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

To examine whether race moderates the relationships between baseline predictors of functioning and baseline measures of functioning, a series of moderated multiple regression models was conducted. For each cognition and/or symptom variable (e.g., AIHQ, PANSS Total score), a regression model was fitted predicting baseline functioning (e.g., SLOF) from the predictor and the dichotomous variable of race. An interaction term of predictorXrace (e.g., AIHQXrace) was then added as an additional independent variable to assess whether moderation occurred.

Aim 3: Racial Differences in Oxytocin Treatment Effectiveness

To explore racial differences in the effect of intranasal oxytocin on functioning and secondary outcomes associated with functioning (i.e., social cognition and symptom severity), longitudinal mixed models were used. In these models, change from baseline was the outcome,

with treatment group, race, and time, treatmentXrace, treatmentXtime, timeXrace, treatmentXtimeXrace, and baseline score for the outcome as predictors. Models were estimated for each outcome measure. An unstructured covariance pattern was specified for each model to account for correlations within each individual's responses across repeated measures. Change from baseline was estimated with least-squares mean. Imputation for missing data was not performed given a high degree of missingness and small sample size, which make model estimations unstable. For significant and trend-level findings, effect sizes were calculated using the quotient of least-squares mean and pooled standards deviation at baseline (i.e., Cohen's *d*). Given the exploratory nature of this study, outcome measures were not corrected for multiple comparisons.

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 were no significant differences between White and Black participants in age, gender, symptom onset age, duration of symptoms, nor history of substance abuse. However, 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), $p < .05$. Additionally, there were significant racial differences in diagnosis type ($\chi^2 = 12.09$, $p < .01$). A greater proportion of Black individuals received schizophrenia diagnoses (paranoid type and undifferentiated type) compared to White individuals. Conversely, a greater proportion of White individuals received schizoaffective diagnoses (depressed and bipolar) compared to Black individuals. Lastly, the racial difference in prior hospitalizations trended toward statistical significance with White individuals (M = 9.69. SD = 15.23) having a higher number of hospitalizations on average compared to Black individuals (M = 4.58, SD = 3.58), $p < .10$. Given existing research demonstrating associations between education and our 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 Predictors of Functioning

To assess differences in neurocognition, a one-way ANCOVA was conducted to compare differences in RBANS scores by race, controlling for education. White and Black participants

significantly differed in scores on the RBANS after controlling for education, F (1, 55) = 12.38, $p < .001$, with White participants scoring higher than Black participants.

A one-way ANCOVA was conducted to assess differences in social cognition skills-based tasks by race, controlling for education. There were no significant differences between racial groups in skills-based social cognition when controlling for education, $p > .10$.

In regard to social cognitive biases, 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 scores (ps > .10).

To assess racial differences in symptom severity, a one-way MANOVA was conducted with Total, Positive, Negative, and General Symptom Subscales of the PANSS as the dependent variables and racial group as the independent variable. There was a statistically significant difference in PANSS scores based on racial group, F (3, 60) = 3.07, $p < .05$, Wilk's $\Lambda = 0.87$, partial $\eta^2 = 0.13$. Post-hoc analyses revealed that the average scores on the PANSS positive symptom subscale trended toward statistical significance ($p = .09$), with Black participants having higher scores compared to Whites. However, no other significant differences between White and Black participants in baseline PANSS scores emerged. See **Table 2** for a summary of racial group differences in symptom and cognition variables, including full report of adjusted means and standard error. Though this aim was focused on assessing racial differences in established *predictors* of functioning, racial differences in baseline measures of functioning are also included in **Table 2**.

Race as a Moderator of Functioning

Prior to examining how race may act as a moderator, the relationship between neurocognition, social cognition, symptom severity and measures of functioning (i.e., informant and participant-rated SLOF and SSPA) were first evaluated via bivariate correlations as summarized in **Table 3**. In regard to neurocognition, there were no significant relationships observed between the RBANS and either of the functioning measures. In regard to social cognition, a significant negative relationship was observed between the AIHQ and the SLOF participant-rated scale, such that lower blame bias was associated with greater self-reported level of functioning. As for symptoms, significant negative relationships were also observed between the PANSS General and Total scales and the SLOF participant-rated scale. For both of these scales, lower ratings of symptoms were associated with higher self-reported level of functioning. Finally, a significant negative relationship was observed between PANSS General scale and the SLOF informant-rated scale, such that lower ratings of general symptoms was associated with higher informant-reported level of functioning (e.g., family member). No other significant relationships were observed between either SLOF participant-rated or informant-rated scales and the social cognition skills or other symptom variables. Additionally, no significant relationships were observed between the SSPA and any of the cognition or symptom variables (all *p*s > .10).

