8-1-2022

# Stability of Neurocognitive Abilities in Heterogeneous Subgroups of Schizophrenia

Megan L. Becker Wright

# STABILITY OF NEUROCOGNITIVE ABILITIES IN HETEROGENEOUS SUBGROUPS OF SCHIZOPHRENIA

By

Megan L. Becker Wright

Bachelor of Arts – Psychology
California State University
May 2013

Master of Arts – General/Experimental Psychology
California State University
December 2016

A dissertation submitted in partial fulfillment
of the requirements for the

Doctor of Philosophy–Clinical Psychology

Department of Psychology
College of Liberal Arts
The Graduate College

University of Nevada, Las Vegas
August 2022

UNLV | GRADUATE COLLEGE

## Dissertation Approval

The Graduate College
The University of Nevada, Las Vegas

October 21, 2021

This dissertation prepared by

Megan L. Becker Wright

entitled

Stability of Neurocognitive Abilities in Heterogeneous Subgroups of Schizophrenia

is approved in partial fulfillment of the requirements for the degree of

Doctor of Philosophy–Clinical Psychology
Department of Psychology

Daniel Allen, Ph.D.
*Examination Committee Chair*

Kimberly Barchard, Ph.D.
*Examination Committee Member*

Stephen Benning, Ph.D.
*Examination Committee Member*

Samantha John, Ph.D.
*Graduate College Faculty Representative*

Kathryn Hausbeck Korgan, Ph.D.
*Vice Provost for Graduate Education &*
*Dean of the Graduate College*

## Abstract

Considerable work has been devoted to characterizing the latent structure of cognition in schizophrenia (SZ) to understand important clinical outcomes associated with generalized or specific deficits but findings are limited in a number of ways. Previous work has not assessed bifactor and other complex models of cognition in SZ, which might provide a better understanding of the structure of cognitive abilities. It is also unclear whether the latent structure of cognitive abilities is similar between men and women with SZ or whether the latent structure of cognitive abilities is stable over time with repeated assessment. These limitations must be addressed before cognitive tests can be meaningfully interpreted in SZ, applied to investigate sex-based differences, or used longitudinally to judge changes in cognition in response to treatment and disease progression. To address these limitations, this dissertation conducted three studies aimed to: (I) assess a bifactor and other complex models of cognition in SZ, (II) compare the factor structure of men and women with SZ, and (III) examine the stability of the latent structure of cognition in SZ over repeated assessment. Each study used archival data from the National Institute of Mental Health Data Archive. The first study included 813 individuals with SZ who were divided into a baseline calibration sample ($n$ = 413) and a cross-validation sample ($n$ = 400). The second study examined whether the factor structure was the same (invariant) between men and women with SZ at a baseline assessment (men $n$ = 612; women $n$ = 201) and then again approximately two months later (men $n$ = 549; women $n$ = 198). The third study examined longitudinal invariance of the factor structure across four repeated assessments ($n$ = 205) that included a baseline assessment and follow up assessments that occurred approximately two, six, and 18 months later. Results of these studies indicated that a bifactor seven-factor model that includes one general factor and seven specific factors (Processing Speed, Phonemic

Fluency, Semantic Fluency, Reasoning, Working Memory, Verbal Memory, and Vigilance) best characterized the latent structure of cognition in SZ. The same bifactor seven-factor model was found to be invariant between men and women with SZ at two assessments. Subsequent comparison of the factor scores between men and women showed that women performed higher on Semantic Fluency, Verbal Memory, and General cognition, that men scored higher on Vigilance, and that there were no statistically significant differences between their performance scores on Processing Speed, Phonemic Fluency, Reasoning, and Working Memory. Further, the bifactor seven-factor model was longitudinally invariant across four assessments that spanned approximately 16.5 months. These results contribute to extant literature that has previously characterized cognition in SZ by demonstrating that cognition may be best understood by a more complex model that incorporates both general deficit and specific deficit conceptualizations. This model remained invariant between men and women allowing for direct comparisons of cognitive abilities and identification of a pattern of differences that was consistent with some prior literature. Finally, the longitudinal stability of the bifactor model suggests that tests are measuring equivalent latent constructs despite fluctuations in abilities that might be expected because of modifying factors of disorder state (e.g., symptoms, medication, course), and so can be appropriately used to investigate longitudinal changes in cognition.
*Keywords*: cognition, schizophrenia, factor analysis, bifactor, CATIE

## Table of Contents

Abstract ..... iii

List of Tables ..... vii

List of Figures ..... vii

Chapter I: Introduction ..... 1

Chapter II: Bifactor Model of Cognition in Schizophrenia: Evidence for General and Specific Abilities ..... 3

- Abstract ..... 5
- Introduction ..... 6
- Method ..... 10
- Results ..... 13
- Discussion ..... 14
- References ..... 20
- Supplementary Materials ..... 38

Chapter III: Latent Structure of Cognitive Tests is Invariant in Men and Women with Schizophrenia ..... 43

- Abstract ..... 46
- Introduction ..... 47
- Method ..... 49
- Results ..... 53
- Discussion ..... 55
- References ..... 59
- Supplementary Materials ..... 72

Chapter IV: Stability of bifactor structure of cognition in schizophrenia with repeated assessment ..... 77

Abstract ..... 80

Introduction ..... 81

Method ..... 83

Results ..... 87

Discussion ..... 88

References ..... 93

Supplementary Materials ..... 110

Chapter V: Conclusion ..... 113

Appendix A. IRB Exemption Letter ..... 117

Appendix B. Use of Previously Published Material ..... 118

Curriculum Vitae ..... 119

## List of Tables

Chapter II: Bifactor Model of Cognition in Schizophrenia: Evidence for General and Specific Abilities ..... 3

Table 1. Cognitive Domains Included from Previous Factor Analyses ..... 30

Table 2. Baseline Demographics of Calibration, Cross-Validation, and Total Sample ..... 31

Table 3. Scores Included in Factors ..... 33

Table 4. Results of Fit Indices Using Robust Methods with Standard Error Correction ..... 34

Supplementary Materials ..... 38

Chapter III: Latent Structure of Cognitive Tests is Invariant in Men and Women with Schizophrenia ..... 43

Table 1. Assessment 1 Demographics ..... 67

Table 2. Results of Fit Indices for Men and Women with SZ ..... 68

Table 3. Measurement Invariance of the Bifactor Seven-Factor Model ..... 69

Supplementary Materials ..... 72

Chapter IV: Longitudinal stability of the latent structure of cognition in schizophrenia ..... 77

Table 1. Baseline Demographics ..... 101

Table 2. Descriptive Statistics ..... 103

Table 3. Scores Included in Factors ..... 105

Table 4. Fit Indices of the Factor Models for Each Assessment ..... 106

Table 5. Factor Loadings for the Bifactor Seven-factor Model at Four Assessments ..... 107

Table 6. Measurement Invariance Estimates at Four Assessments ..... 109

## List of Figures

Chapter II: Bifactor Model of Cognition in Schizophrenia: Evidence for General and Specific Abilities ..... 3