For each of the significant relationships described above, linear regressions were run to test whether the cognition and symptoms variables significantly predicted the associated functioning outcome. In regard to social cognition, the AIHQ was a significant predictor of the SLOF-patient-rated scale such that lower blame bias predicted higher self-reported functioning, F (1, 58) = 5.92, R^2 = .078, b = -0.722, SE = 0.28, p < .05. For the symptom variables, the PANSS Total scale significantly predicted self-reported level of functioning on the SLOF, with lower ratings of total symptoms predicting higher self-reported functioning, F (1, 58) = 10.76, R^2

$^{=}$ .144, *b* = -.379, SE = 0.116), *p* < .01. Finally, the PANSS General scale significantly predicted both self-reported (*F* (1, 58) = 11.90, $R^{2\,=}$ .158, *p* < .001) and informant-reported levels of functioning on the SLOF (*F* (1, 58) = 5.59, $R^{2\,=}$ .105, *p* < .05). Lower ratings of general symptoms predicted higher levels of self-reported (*b* = -.724, SE = .210, *p* < .001) and informant-reported functioning (*b* = -.716, SE = .303, *p* < .05).

Moderated multiple regression models were created for each of the significant predictive relationships between cognition/symptom variables (i.e., AIHQ, PANSS Total and General scales) and functioning measures (i.e., informant and participant- rated SLOF) reported above. Race moderated the effect of PANSS general symptoms on informant-reported level of functioning, *F* (3, 36) = 5.02, ΔR^2 = .103, *p* < .05. Specifically, there was a significant negative linear relationship between PANSS general symptoms and informant-reported level of functioning among White individuals, such that lower ratings of symptoms predicted higher functioning, (*b* = -1.29, SE = 0.389, *p* < .001); however, this relationship did not exist among Black individuals (*b* = .003, SE = 0.426, *p* = .99). Race did not moderate the relationship between any other cognition or symptom variables and functioning measures (for all ΔR^2s, *p* > .05).

To further explore the moderating role of race in the relationship between the PANSS general symptoms and the informant-rated SLOF, additional moderated regressions were conducted for the informant-rated SLOF subscales: Interpersonal Relationships, Social Acceptability, Activities, and Work Skills. Race moderated the relationship between the PANSS general symptoms and the Interpersonal Relationships subscale (*F* (3, 41) = 4.25, ΔR^2 = .096, *p* < .05). This moderation followed a similar patten as was found with the overall informant-rated SLOF. Specifically, there was a significant negative linear relationship between PANSS general

symptoms and informant-reported level of functioning in interpersonal relationships among White individuals, such that lower ratings of symptoms predicted higher functioning in interpersonal relationships, (b = -.331, SE = .167, p < .001); however, this relationship did not exist among Black individuals (b = .176, SE = 0.181, p = .34). Race was not a moderator of the relationship between the PANSS general symptoms and any other subscales of the informant-rated SLOF (for all ΔR^2s, p > .05).

Racial Differences in Oxytocin Treatment Effectiveness

Longitudinal mixed models were used to explore whether there were differences in the effect of intranasal oxytocin on functioning outcomes, social cognition, and symptom severity as a function of race. Among all functioning outcomes, there were no significant three-way interactions of treatmentXtimeXrace. In sum, there were no significant differences in the effect of treatment on functioning between Black and White participants across time (see **Table 4)**.

Among the social cognition variables, there was a significant three-way interaction of treatmentXtimeXrace, indicating a significant difference in the effect of treatment between Black and White participants on the IPT (p < .05, Cohen's d = 1.04; see **Table 5**). The change from baseline to 12 weeks between oxytocin and placebo groups for Black participants was significantly different from the change observed between oxytocin and placebo groups for White participants at this time point. While Black participants did not demonstrate between-group differences on the IPT at 12 weeks, White participants did demonstrate a between-group difference on this measure that was bordering statistical significance (p = .06, Cohen's d = -.60). Of note, this difference was trending in favor of the placebo group. Thus, White participants in the placebo group demonstrated improvement from baseline on the IPT (Cohen's d = .32), while White participants in the oxytocin group did not.

Among the PANSS scales, there was a significant three-way interaction of treatmentXtimeXrace, indicating a significant difference in the effect of treatment between Black and White participants on the PANSS positive symptom scale ($p < .05$, Cohen's $d = -.83$; see **Table 6**). The change from baseline to 6 weeks between the oxytocin and placebo groups for Black participants was significantly different from the change observed between oxytocin and placebo groups for White participants at this time point. For Black participants, there was not a statistically significant between-group difference in positive symptoms, though there was a significant within-group improvement among Black participants in the oxytocin group. In contrast, for White participants, there was a significant between-group difference, such that the placebo group demonstrated statistically significant improvement of positive symptoms ($p < .05$, Cohens $d = .24$) while the oxytocin group did not. There were no significant treatment differences as function of race for any other outcome measures; however, within each racial group, some measures demonstrated between-group changes by treatment group and within-group changes by treatment group. Given that these two-way interactions were not directly related to the primary research question, these results are not fully discussed here.

DISCUSSION

This study conducted secondary data analysis on a double-blind, randomized treatment study to **(1)** examine baseline racial differences in established predictors of functioning (i.e., neurocognition, social cognition, and symptom severity); **(2)** investigate whether race moderated the strength of the relationship between these predictors and functioning; and **(3)** explore whether there were racial differences in the effects of intranasal oxytocin in improving functioning, social cognition, and symptom severity among Black and White individuals with schizophrenia.

In regard to the first aim of this study, the hypothesis that significant racial differences would exist in established predictors of functioning between Black and White individuals at baseline was partially supported. Black participants demonstrated worse neurocognitive performance relative to White individuals, even when controlling for education. The present findings replicate previous studies showing that Black Americans with schizophrenia obtain lower scores on measures of neurocognition relative to Whites (Keefe et al., 2006 ; Nagendra, Halverson, et al., 2020 ; Nagendra, Schooler, et al., 2018). A robust body of research in nonclinical populations has also demonstrated similar trends of racial disparities in cognitive assessments, and have suggested that these 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).

Conversely, there were no significant racial differences in social cognition. 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, Lysaker, & Minor, 2021 ; Pinkham et al., 2017). One reason for this null finding may be due to how social cognition was measured in the present study. In an effort to reduce Type 1 errors associated with multiple comparisons, a social cognition skills composite score was created for participants that was comprised of scores on the Eyes Task, the ER-40, and the IPT. Previous studies looking at racial differences in social cognition focused on single measures of social cognition, thus the use of a composite score may have obscured significant group differences.

Additionally, no significant differences were observed among the symptom variables, with the exception of a trend-level difference in PANSS positive symptoms (i.e., Black participants being rated as having higher positive symptoms relative to Whites). Again, these insignificant results may be explained by the method of measuring symptoms used in the current study. Though previous studies have found Black/White differences in symptom severity, they have utilized different procedures for assessing symptoms. For example, some studies have used item level analysis of individual PANSS items (Barrio et al., 2003 ; Monette et al., 2021) , while others have used a five-factor model of the PANSS items to characterize symptoms (Nagendra, Schooler, et al., 2018). Moreover, other studies have used alternative instruments other than the PANSS to assess racial differences in symptoms (Adebimpe et al., 1981 ; Chu et al., 1985 ; Fabrega et al., 1988). The present study utilized the PANSS in its traditional form by assessing differences in total symptoms and the three subscales of positive, negative, and general symptoms, which may have contributed to the difference between the current findings and prior studies.

Another possible explanation for the null findings may be related to the inclusion criteria for the study. To ensure that individuals were functioning at a deficit level relative to a normative

sample, participants enrolled in this study had to score below a 24 on the Eyes Task (0.5 standard deviation below the mean in a large normative sample). If participants scored above this cutoff on the Eyes Test, then they had to have a score of three or greater on the following PANSS items: suspiciousness/persecution, hostility, passive/apathetic social withdrawal, uncooperativeness, active social avoidance in order to be eligible to participant in the study. As such, this study selected for participants that performed at relatively similar deficit levels on these measures. This may have subsequently reduced the amount of variation across racial groups. That said, it is also possible that the lack of significant racial differences in these known predictors of functioning (i.e., social cognition and symptom severity) indicates that other domains should be considered in exploring predictors relevant for understanding racial disparities in functional outcomes.

One domain that may be relevant for understanding racial disparities in functioning may lie in socioeconomic status (SES). Indeed, past studies of individuals with schizophrenia have established significant overlap between being Black and being of lower socioeconomic status (Nagendra, Schooler, et al., 2018 ; Rosenheck et al., 2006). Further significant associations have been found between SES, predictors of functioning, and real-world outcomes among individuals with schizophrenia. For example, SES has been found to partially mediate the relationship between race and neurocognition (Nagendra, Halverson, et al., 2020) and has been associated with greater risk for hospitalizations and reduced well-being in schizophrenia samples (Goldberg et al., 2011). Though the present analyses controlled for education level – a domain sometimes used to index SES – the current dataset did not include other commonly used indicators of SES such as income, occupational status, or poverty status (Diemer, Mistry, Wadsworth, López, & Reimers, 2013) that would allow for more sensitive exploration of SES differences by race. As

such, future work should explore the nuanced interplay between race and SES in effort to better understand racial disparities in functioning in schizophrenia.