Figure 1. Bifactor Seven-Factor Model for the Calibration and Cross-Validation Samples .... 36

Supplementary Materials ..... 38

Figure 1. Hierarchical Model Compared to Bifactor Model ..... 42

Chapter III: Latent Structure of Cognitive Tests is Invariant in Men and Women with Schizophrenia ..... 43

Figure 1. Bifactor Seven-factor Model Loadings for Men (M) and Women (W) at Assessments 1 and 2 ..... 70

Figure 2. Specific and General Standardized Factor Scores for Men (M) and Women (W) .... 71

## Chapter I: Introduction

Neurocognition in schizophrenia (SZ) has been the focus of much investigation because neurocognitive deficits are core features of the disorder and predict important clinical outcomes. The central role of neurocognitive deficits was apparent from early conceptualizations of SZ, which Kraepelin (1899) designated as dementia praecox or premature dementia. He identified SZ as a form of dementia because it was characterized by disordered intellectual functioning. However, unlike other forms of dementia, most individuals with SZ did not exhibit a progressive decline in cognitive abilities, and some demonstrated full recovery. Disordered cognition remained a hallmark feature of the disorder. The research available on disturbances in cognition and associated underlying neuropathology in SZ is now quite extensive, but significant questions remain unanswered.

First, there is an ongoing debate as to whether the neurocognitive deficits in SZ are generalized, (i.e., most or all cognitive abilities are negatively impacted) or whether there are differential profiles of deficits that would suggest neuropathology is confined to specific brain regions and neural circuits. Investigations of neurocognitive heterogeneity suggest variability in cognitive profiles of individuals with SZ, such that some individuals exhibit generalized deficits, whereas others have profiles characterized by deficits in some abilities with sparing of others. Second, studies investigating the latent structure of cognitive abilities in SZ have not established differences between men and women, although such differences might be anticipated given that other important differences between men and women with SZ are apparent (e.g., age of onset, severity of illness, severity of social and academic premorbid deficits). Similarly, the longitudinal stability of the latent structure of cognitive abilities has not been examined, although

changes in cognition due to symptom fluctuations, alterations in medication regimens, practice effects, and other factors might be expected to modify latent structure.

The three studies in this dissertation examine each of these three issues. The aim of the first study was to assess whether cognition in SZ was best characterized by a general latent construct, a number of specific latent constructs, or a combination of both general and specific constructs, and then to determine if the best model could be replicated. The second study examined the latent structure of cognitive abilities in a heterogeneous subgroup of SZ (men and women) to determine if the same model would best characterize the latent structure in both men and women at baseline and follow-up assessment, or if there were differences in latent structure based on binary sex. The third paper investigated whether the latent structure of cognitive abilities in SZ remained stable following four repeated assessments. This dissertation used data from the National Institute of Mental Health (NIMH) Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), which was a multi-site study conducted in the early 2000's and contains neurocognitive, symptom, laboratory test, genomic, and medication data for adults with SZ.

## Chapter II: Bifactor Model of Cognition in Schizophrenia: Evidence for General and Specific Abilities

Note: Study I was published in the *Journal of Psychiatric Research*.

Becker, M. L., Ahmed, A. O., Benning, S. D., Barchard, K. A., John, S. E., & Allen, D. N. (2021). Bifactor model of cognition in schizophrenia: Evidence for general and specific abilities. *Journal of Psychiatric Research*, *136*, 132-139. https://doi.org/10.1016/j.jpsychires.2021.01.051.

# BIFACTOR MODEL OF COGNITION IN SCHIZOPHRENIA: EVIDENCE FOR GENERAL AND SPECIFIC ABILITIES

Megan L. Becker[1]

Anthony O. Ahmed[2]

Stephen D. Benning[1]

Kimberly A. Barchard[1]

Samantha E. John[1]

Daniel N. Allen[1]

1. Department of Psychology, University of Nevada, Las Vegas, Las Vegas, NV

2. Department of Psychiatry, Weill Cornell Medicine, White Plains, NY

*Address correspondence to: Daniel N. Allen, Ph.D., Department of Psychology, University of Nevada Las Vegas, 4505 Maryland Parkway, Las Vegas, NV 89154. Phone: 702.895.0121. Fax: 702.895.0195. Email: daniel.allen@unlv.edu

Number of Tables: 4; Number of Figures: 1; Abstract Words (160); Manuscript Words 3,114)

**Abstract**

Background: Despite extensive study of cognition in schizophrenia, it remains unclear as to whether cognitive deficits and their latent structure are best characterized as reflecting a generalized deficit, specific deficits, or some combination of general and specific constructs. Method: To clarify latent structure of cognitive abilities, confirmatory factor analysis was used to examine the latent structure of cognitive data collected for the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) for Schizophrenia study. Baseline assessment data ($n$ = 813) were randomly divided into calibration ($n$ = 413) and cross-validation samples ($n$ = 400). To examine whether generalized or specific deficit models provided better explanation of the data, we estimated first-order, hierarchical, and bifactor models. Results: A bifactor model with seven specific factors and one general factor provided the best fit to the data for both the calibration and cross-validation samples. Conclusions: These findings lend support for a replicable bifactor model of cognition in schizophrenia, characterized by both a general cognitive factor and specific domains. This suggests that cognitive deficits in schizophrenia might be best understood by separate general and specific contributions

Student Contribution Statement: Megan Becker Wright's role on this manuscript included study conceptualization, data preparation, statistical analyses and interpretation, writing the first draft of the manuscript, and overseeing the revision process with coauthors.

## Introduction

Early conceptualizations of schizophrenia (SZ) as dementia praecox acknowledged SZ as a brain disorder with cognitive deficits as a core feature (Bleuler, 1908). Since then, an extensive literature has developed regarding neuropsychological deficits in SZ and other psychotic disorders. Some of the findings from this literature suggest 1) cognitive abnormalities in SZ include generalized and specific deficits; 2) there are substantial interindividual differences in pattern and severity of cognitive deficits (Allen et al., 2001; Heinrichs and Awad, 1993), and 3) cognitive deficits predict functional capacity and outcomes (Ahmed et al., 2015a; Fett et al., 2011; Kalache et al., 2015; Green et al., 2004, 2000). There has been substantial debate with regard to whether a generalized deficit or specific cognitive deficits are at the core of SZ, or if some combination of specific and generalized deficits best characterize the disorder. Specific deficit approaches have focused on identification of "differential deficits" or patterns of preserved and impaired abilities, the latter of which might reflect dysfunction of specific brain regions or circuits. Factor analysis of multidimensional first-order models has been extensively used to identify specific first-order cognitive dimensions assessed by neuropsychological tests in SZ and has produced marked variability across studies (Fioravanti et al., 2012). Variability among studies is likely due to differences in neuropsychological tests included in the analyses, whether exploratory or confirmatory approaches were used, and extent to which sample characteristics (e.g., clinical state, sex, age) and size vary across studies. However, some of the commonalities across studies are summarized in Table 1. Studies consistently identify Processing Speed, Executive Function/Reasoning, Working Memory, Verbal Memory, and Attention/Vigilance cognitive factors. Additional factors such as Crystallized Verbal abilities, Visual Learning and Memory, and Social Cognition have also emerged when measures for these

domains are included in analyses. Identification of these common cognitive domains provides support for the potential usefulness of neuropsychological tests to investigate differential deficits in SZ.