In addition to SES, another domain that has received relatively little attention in existing research on racial disparities in schizophrenia, is stress exposure. While a robust literature exists describing the role of stress exposure in the etiology of schizophrenia (Corcoran et al., 2003 ; Norman & Malla, 1993 ; Walker, Kestler, Bollini, & Hochman, 2004), no studies to date have investigated stress as predictor that may relate to racial disparities in functioning in schizophrenia. Notably, a few studies have demonstrated a negative relationship between stress and functioning among schizophrenia patients (Berger et al., 2018 ; Buonocore et al., 2019 ; Yanos & Moos, 2007). Additionally, it is known that Black individuals, as well as other racial/ethnic minorities, may be more susceptible to experiencing stress relative to White peers due to interpersonal and systemic racism (Berger & Sarnyai, 2015 ; Brown et al., 2020 ; Clark et al., 1999). Taken together, these findings imply that exposure to stress may be a particularly relevant pathway by which Black Americans with schizophrenia experience poorer outcomes. Unfortunately, the current study was unable to assess whether Black participants experienced greater exposure to stress compared to Whites and how such differences related to measures of functioning, thus this may be a natural next step for future research.

In regard to the second the 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 factors and functioning would be moderated by participants' race. One measure of social cognition, the AIHQ, predicted functioning as measured by the SLOF, but this relationship was not moderated by race. The PANSS total and general symptoms subscale also predicted functioning as

measured by the SLOF, and race was found to moderate the relationship between PANSS general symptoms and informant-rated functioning measured by the SLOF. These analyses indicated that PANSS general symptoms were a significant predictor of informant-rated functioning for White participants, but not for Black participants.

This is the first study to demonstrate that race moderates the relationship between symptom severity and functioning among Black and White individuals with schizophrenia, which is notable given the strong relationship between symptomatology and functioning (Eack & Newhill, 2007 ; Ventura, Hellemann, Thames, Koellner, & Nuechterlein, 2009). Further, this finding offers evidence that established predictors of functioning in schizophrenia may not operate in the same way across racial lines. However, given that this was the only significant moderation by race, the present results largely suggest that the other social cognition and symptom variables (i.e., AIHQ, PANSS subscales) predict functional outcomes comparably in Black and White individuals.

It should be noted that significant predictive relationships were not observed between the neurocognition social cognition variables, with the exception of the AIHQ, which is in contrast to previous studies showing that neurocognition, social cognition are significant predictors of functioning outcomes (Fett et al., 2011 ; Halverson, Orleans-Pobee, et al., 2019). Once again, how these variables were measured in the present study may offer a potential explanation for these null results. For example, neurocognition was assessed using composite scores on the RBANS, rather than looking at the individual domains that make up the battery (e.g., immediate memory, attention, language, etc.) Prior studies have found that specific domains of neurocognition 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 the measures of functioning. As previously mentioned, total and composite scores were used to reduce Type 1 errors due to multiple comparisons. Nevertheless, these findings, along with those of the first aim, ultimately indicate the need to explore other domains that may better explain racial disparities in functional outcomes.

The final aim of this study was to determine whether there were racial differences in the effectiveness of intranasal oxytocin in improving functioning, social cognition, and symptom severity among Black and White individuals with schizophrenia. Ultimately, only one measure of social cognition, the IPT, and one subscale of symptoms, PANSS positive symptoms, showed differences as a function of race and treatment group over time. While Black participants showed no significant differences between oxytocin or placebo treatment at any time point, White participants in the placebo group exhibited a decrease in positive symptoms relative to White participants in the oxytocin group after 6 weeks of treatment. Following a similar trend, White participants in the placebo group exhibited improvement on the IPT relative to White participants in the oxytocin group after 12 weeks of treatment that bordered on statistical significance. As such, the present findings do not offer strong evidence of racial differences in the effectiveness of intranasal oxytocin as an adjunctive treatment for schizophrenia. Moreover, findings do not suggest that oxytocin significantly improves functioning, social cognition, or symptoms for either Black or White individuals with schizophrenia. These findings align with previous work, including the parent study from Jarskog et al. (2017), showing limited effects of oxytocin on these outcomes in schizophrenia (Halverson, Jarskog, et al., 2019 ; Martins, Paduraru, & Paloyelis, 2021).