However, there have also been questions about the utility of various specific cognitive domains that are commonly identified in those with SZ, as opposed to composite scores that represent one or more general cognitive abilities (Bismark et al., 2018; Dickinson et al., 2004; Harvey et al., 2013; Heinrichs and Awad, 1993). Historically, early conceptualization of a general deficit model focused on a unitary disease process underlying cognition in SZ, albeit with differing expression, and a substantial literature has developed that documents impairment across most cognitive tests when SZ is compared to healthy controls (Heinrichs and Zakzanis, 1998; Dickinson et al., 2007). Studies indicating substantial shared variance between specific cognitive test scores also provide support for a common cognitive factor that accounts for the observed deficits across many specific domains (Dickinson et al., 2008a, 2008b). Measurement issues inherent in the tests present additional challenges to understanding specific neurocognitive deficits in SZ. For example, scores produced by neuropsychological tests typically are not pure indicators of a specific cognitive ability, but often reflect both lower- and higher-level abilties. Lower-level perceptual or motor deficits can impact higher order cognitive function, including working memory and executive function (Friedman and Miyake, 2017; Gold et al., 2018; Lesh et al., 2011). Some theorists posit that deficits in one domain may impact other domains, thereby resulting in the appearance of a general cognitive deficit (Heinrichs and Zakzanis, 1998; Green et al., 2013). Thus, factorial structure is likely impacted because general deficits across cognitive abilities resulting from impaired higher-level (e.g., executive function) cognitive processes may obscure the separation of specific cognitive domains (Hill et al., 2008). Hierarchical factor

analytic models provide support for a latent structure of cognitive abilities in SZ where first order specific cognitive factors load onto a higher order general factor (Dickinson et al., 2006, 2008b).

Despite this rather extensive work, there are still some important issues that require clarification regarding the latent structure of cognition in SZ. To date, first-order and hierarchical models served to test conjectures about the nature of a generalized cognitive deficit as a unitary disease process, the unique contributions of separate cognitive domains, and the contributions of generalized cognition indirectly through specific factors. From this work, hierarchical models gained increasing acceptance for their representation of the generalized deficit model in which certain test scores load on specific domains, which in turn load on a generalized deficit domain (Dickinson et al., 2006, 2008b; Heinrichs and Zakzanis, 1998). However the considerable heterogeneity across multiple aspects of pathology in SZ, including cognition, appears inconsistent with a unitary pathology generalized deficit model as well as specific deficit models identified using hierarchical and first-order factor analysis, respectively. Bifactor models of cognition offer an alternative to first-order and hierarchical models although they have not been tested in SZ (McCleery et al., 2015). Further, bifactor models may be useful for further elucidating the unique contributions of both general and specific deficits by allowing for their separation, unlike hierarchical models. Such a structure may better account for the cognitive heterogeneity demonstrated using cluster analysis and other classification approaches, which identifies subgroups of individuals with SZ who have distinct neurocognitive profiles. Some subgroups are differentiated by level of performance differences (e.g., average performance, impaired performance) while others display unique patterns of deficit and sparing (e.g., executive deficit subgroup, verbal memory deficit subgroup) (Allen et al., 2001; Heinrichs and

Awad, 1998; Goldstein, 1990; Seaton et al., 2001). Bifactor characterization may better account for individuals with unitary deficits and those with clearer separation of abilities, whether their abilities resemble cognition in healthy controls or deficits attributable to localized anatomical correlates. Further, a bifactor model would aid in determining if cognition in SZ is better understood with scores having direct latent contributions from a generalized deficit versus specific deficits, in comparison to previously examined indirect contributions of generalized deficit through specific domains. Thus, this comparison may provide new insight into cognition in SZ and possibly provide a more theoretically accurate representation of the latent structure of abilities (see Supplemental Figure 1) (Gignac, 2016). From a psychometric perspective, bifactor models require many more parameters to fit than hierarchical models. However, the hierarchical model imposes a proportionality constraint such that the ratio of general to group factor variance must be the same in each first-order factor; the violation of this constraint is why bifactor models fit better even accounting for their reduced parsimony (Gignac, 2016). The unique variance within general and group factors can be estimated directly in the bifactor model, whereas the proportionality constraint makes that kind of estimation untenable in hierarchical models.

Based on these considerations, the current study was conducted to extend research findings regarding latent structure of cognitive abilities in SZ by comparing first-order correlated factor models to hierarchical and bifactor models. Bifactor models were examined to further investigate the extent to which there was support for generalized and specific latent constructs. The hierarchical five-factor model conceptualized by Keefe et al. (2006) (Processing Speed, Verbal Memory, Working Memory, Reasoning, and Vigilance as the first-order factors loading onto the generalized second-order factor) was expected to provide the best fit of the data. Alternative models included a unitary model, to represent a generalized cognitive deficit, and

six- and seven-factor models. Six-factor models were selected based on known verbal fluency deficits in SZ, which separated Verbal Fluency measures from Processing Speed (Tyburski et al., 2015). Previous work has also noted differences in performance on verbal fluency measures among those with SZ, with greater impairment on semantic fluency tasks relative to phonemic fluency (Bozikas et al., 2005; Henry and Crawford, 2005; Phillips et al., 2004). Thus, a seven-factor model that split Verbal Fluency to further differentiate Semantic from Phonemic Fluency was also examined (see Table 3).

## Method

### *Participants*

The Clinical Antipsychotic Trials and Intervention Effectiveness (CATIE) study included 1,493 participants from multiple sites throughout the United States who had a DSM-IV diagnosis of SZ, and who were between the ages of 18 and 65, able to take oral medication, demonstrated adequate decision making, and provided informed consent (Keefe et al., 2006; Stroup et al., 2003). Of the original 1,493 participants, only individuals with complete cognitive data (excluding social cognition) at the baseline assessment were included in the analyses ($n$ = 839). Twenty-six additional participants were excluded because they were multivariate outliers according to a $p < .001$ cutoff for Mahalonobis distance. The final data set included 813 cases that were randomly split into two samples, one that served as a calibration group ($n$ = 413) and the other as a cross-validation ($n$ = 400) group. Demographic and descriptive data for these groups are presented in Table 2 and Supplemental Table 2, respectively. This study used deidentified archival data that were determined to be exempt by the local institutional review board for the protection of human subjects.

### *Measures*

The CATIE cognitive battery consists of the following measures: WRAT-III Reading Test (Wilkinson, 1993), Controlled Oral Word Association Test (COWAT) (Benton and Hamscher, 1978), Category Instances (Benton and Hamscher, 1978), Wechsler Intelligence Scale for Children Revised-Third Edition (WISC-III) Mazes (Wechsler, 1991), Hopkins Verbal Learning Test (HVLT-R) (Brandt, 1991), Face Emotion Discrimination Task (FEDT) (Kerr and Neale, 1993), Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol (Wechsler, 1974), Letter-Number Span Test (Gold et al., 1997), Grooved Pegboard (Lafayette Instrument Company, 1989), Computerized Continuous Performance Test-Identical Pairs (CPT-IP) (Cornblatt et al., 1998), Computerized Test of Visuospatial Working Memory (CTVWM) (Hershey et al., 1999), and a computerized, 64-card version of the Wisconsin Card Sorting Test (WCST) (Heaton et al., 1993). Although factor analytic studies have provided evidence that social cognition is a separate cognitive domain in SZ, social cognition measures were excluded from these analyses because those data were verified to be unacceptably skewed, which was also reported in prior work (Allen et al., 2007; Keefe et al., 2006).

***Procedures***

The CATIE Neurocognitive Assessment Training Unit trained staff in the protocols for data collection, editing, and transmission at each site. Assessment certification with a Neurocognitive Assessment Training Unit evaluator ensured that uniform testing occurred across sites and helped assessors anticipate responses to various challenges that might occur with testing (Keefe et al., 2003). The Neurocognitive Assessment Unit Data randomly audited the data entered from each site into a web-based system to verify and correct score entry. In addition to the baseline assessment examined in this study, cognitive data were collected at two, six, and 18

month timepoints, with data also collected if the study drug was switched or if the participant continued past 18 months.

***Data Analysis***

Data met the assumptions of confirmatory factor analysis regarding homoscedasticity and linearity. Parameter estimates were produced with conventional standard errors, as most variables did not violate normality, and those that did were corrected. Models evaluated in the current study are presented in Table 3. A unidimensional one-factor model was evaluated as an informed baseline model that hypothesized all test scores loaded on one general cognitive factor. The first-order five-factor model we evaluated was based on the report of Keefe et al., which reported a hierarchical model composed of five domain scores, including Processing Speed, Reasoning, Working Memory, Verbal Memory, and Vigilance factors (Keefe et al., 2006). A six-factor model separated Verbal Fluency from Processing Speed, based on studies of SZ that identified verbal fluency deficits (Tyburski et al., 2015). Finally, a seven-factor model split phonemic and semantic fluency into separate constructs, based on research suggesting that these two verbal fluency measures are differentially sensitive to cerebral dysfunction in SZ (Ojeda et al., 2010; Piras et al., 2019). In addition, hierarchical and bifactor models were examined for the five-, six-, and seven-factor models. Hierarchical models are consistent with the view that a generalized factor indirectly contributes to the latent structure of scores through specific domains. Bifactor models were included to test for separate latent contributions of general and specific factors, consistent with generalized versus specific ability conceptualizations of cognitive deficit in SZ.

All factor models were estimated in *Mplus* version 5 using maximum likelihood as an estimator (Muthén and Muthén, 2007). Overall model fit was assessed using several goodness-of-fit indices. These included the model chi-square, a test that indicates agreement between the model and the hypothesized model (Hu and Bentler, 1999). Because the chi-square is sensitive to sample size (i.e., chi-square may be significant for good fitting models if sample size is large), a number of other goodness of fit statistics were examined including the comparative fit index (CFI), root mean squared error of approximation (RMSEA), Akaike's information criterion (AIC), and the Bayesian information criterion (BIC). The CFI is an incremental fit index that is less sensitive to sample size than the chi square and compares the independence model to the hypothesized model (Bentler, 1990). The RMSEA is a parsimony adjusted index that evaluates the fit between the hypothesized model and the population covariance matrix (Steiger, 1990). The AIC and BIC were used to compare the relative fit of competing models. The AIC is a relative fit index of model parsimony that allows comparison between non-nested models by taking into account degrees of freedom in the model (Akaike, 1987). The BIC is also a relative fit index that has a stricter penalty for overparameterized models than the other indices used for these analyses (Vrieze, 2012). Model fit was considered good if CFI values were equal to or greater than .95, and RMSEA values were less than or equal to .06 (Hu and Bentler, 1999). Relative fit was determined by lower AIC and BIC values (Akaike, 1987; Dziak et al., 2020). All models were initially fit to the data in the calibration group, and the best fitting model was then evaluated in the cross-validation group.

## Results

Table 4 shows the goodness of fit indices for calibration and cross-validation models. As the table indicates, most of the models provided a poor fit of the data. The bifactor six-factor

model had good fit in the calibration group, although the bifactor seven-factor model provided the best fit in the calibration group based on all of the goodness of fist statistics. In this regard, both the AIC and the BIC were lowest for this model, indicating that despite its increased complexity, it provided a better fit of the data in comparison to the six-factor model. The bifactor seven-factor model was then estimated for the cross-validation group and goodness of fit statistics indicated excellent model fit.

Bifactor seven-factor models and factor loadings for the calibration and cross-validation groups are presented in Figure 1. As shown from the figure, most of the variables had strong loadings on their respective specific factors, with greater loading variability on the general factor, which is to be expected. WCST final sorts demonstrated low loadings on both factors, whereas other scores with low loadings on specific factors showed much higher loadings on the general factor (Digit Symbol, LNS, Mazes).

## Discussion

The purpose of this study was to examine the latent structure of cognitive abilities in SZ to determine whether bifactor models, consistent with generalized and specific cognitive deficits, might better explain the latent structure of neurocognition in SZ. A bifactor model was identified as the best fitting model in calibration and cross-validation samples. This model consisted of seven specific factors (Processing Speed, Phonemic Fluency, Semantic Fluency, Reasoning, Working Memory, Verbal Memory, and Vigilance) and one general factor. Processing Speed, Executive Function/Reasoning, Working Memory, Verbal Memory, and Attention or Vigilance are commonly identified as separable dimensions in the factor analytic literature (see Table 1). The preferred bifactor seven-factor model resulted from the separation of the Processing Speed construct into Processing/Motor Speed, Phonemic Fluency, and Semantic Fluency constructs.

The BIC, which is less biased toward overparameterized models suggested that the increased model complexity moving from five to seven factors did not account for the superior fit of the bifactor seven-factor model (Vrieze, 2012). Additionally, there is empirical support for this seven-factor model. For example, studies of SZ using cognitive scores have demonstrated more severe impairment in semantic fluency compared to phonemic fluency (Bozikas et al., 2005; Henry and Crawford, 2005; Phillips et al., 2004). There are also GABAergic mediated differences for the Verbal Fluency split, as those with SZ had higher cerebellar GABA concentrations and poorer performance on phonemic fluency relative to controls (Piras et al., 2019). Further, differences between semantic and phonemic processing in SZ have been observed in near-infrared spectroscopy (NIRS), as semantic tasks elicit greater frontal activation, which is opposite of healthy adults, and may indicate heightened task difficulty (Kubota et al., 2005). However, NIRS studies on Verbal Fluency have had mixed results (Koike et al, 2013).