Given these results, it is also possible that other domains should be considered when investigating the effects of oxytocin among Black individuals with schizophrenia. As previously

mentioned, stress exposure and reactivity may be an especially important domain to be considered in research among Black Americans with schizophrenia. However, a majority of the studies investigating the effects of intranasal oxytocin on individuals with schizophrenia have primarily focused on oxytocin-induced changes in social cognition and symptomology (Bradley & Woolley, 2017 ; Martins et al., 2021). Yet, some existing research offers promising insight into how oxytocin may produce more adaptive stress responding in healthy populations (see Olff et al., 2013 for a review). For example, studies in nonclinical samples have found that participants administered intranasal oxytocin responded to stressors with more adaptive physiological reactivity (i.e., reduced cortisol response, more efficient autonomic nervous system activity) relative to participants receiving a placebo (Kubzansky, Mendes, Appleton, Block, & Adler, 2012 ; Quirin, Kuhl, & Düsing, 2011). If oxytocin is able to produce similar enhancements in physiological responses to stress among individuals with schizophrenia, it may have important implications for recovery-related outcomes. Given this, future research could explore how oxytocin impacts stress-related psychophysiology, which could have indirect effects on functioning and recovery in schizophrenia.

Limitations

The current study had a number of limitations that should be considered. First, this study utilized a subset of data from a larger double-blind randomized controlled trial on the effects 12 weeks of daily intranasal oxytocin on treatment outcomes in people with schizophrenia, and while the original study was one of the largest oxytocin trials in schizophrenia to date, the study was still not adequately powered (Jarskog et al., 2017). This study was similarly underpowered given that it used an even smaller sample because some subjects from the overall sample were excluded if they did not identify as either Black or White and the sample was also

split roughly in half in order to look at group differences by race. Additionally, given the extended duration of this study, there was substantial missing data for the longitudinal analyses, thus reducing the sample sizes for these analyses as noted in tables 4-6. Due to this small sample size and high degree of missing data, the present study should be considered as exploratory. Moreover, because this dataset was not collected with the intent to investigate racial differences in the domains explored in the present study, other relevant variables that may explain any observed differences were not included (e.g., SES, general stress exposure, race-related stress exposure, etc.), consequently limiting the ability for a more nuanced investigate of mechanisms contributing to racial disparities in schizophrenia. Relatedly, the neurocognitive, social cognitive, and symptom measures used in the present have not undergone cross-cultural validation, thus complicating interpretations of differences between races, as they may be related to cultural differences.