The general factor was most strongly defined through tests of Processing Speed (Digit Symbol), Working Memory (LNS), and nonverbal reasoning (Mazes) in the calibration and cross-validation groups. This pattern suggests that the more generalized cognitive deficit in SZ is associated with impairment in these cognitive domains, which has the overall effect of producing more generalized decrements in performance across the seven specific cognitive factors. Working memory and executive function are reported to separately account for variance in general cognition in SZ, a finding that is consistent with the general factor identified here (Gold et al., 2018). Not only did Digit Symbol, LNS, and Mazes demonstrate high loadings on the general factor, they had low loadings on their specific factors, providing further support for the general factor having a greater influence on performance for these tests. The bifactor model is also consistent with multigroup factor analyses that report significantly higher factor loadings

and higher correlations between cognitive domains for those with SZ compared to controls, both of which suggest a more generalized latent structure of cognitive ability (Dickinson et al., 2006). Certainly, such results may be called broad rather than generalized as some have proposed, to allow for greater precision reflecting the overlap of some, but not the majority, of scores with latent contributions from this over-arching factor (Gold and Dickinson, 2013).

These results extend previous findings that reported superior fit of hierarchical models, as they provided direct comparison of a bifactor model to competing hierarchical and first-order models. To our knowledge, this is the first study to examine bifactor models of cognition in SZ. The results of this work suggest that the latent structure of cognition in SZ is characterized by both a general factor and specific factors. This finding may provide insight into the long-standing theoretical debate regarding a generalized cognitive deficit in SZ versus specific deficits. Studies examining cognitive heterogeneity in individuals with SZ suggest that a generalized deficit model is likely an oversimplification of cognition in SZ. These studies have identified average performing and impaired subgroups of individuals with SZ, which is consistent with a general factor influencing cognition. However, they have also identified subgroups of patients that exhibit unique differentiated cognitive profiles, with preservation of some abilities and impairment of others, a finding that is more consistent with specific ability conceptualizations of SZ cognition. Perhaps this lack of consensus regarding general and specific deficit models is predominantly due to failure to test models that incorporate separation of general and specific cognitive constructs, thereby providing only partial characterizations of cognition in SZ.

The current results should be interpreted with a number of limitations in mind. Despite acceptable goodness of fit statistics for the bifactor seven-factor model, some of the CATIE variables had low loadings on their respective factors, indicating such measures as Digit Symbol

and Mazes may only assess general cognitive functioning. Also, five of the seven factors were composed of scores from a single test, which may raise concerns about the contributions of method variance (rather than cognitive construct) driving the CFA results (Lesh et al., 2011). This limitation arises from the purpose of the testing conducted in the CATIE study, which precluded more comprehensive assessments that could include more than one measure for each of the cognitive constructs. It is likely that use of more or different tests would result in different latent structures for specific domains than the one identified here. However, this limitation does not diminish the main findings of consistency of latent bifactor structure between samples or conceptualizing the structure of cognition in SZ according to a general and more specific factors. It is also the case that we did not directly evaluate the relative contribution of the general and specific factors to overall performance on the cognitive tests. Some have suggested that a general factor accounts for most of the variance in cognitive test performance (Dickinson et al., 2008b). Although the findings of this study speak to a bifactor structure for the CATIE battery specifically, they suggest that follow-up studies should include batteries of tests aimed at assessing multiple domains with scores from more than one test comprising a given domain to better characterize cognition in SZ. Given that this sample was composed primarily of individuals in the chronic phase of illness, the results of this study may not generalize to populations at risk for psychosis or those with first episode psychosis. Additional investigation of a bifactor structure for SZ within these groups is warranted, as is further investigation of a bifactor cognitive structure for more diverse ethnoracial groups and those outside of the United States.

From a group level perspective, the bifactor structure identified here may provide additional insight into cluster analytic and latent class/profile analyses that have investigated

whether subgroups of individuals with SZ might be identified based on cognitive profiles (Goldstein, 1990; Lim et al., 2020; Seaton et al., 2001). These studies support investigation of cognitive subgroups in SZ that may differ in patterns of cognitive deficits, symptom profiles, morphological alterations, and clinical outcomes that can inform treatment choice and appropriate allocation of resources (Goldstein, 1990; Lim et al., 2020; Seaton et al., 2001). A bifactor structure represents a purely dimensional representation of cognitive heterogeneity in SZ. It remains unknown if the unveiled bifactor structure is valid for all putative cognitive subgroups. Factor mixture modeling is a latent variable modeling approach that combines factor analysis with latent class/profile analysis and has seen application in the study of SZ heterogeneity (Ahmed et al., 2015b, 2018; Miettunen et al., 2016). It could thus allow for a closer approximation of the heterogeneity of cognitive deficits in SZ by simultaneously capturing cognitive dimensions and subgroups reported in other studies. The flexibility of this approach would be particularly useful for determining if the bifactor structure co-exists with, and is invariant across non-arbitrary subgroups.

This bifactor characterization of cognition in SZ supports the differentiation of score profiles. For instance, some people with SZ may show deficits across multiple domains (e.g., processing speed, semantic fluency, reasoning, verbal memory, and vigilance) consistent with a generalized deficit. Others may demonstrate deficits within a distinct domain such as processing speed that, once accounted for, explains deficits in performance across other tests. Still others may show impaired scores across nearly all domains with even more profound impairment in specific domains (such as phonemic fluency and working memory) that would indicate a combination of generalized and specific deficits. Nevertheless, some people with SZ who do not show cognitive deficits and are otherwise “average performing” would still show minor

variations in test scores around a typical level of functioning. When interpreting test scores, this bifactor characterization provides evidence for examining both composite scores and scores that are more directly linked to specific cognitive deficits, as opposed to interpreting only composite scores. This interpretive method would aid in detecting an individual's unique pattern of performance and level of deficit, if present. Future studies may examine the relationship between a broad or generalized factor and various functional outcomes in SZ as well as investigate the relative contributions of specific domains to cognitive and functional deficits in order to determine if bifactor models are more useful for predicting outcomes than first-order or hierarchical models.

**Acknowledgments**

Data and/or research tools used in the preparation of this manuscript were obtained from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) for Schizophrenia database from the National Institute of Mental Health (NIMH) Data Archive (NDA). NDA is a collaborative informatics system created by the National Institutes of Health to provide a national resource to support and accelerate research in mental health. *[NIMH Data Archive DOI: 10.15154/1519574]*. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or of the Submitters submitting original data to NDA.