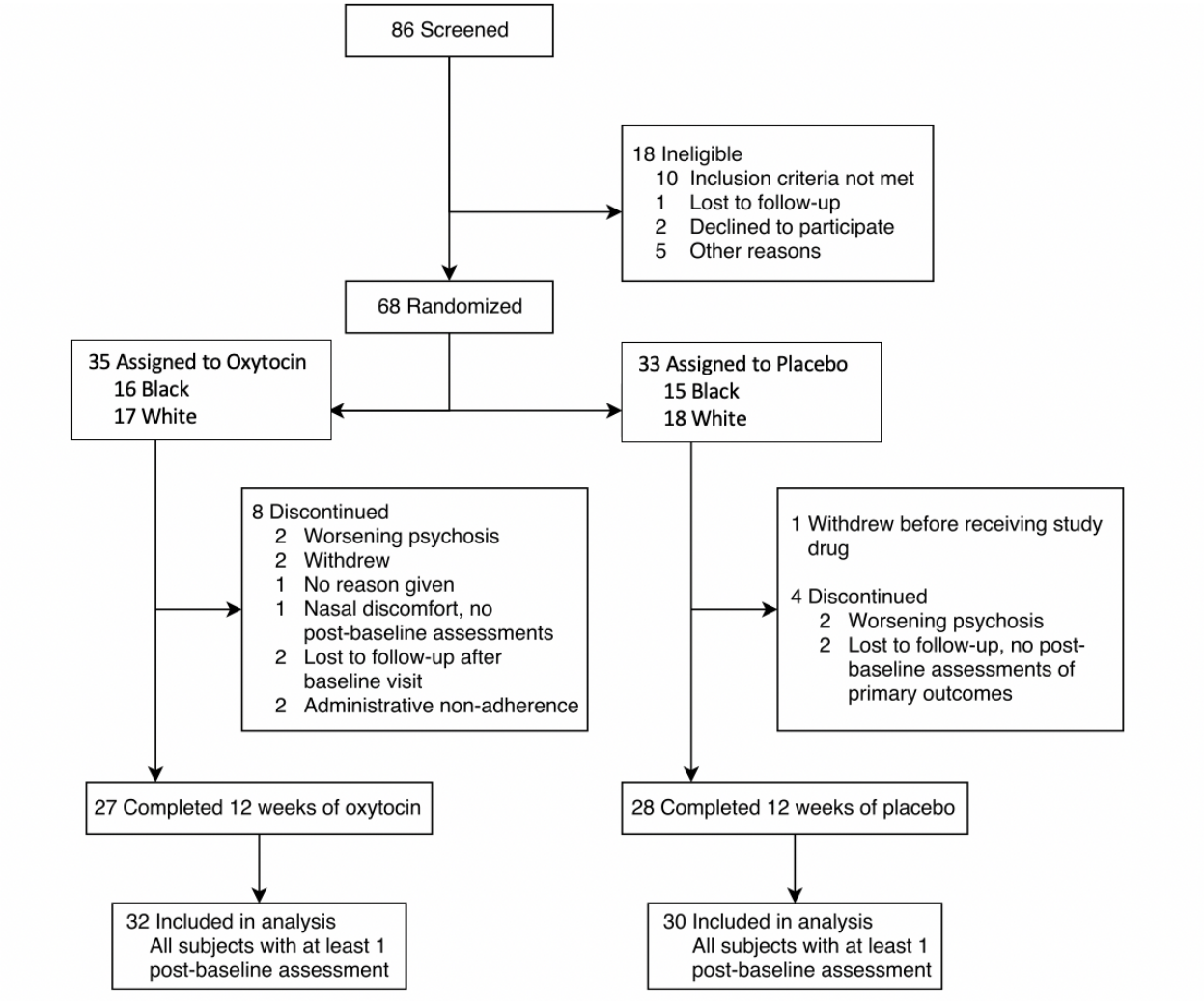
Conclusion

Given the well-documented disparities between Black and White Americans with schizophrenia, research exploring pathways through which these disparities manifest is of paramount importance. The present study adds to the growing work in this area by highlighting the need to investigate additional predictors of functioning beyond neurocognition, social cognition, and symptom severity and demonstrating that the relationship between some of these established predictors of functioning may vary depending on race. Additionally, this study provides evidence that racial differences largely do not exist in the effect of intranasal oxytocin on functioning, social cognition, and symptom severity. Future work should seek to continue to explore relevant domains in explaining racial differences in schizophrenia outcomes (e.g., SES, stress exposure), as well as investigate other extant treatments that may differentially impact

Black vs. White Americans with schizophrenia. Research along these lines will be a critical steppingstone in addressing 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**.**

FIGURES

Figure 1. Flowchart of study inclusion and data analysis adapted from Jarskog et al. (2017)



TABLES

Table 1. Sociodemographic Characteristics

Variable		Black M (SD) or % (N)		White M (SD) or % (N)
	N		N	
Age, M (SD)	31	38.55 (11.76)	35	41.66 (12.61)
Gender (male), % (N)	31	70.97 (22)	35	74.29 (26)
Years of Education, M (SD)*	31	12.23 (1.61)	29	13.66 (1.99)
Diagnosis, % (N)**	31		34	
Schizophrenia – Paranoid		64.52 (20)		38.23 (13)
Schizophrenia – Undifferentiated		16.13 (5)		2.94 (1)
Schizoaffective – Depressed		16.13 (5)		38.23 (13)
Schizoaffective – Bipolar		3.22 (1)		
Symptom Onset Age, M (SD)	30	22.80 (9.55)	33	21.76 (9.11)
Duration of Symptoms, M (SD)	30	15.73 (11.70)	33	20.42 (12.40)
Prior Hospitalizations, M (SD)†	31	4.58 (3.58)	35	9.69 (15.23)
History of Substance Abuse, % (N)	31	48.57 (13)	35	41.94 (17)

** $p < .01$, * $p < .05$, † $p < .10$

Table 2. Baseline Differences in Cognition and Symptom Variables by Race

Variable		Black, M (SE)		White M (SE)
	N		N	
Neurocognition[a]*	29	63.91 (2.01)	27	74.505 (2.09)
Social Cognition[a]				
Skills-Based Composite	29	-0.176 (0.15)	27	0.161(0.15)
AIHQ	28	12.50 (0.94)	28	12.86 (0.94)
Trustworthiness Task	29	8.13 (6.61)	28	15.78 (6.74)
PANSS[b]				
Positive Symptoms†	29	18.10 (5.24)	35	16.17 (3.37)
Negative Symptoms	29	18.24 (4.83)	35	17.57 (4.77)
General Symptoms	29	31.93 (6.50)	35	32.06 (5.84)
Total Symptoms	29	68.28 (10.88)	35	65.80 (11.56)
Functioning[a]				
SLOF-I Total†	15	126.18 (3.59)	20	116.92 (3.07)
SLOF-P Total†	27	133.83 (2.16)	27	127.43 (2.16)
SSPA GSS†	28	3.27 (0.11)	27	2.94 (0.11)