## References


Ahmed, A. O., Hunter, K. M., Goodrum, N. M., Batten, N.-J., Birgenheir, D., Hardison, E., Dixon, T., & Buckley, P. F. (2015). A randomized study of cognitive remediation for forensic and mental health patients with schizophrenia. *Journal of Psychiatric Research*, *68*, 8–18. https://doi.org/10.1016/j.jpsychires.2015.05.013

Ahmed, A. O., Strauss, G. P., Buchanan, R. W., Kirkpatrick, B., & Carpenter, W. T. (2015). Are negative symptoms dimensional or categorical? Detection and validation of deficit schizophrenia with taxometric and latent variable mixture models. *Schizophrenia Bulletin*, *41*(4), 879–891. https://doi.org/10.1093/schbul/sbu163

Ahmed, A. O., Strauss, G. P., Buchanan, R. W., Kirkpatrick, B., & Carpenter, W. T. (2018). Schizophrenia heterogeneity revisited: Clinical, cognitive, and psychosocial correlates of statistically-derived negative symptoms subgroups. *Journal of Psychiatric Research*, *97*, 8–15. https://doi.org/10.1016/j.jpsychires.2017.11.004

Akaike, H. (1987). Factor analysis and AIC. In *Selected papers of Hirotugu Akaike* (pp. 371-386). Springer, New York, NY.

Allen, D. N., Goldstein, G., & Weiner, C. (2001a). Differential neuropsychological patterns of frontal- and temporal-lobe dysfunction in patients with schizophrenia. *Schizophrenia Research*, *48*(1), 7–15. https://doi.org/10.1016/S0920-9964(00)00115-8

Allen, D. N., Goldstein, G., & Weiner, C. (2001b). Differential neuropsychological patterns of frontal- and temporal-lobe dysfunction in patients with schizophrenia. *Schizophrenia Research*, *48*(1), 7–15. https://doi.org/10.1016/S0920-9964(00)00115-8

Allen, D. N., Strauss, G. P., Donohue, B., & van Kammen, D. P. (2007). Factor analytic support for social cognition as a separable cognitive domain in schizophrenia. *Schizophrenia Research*, *93*(1–3), 325–333. https://doi.org/10.1016/j.schres.2007.02.008

Bentler, P. M. (1990). Comparative fit indexes in structural models. *Psychological Bulletin*, *107*(2), 238–246. https://doi.org/10.1037/0033-2909.107.2.238

Benton, A. L., & Hamscher, K. (1978). Multilingual Aphasia Examination Manual (revised) Iowa City. *IA: University of Iowa*.

Bleuler, E. (1908). Die Prognose der Dementia praecox (Schizophrenie-Gruppe). *Allg Z f Psychiat Psychisch-Gerichitliche Medizin*, *65*, 436-464.

Bismark, A. W., Thomas, M. L., Tarasenko, M., Shiluk, A. L., Rackelmann, S. Y., Young, J. W., & Light, G. A. (2018). Reverse translated and gold standard continuous performance tests predict global cognitive performance in schizophrenia. *Translational Psychiatry*, *8*(1), 80. https://doi.org/10.1038/s41398-018-0127-5

Bozikas, V., Kosmidis, M., & Karavatos, A. (2005). Disproportionate impairment in semantic verbal fluency in schizophrenia: Differential deficit in clustering. *Schizophrenia Research*, *74*(1), 51–59. https://doi.org/10.1016/j.schres.2004.05.001

Brandt, J. (1991). The Hopkins verbal learning test: Development of a new memory test with six equivalent forms. *Clinical Neuropsychologist*, *5*(2), 125–142. https://doi.org/10.1080/13854049108403297

Burton, C. Z., Vella, L., Harvey, P. D., Patterson, T. L., Heaton, R. K., & Twamley, E. W. (2013). Factor structure of the MATRICS consensus cognitive battery (Mccb) in schizophrenia. *Schizophrenia Research*, *146*(1–3), 244–248. https://doi.org/10.1016/j.schres.2013.02.026

Cornblatt, B. A., Risch, N. J., Faris, G., Friedman, D., & Erlenmeyer-Kimling, L. (1988). The continuous performance test, identical pairs version (Cpt-ip): I. new findings about sustained attention in normal families. *Psychiatry Research*, *26*(2), 223–238. https://doi.org/10.1016/0165-1781(88)90076-5

Dickinson, D., & Gold, J. M. (2007). Less unique variance than meets the eye: Overlap among traditional neuropsychological dimensions in schizophrenia. *Schizophrenia Bulletin*, *34*(3), 423–434. https://doi.org/10.1093/schbul/sbm092

Dickinson, D., Iannone, V. N., Wilk, C. M., & Gold, J. M. (2004). General and specific cognitive deficits in schizophrenia. *Biological Psychiatry*, *55*(8), 826–833. https://doi.org/10.1016/j.biopsych.2003.12.010

Dickinson, D., Ragland, J., Calkins, M., Gold, J., & Gur, R. (2006). A comparison of cognitive structure in schizophrenia patients and healthy controls using confirmatory factor analysis. *Schizophrenia Research*, *85*(1–3), 20–29. https://doi.org/10.1016/j.schres.2006.03.003

Dickinson, D., Ragland, J. D., Gold, J. M., & Gur, R. C. (2008). General and specific cognitive deficits in schizophrenia: Goliath defeats David? *Biological Psychiatry*, *64*(9), 823–827. https://doi.org/10.1016/j.biopsych.2008.04.005

Dickinson, D., Ramsey, M. E., & Gold, J. M. (2007). Overlooking the obvious: A meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. *Archives of General Psychiatry*, *64*(5), 532. https://doi.org/10.1001/archpsyc.64.5.532

Dziak, J. J., Coffman, D. L., Lanza, S. T., Li, R., & Jermiin, L. S. (2020). Sensitivity and specificity of information criteria. *Briefings in Bioinformatics*, *21*(2), 553–565. https://doi.org/10.1093/bib/bbz016

Fett, A.-K. J., Viechtbauer, W., Dominguez, M.-G., Penn, D. L., van Os, J., & Krabbendam, L. (2011). The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: A meta-analysis. *Neuroscience & Biobehavioral Reviews*, *35*(3), 573–588. https://doi.org/10.1016/j.neubiorev.2010.07.001

Fioravanti, M., Bianchi, V., & Cinti, M. E. (2012). Cognitive deficits in schizophrenia: An updated metanalysis of the scientific evidence. *BMC Psychiatry*, *12*(1), 64. https://doi.org/10.1186/1471-244X-12-64

Friedman, N. P., & Miyake, A. (2017). Unity and diversity of executive functions: Individual differences as a window on cognitive structure. *Cortex*, *86*, 186–204. https://doi.org/10.1016/j.cortex.2016.04.023

Gignac, G. E. (2016). The higher-order model imposes a proportionality constraint: That is why the bifactor model tends to fit better. *Intelligence*, *55*, 57–68. https://doi.org/10.1016/j.intell.2016.01.006

Gladsjo, J. A., McAdams, L. A., Palmer, B. W., Moore, D. J., Jeste, D. V., & Heaton, R. K. (2004). A six-factor model of cognition in schizophrenia and related psychotic disorders: Relationships with clinical symptoms and functional capacity. *Schizophrenia Bulletin*, *30*(4), 739–754. https://doi.org/10.1093/oxfordjournals.schbul.a007127

Gold, J. M. (1997). Auditory working memory and Wisconsin card sorting test performance in schizophrenia. *Archives of General Psychiatry*, *54*(2), 159. https://doi.org/10.1001/archpsyc.1997.01830140071013