[a]Mean and standard error adjusting for group differences in education
[b]Unadjusted mean and standard deviation reported
** $p < .01$, * $p < .05$, † $p < .10$

Table 3. Bivariate Correlations of Baseline Predictors and Functioning Outcomes

	SSPA GSS	SLOF-I Total	SLOF-P Total	RBANS	SC Skills	AIHQ Blame Score	Trust-Worthiness Task	PANSS General	PANSS Positive	PANSS Negative	PANSS Total
RBANS	0.19	0.08	-0.07	1	0.38**	0.12	-0.03	-0.12	-0.12	-0.07	-0.14
SC Skills	0.05	-0.06	-0.11	0.38**	1	-0.07	-0.22	-0.16	-0.07	-0.03	-0.13
AIHQ Blame Score	-0.10	-0.02	-0.31*	0.12	-0.07	1	-0.14	0.14	0.04	0.10	0.13
Trust Task	-0.15	-0.20	0.03	-0.03	-0.22	-0.14	1	-0.03	-0.01	-0.02	-0.03
PANSS General	-0.19	-0.36*	-0.42**	-0.12	-0.16	0.14	-0.03	1	0.71**	0.19	0.91**
PANSS Positive	-0.01	-0.15	-0.23	-0.12	-0.07	0.04	-0.01	0.71**	1	-0.09	0.75**
PANSS Negative	-0.17	-0.17	-0.20	-0.07	-0.03	0.10	-0.01	0.19	-0.09	1	0.49**
PANSS Total	-0.17	-0.31	-0.40**	-0.14	-0.13	0.13	-0.03	0.91**	0.75**	0.49**	1

Abbreviations: SSPA GSS, Social Skills Performance Assessment Global Social Skill; SLOF-I, Specific Levels of Functioning Scale - Informant; SLOF-P, SLOF-Participant; AHIQ, Ambiguous Hostile Intentions Questionnaire; PANSS, Positive and Negative Syndrome Scale.
** $p < .01$, * $p < .05$, † $p < .10$

Table 4. Change from Baseline for Outcomes of Functioning

		Black							White						
		Oxytocin			*Placebo*				*Oxytocin*			*Placebo*			
Outcome variable	Time point (wk)	N	LS mean (SE)	P-value diff>0[a]	N	LS mean (SE)	P-value diff>0[a]	P-value Trt diff[b]	N	LS mean (SE)	P-value diff>0[a]	N	LS mean (SE)	P-value diff>0[a]	P-value Trt diff[b]	P-value Trt by Race[c]
SSPA GSS	12	10	-0.22 (0.15)	0.148	10	-0.03 (0.15)	0.839	0.374	12	-0.03 (0.14)	0.806	13	-0.20 (0.13)	0.143	0.397	0.222
SLOF-I Total	12	6	1.34 (3.80)	0.729	3	-3.62 (5.55)	0.521	0.469	9	2.26 (3.11)	0.477	8	0.57 (3.30)	0.865	0.712	0.690
SLOF-P Total	12	11	-4.30 (2.86)	0.140	8	-6.18 (3.47)	0.083†	0.678	13	-0.27 (2.64)	0.920	14	1.30 (2.56)	0.614	0.670	0.556

Abbreviations: LS, least squares; SSPA GSS, Social Skills Performance Assessment Global Social Skill; SLOF-I, Specific Levels of Functioning Scale - Informant; SLOF-P, SLOF-Participant. All models adjusted for baseline value.