Gold, J. M., & Dickinson, D. (2013). "Generalized cognitive deficit" in schizophrenia: Overused or underappreciated? *Schizophrenia Bulletin*, *39*(2), 263–265. https://doi.org/10.1093/schbul/sbs143

Gold, J. M., Robinson, B., Leonard, C. J., Hahn, B., Chen, S., McMahon, R. P., & Luck, S. J. (2018). Selective attention, working memory, and executive function as potential independent sources of cognitive dysfunction in schizophrenia. *Schizophrenia Bulletin*, *44*(6), 1227–1234. https://doi.org/10.1093/schbul/sbx155

Goldstein, G. (1990). Neuropsychological heterogeneity in schizophrenia: A consideration of abstraction and problem-solving abilities. *Archives of Clinical Neuropsychology*, *5*(3), 251–264. https://doi.org/10.1016/0887-6177(90)90024-J

Green, M. F., Kern, R. S., Braff, D. L., & Mintz, J. (2000). Neurocognitive deficits and functional outcome in schizophrenia: Are we measuring the "right stuff"? *Schizophrenia Bulletin*, *26*(1), 119–136. https://doi.org/10.1093/oxfordjournals.schbul.a033430

Green, M. F., Kern, R. S., & Heaton, R. K. (2004). Longitudinal studies of cognition and functional outcome in schizophrenia: Implications for MATRICS. *Schizophrenia Research*, *72*(1), 41–51. https://doi.org/10.1016/j.schres.2004.09.009

Harvey, P. D., Raykov, T., Twamley, E. W., Vella, L., Heaton, R. K., & Patterson, T. L. (2013). Factor structure of neurocognition and functional capacity in schizophrenia: A multidimensional examination of temporal stability. *Journal of the International Neuropsychological Society*, *19*(6), 656–663. https://doi.org/10.1017/S1355617713000179

Heaton, R. K. (1981). Wisconsin card sorting test manual. *Psychological assessment resources*.

Heinrichs, R. W., & Awad, A. G. (1993). Neurocognitive subtypes of chronic schizophrenia. *Schizophrenia Research*, *9*(1), 49–58. https://doi.org/10.1016/0920-9964(93)90009-8

Heinrichs, R. W., & Zakzanis, K. K. (1998). Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. *Neuropsychology*, *12*(3), 426–445. https://doi.org/10.1037/0894-4105.12.3.426

Henry, J., & Crawford, J. (2005). A meta-analytic review of verbal fluency deficits in schizophrenia relative to other neurocognitive deficits. *Cognitive Neuropsychiatry*, *10*(1), 1–33. https://doi.org/10.1080/13546800344000309

Hershey, T., Selke, G., Fucetola, R., & Newcomer, J. W. (1999). Spatial long-term memory but not working memory decreases over time in schizophrenia. In *Society for Neuroscience Abstracts* (Vol. 25, No. Part 1, p. 572).

Hill, S. K., Sweeney, J. A., Hamer, R. M., Keefe, R. S. E., Perkins, D. O., Gu, H., Mcevoy, J. P., & Lieberman, J. A. (2008). Efficiency of the CATIE and BACS neuropsychological batteries in assessing cognitive effects of antipsychotic treatments in schizophrenia. *Journal of the International Neuropsychological Society*, *14*(02). https://doi.org/10.1017/S1355617708080570

Hu, L., & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling: A Multidisciplinary Journal*, *6*(1), 1–55. https://doi.org/10.1080/10705519909540118

Instrument, L. (1989). Grooved pegboard: instruction/owner's manual. *Lafayette Instrument*.

Kalache, S. M., Mulsant, B. H., Davies, S. J. C., Liu, A. Y., Voineskos, A. N., Butters, M. A., Miranda, D., Menon, M., Kern, R. S., & Rajji, T. K. (2015). The impact of aging, cognition, and symptoms on functional competence in individuals with schizophrenia across the lifespan. *Schizophrenia Bulletin*, *41*(2), 374–381. https://doi.org/10.1093/schbul/sbu114

Keefe, R. S. E., Bilder, R. M., Harvey, P. D., Davis, S. M., Palmer, B. W., Gold, J. M., Meltzer, H. Y., Green, M. F., Miller, D. D., Canive, J. M., Adler, L. W., Manschreck, T. C., Swartz, M., Rosenheck, R., Perkins, D. O., Walker, T. M., Stroup, T. S., McEvoy, J. P., & Lieberman, J. A. (2006). Baseline neurocognitive deficits in the catie schizophrenia trial. *Neuropsychopharmacology*, *31*(9), 2033–2046. https://doi.org/10.1038/sj.npp.1301072

Keefe, R. S. E., Mohs, R. C., Bilder, R. M., Harvey, P. D., Green, M. F., Meltzer, H. Y., Gold, J. M., & Sano, M. (2003). Neurocognitive assessment in the clinical antipsychotic trials of intervention effectiveness (Catie) project schizophrenia trial: Development, methodology, and rationale. *Schizophrenia Bulletin*, *29*(1), 45–55. https://doi.org/10.1093/oxfordjournals.schbul.a006990

Kerr, S. L., & Neale, J. M. (1993). Emotion perception in schizophrenia: Specific deficit or further evidence of generalized poor performance? *Journal of Abnormal Psychology*, *102*(2), 312–318. https://doi.org/10.1037/0021-843X.102.2.312

Koike, S., Nishimura, Y., Takizawa, R., Yahata, N., & Kasai, K. (2013). Near-infrared spectroscopy in schizophrenia: A possible biomarker for predicting clinical outcome and treatment response. *Frontiers in Psychiatry*, *4*. https://doi.org/10.3389/fpsyt.2013.00145

Kubota, Y., Toichi, M., Shimizu, M., Mason, R. A., Coconcea, C. M., Findling, R. L., Yamamoto, K., & Calabrese, J. R. (2005). Prefrontal activation during verbal fluency tests in schizophrenia—A near-infrared spectroscopy (Nirs) study. *Schizophrenia Research*, *77*(1), 65–73. https://doi.org/10.1016/j.schres.2005.01.007

Lafayette Instrument Company, 1989. Grooved Pegboard Instruction Manual, Model 32025. Lafayette Instrument Company, Lafayette, Indiana.