[a] Test for within-group change by treatment group within racial group

[b] Test for between-group change by treatment group within racial group

[c] Test for between-group change by treatmentxrace group

** $p < .01$, * $p < .05$, † $p < .10$

Table 5. Change from Baseline for Outcomes of Social Cognition

		Black							White						
		Oxytocin			*Placebo*				*Oxytocin*			*Placebo*			
Outcome variable	Time point (wk)	N	LS mean (SE)	P-value diff>0[a]	N	LS mean (SE)	P-value diff>0[a]	P-value Trt diff[b]	N	LS mean (SE)	P-value diff>0[a]	N	LS mean (SE)	P-value diff>0[a]	P-value Trt diff[b]	P-value Trt by Race[c]
AIHQ Blame Score	6	10	1.20 (1.09)	0.279	11	0.76 (1.04)	0.471	0.771	16	-0.14 (0.87)	0.877	15	0.23 (0.90)	0.798	0.772	0.681
	12	10	1.30 (1.09)	0.241	11	-0.61 (1.04)	0.563	0.214	14	-1.44 (0.90)	0.118	15	-1.37 (0.90)	0.133	0.957	0.321
ER-40	6	11	0.91 (0.85)	0.288	11	1.84 (0.85)	0.035*	0.446	16	0.98 (0.70)	0.170	15	0.65 (0.74)	0.384	0.748	0.429
	12	11	-0.27 (0.85)	0.755	11	1.38 (0.85)	0.110	0.176	14	0.01 (0.74)	0.989	15	0.71 (0.74)	0.338	0.507	0.556
Eyes Task	6	11	-0.42 (0.98)	0.669	11	-2.89 (0.95)	0.004**	0.074†	16	-0.13 (0.79)	0.875	15	-0.10 (0.82)	0.905	0.981	0.162
	12	11	-0.97 (0.98)	0.328	11	-1.07 (0.95)	0.267	0.938	14	-0.52 (0.84)	0.540	15	0.90 (0.82)	0.280	0.229	0.396
IPT	6	11	0.24 (0.63)	0.707	10	-1.06 (0.65)	0.113	0.159	16	0.39 (0.52)	0.460	15	0.68 (0.53)	0.210	0.697	0.184
	12	11	-0.22 (0.63)	0.730	10	-1.36 (0.65)	0.043*	0.214	13	-0.70 (0.57)	0.228	15	0.81 (0.53)	0.135	0.060†	0.033*
Trustworthiness Task	6	11	-0.34 (6.93)	0.961	11	-13.90 (6.95)	0.051*	0.176	16	1.39 (5.72)	0.810	15	4.53 (5.92)	0.448	0.705	0.203
	12	11	2.75 (6.93)	0.694	11	1.10 (6.95)	0.875	0.868	14	-2.82 (5.98)	0.639	15	4.26 (5.92)	0.475	0.404	0.506

Abbreviations: LS, least squares; AHIQ, Ambiguous Hostile Intentions Questionnaire; ER-40, Penn Emotion Recognition Task; IPT, Interpersonal Perception Task. All models adjusted for baseline value.

[a] Test for within-group change by treatment group within racial group

[b] Test for between-group change by treatment group within racial group

[c] Test for between-group change by treatmentxrace group

** $p < .01$, * $p < .05$, † $p < .10$

Table 6. Change from Baseline for Outcomes of Symptoms

		Black							White						
		Oxytocin			*Placebo*				*Oxytocin*			*Placebo*			
Outcome variable	Time point (wk)	N	LS mean (SE)	P-value diff>0[a]	N	LS mean (SE)	P-value diff>0[a]	P-value Trt diff[b]	N	LS mean (SE)	P-value diff>0[a]	N	LS mean (SE)	P-value diff>0[a]	P-value Trt diff[b]	P-value Trt by Race[c]
PANSS General	6	11	-0.45 (1.44)	0.757	11	-3.00 (1.44)	0.043*	0.218	16	-0.97 (1.20)	0.423	15	-3.62 (1.23)	0.005**	0.129	0.968
	12	11	-0.72 (1.44)	0.619	11	-3.00 (1.44)	0.043*	0.270	14	-1.58 (1.26)	0.215	15	-2.82 (1.23)	0.0278	0.483	0.703
PANSS Negative	6	11	-1.05 (1.08)	0.337	11	-0.46 (1.07)	0.670	0.703	16	-1.65 (0.90)	0.072†	15	-0.65 (0.92)	0.486	0.448	0.843
	12	11	-1.14 (1.08)	0.297	11	-0.37 (1.07)	0.732	0.618	14	-0.74 (0.94)	0.438	15	-1.38 (0.92)	0.141	0.632	0.501
PANSS Positive	6	11	-1.97 (0.90)	0.033*	11	-0.99 (0.92)	0.286	0.443	16	0.27 (0.75)	0.717	15	-2.46 (0.77)	0.003**	0.014*	0.030*
	12	11	-2.52 (0.90)	0.007**	11	-0.90 (0.92)	0.332	0.209	14	-0.50 (0.79)	0.533	15	-1.60 (0.77)	0.045*	0.320	0.112
PANSS Total	6	11	-3.60 (2.58)	0.170	11	-4.22 (2.58)	0.108	0.864	16	-2.21 (2.14)	0.307	15	-7.01 (2.20)	0.003**	0.125	0.385
	12	11	-4.51 (2.58)	0.087†	11	-4.04 (2.58)	0.123	0.898	14	-2.59 (2.26)	0.258	15	-6.08 (2.20)	0.008**	0.274	0.415

Abbreviations: LS, least squares; PANSS, Positive and Negative Syndrome Scale. All models adjusted for baseline value.

[a] Test for within-group change by treatment group within racial group

[b] Test for between-group change by treatment group within racial group

[c] Test for between-group change by treatmentxrace group

** $p < .01$, * $p < .05$, † $p < .10$

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