Lesh, T. A., Niendam, T. A., Minzenberg, M. J., & Carter, C. S. (2011). Cognitive control deficits in schizophrenia: Mechanisms and meaning. *Neuropsychopharmacology*, *36*(1), 316–338. https://doi.org/10.1038/npp.2010.156

Lim, K., Smucny, J., Barch, D. M., Lam, M., Keefe, R. S. E., & Lee, J. (2021). Cognitive subtyping in schizophrenia: A latent profile analysis. *Schizophrenia Bulletin*, *47*(3), 712–721. https://doi.org/10.1093/schbul/sbaa157

McCleery, A., Green, M. F., Hellemann, G. S., Baade, L. E., Gold, J. M., Keefe, R. S. E., Kern, R. S., Mesholam-Gately, R. I., Seidman, L. J., Subotnik, K. L., Ventura, J., & Nuechterlein, K. H. (2015). Latent structure of cognition in schizophrenia: A confirmatory factor analysis of the MATRICS Consensus Cognitive Battery (Mccb). *Psychological Medicine*, *45*(12), 2657–2666. https://doi.org/10.1017/S0033291715000641

Miettunen, J., Nordström, T., Kaakinen, M., & Ahmed, A. O. (2016). Latent variable mixture modeling in psychiatric research – a review and application. *Psychological Medicine*, *46*(3), 457–467. https://doi.org/10.1017/S0033291715002305

Múthen, L. K., & Múthen, B. O. (2007). Mplus (version 5.0)[computer software]. *Los Angeles, CA: Author*. https://www.statmodel.com/index.shtml

Nuechterlein, K. H., Barch, D. M., Gold, J. M., Goldberg, T. E., Green, M. F., & Heaton, R. K. (2004). Identification of separable cognitive factors in schizophrenia. *Schizophrenia Research*, *72*(1), 29–39. https://doi.org/10.1016/j.schres.2004.09.007

Ojeda, N., Sánchez, P., Peña, J., Elizagárate, E., Yoller, A. B., Larumbe, J., Gutiérrez, M., Casais, L., & Ezcurra, J. (2010). Verbal fluency in schizophrenia: Does cognitive performance reflect the same underlying mechanisms in patients and healthy controls? *Journal of Nervous & Mental Disease*, *198*(4), 286–291. https://doi.org/10.1097/NMD.0b013e3181d61748

Phillips, T. (2004). Semantic fluency is impaired but phonemic and design fluency are preserved in early-onset schizophrenia. *Schizophrenia Research*, *70*(2–3), 215–222. https://doi.org/10.1016/j.schres.2003.10.003

Piras, F., Piras, F., Banaj, N., Ciullo, V., Vecchio, D., Edden, R. A. E., & Spalletta, G. (2019). Cerebellar GABAergic correlates of cognition-mediated verbal fluency in physiology and

schizophrenia. *Acta Psychiatrica Scandinavica*, *139*(6), 582–594. https://doi.org/10.1111/acps.13027

Reise, S. P., Moore, T. M., & Haviland, M. G. (2010). Bifactor models and rotations: Exploring the extent to which multidimensional data yield univocal scale scores. *Journal of Personality Assessment*, *92*(6), 544–559. https://doi.org/10.1080/00223891.2010.496477

Schretlen, D. J., Peña, J., Aretouli, E., Orue, I., Cascella, N. G., Pearlson, G. D., & Ojeda, N. (2013). Confirmatory factor analysis reveals a latent cognitive structure common to bipolar disorder, schizophrenia, and normal controls. *Bipolar Disorders*, *15*(4), 422–433. https://doi.org/10.1111/bdi.12075

Seaton, B. E., Goldstein, G., & Allen, D. N. (2001). [No title found]. *Neuropsychology Review*, *11*(1), 45–67. https://doi.org/10.1023/A:1009013718684

Steiger, J. H. (1990). Structural model evaluation and modification: An interval estimation approach. *Multivariate Behavioral Research*, *25*(2), 173–180. https://doi.org/10.1207/s15327906mbr2502_4

Stroup, T. S., McEvoy, J. P., Swartz, M. S., Byerly, M. J., Glick, I. D., Canive, J. M., McGee, M. F., Simpson, G. M., Stevens, M. C., & Lieberman, J. A. (2003). The national institute of mental health clinical antipsychotic trials of intervention effectiveness (Catie) project: Schizophrenia trial design and protocol development. *Schizophrenia Bulletin*, *29*(1), 15–31. https://doi.org/10.1093/oxfordjournals.schbul.a006986

Tyburski, E., Sokołowski, A., Chęć, M., Pełka-Wysiecka, J., & Samochowiec, A. (2015). Neuropsychological characteristics of verbal and non-verbal fluency in schizophrenia patients. *Archives of Psychiatric Nursing*, *29*(1), 33–38. https://doi.org/10.1016/j.apnu.2014.09.009

Vrieze, S. I. (2012). Model selection and psychological theory: A discussion of the differences between the Akaike information criterion (Aic) and the Bayesian information criterion (Bic). *Psychological Methods*, *17*(2), 228–243. https://doi.org/10.1037/a0027127

Wechsler, D., & De Lemos, M. M. (1981). Wechsler Adult Intelligence Scale-Revised.

Wechsler, D. (1991). Manual for the Wechsler Intelligence Scale for Children 3rd ed Psychological Corporation. *San Antonio, TX*.

Wilkinson, G. S. (1993). WRAT-3: Wide Range Achievement Test administration manual. Wide Range. *Inc, Wilmington, DE*.

**Table 1. Cognitive Domains Included from Previous Factor Analyses**

| Study | PS | EF | WM | VM | ATT | NVM | CV | SC | IF | Factors |
|---|---|---|---|---|---|---|---|---|---|---|
| Burton et al. (2013) | X | X | X | X | X | X | | | | 3 |
| Gladsjo et al. (2004) | X | X | X | X | X | X | X | | | 6 (ATT and WM) |
| Keefe et al. (2006) | X | X | X | X | X | | | | | Hierarchical, 5 on 1 |
| Ojeda et al. (2010) | X | X | X | X | X | X | | | | 6 |
| McCleery et al. (2015) | X | X | X | X | X | X | | X | | 7 |
| Nuechterlein et al. (2004) | X | X | X | X | X | X | | X | | 7 |
| Schretlen et al. (2013) | X | X | | X | X | X | | | X | 6 |

*Note*. VM = Verbal Memory, ATT = attention or vigilance, PS = processing speed, EF = executive function/reasoning/problem solving, WM = working memory, NVM = non-verbal memory (visual learning and memory), CV = crystalized verbal abilities, SC = social cognition, and IF = ideational fluency. Burton et al. (2013) collapsed factors of the above represented domains. Gladsjo et al. (2004) grouped attention and working memory measures under one factor, which resulted in six factors. Schretlen et al. (2013) had a sample size of 110 adults with schizophrenia.

**Table 2. Baseline Demographics of Calibration, Cross-Validation, and Total Sample**

| | Calibration | Cross-validation | Total |
|---|---|---|---|
| Mean age in years (*SD*) | (*n* = 411) | (*n* = 399) | (*n* = 810) |
| | 38.3 (10.7) | 39.0 (10.7) | 38.7 (10.7) |
| % Male | (*n* = 413) | (*n* = 410) | (*n* = 813) |
| | 78.5 | 72.0 | 75.3 |
| Mean education in years (*SD*) | (*n* = 409) | (*n* = 395) | (*n* = 804) |
| | 11.6 (3.5) | 11.7 (3.4) | 11.7 (3.5) |
| Race/Ethnicity | (*n* = 410) | (*n* = 399) | (*n* = 809) |
| White/Caucasian | 255 | 254 | 509 |
| Black/African American | 137 | 119 | 256 |
| Asian | 7 | 12 | 19 |
| More than one race | 9 | 8 | 17 |
| American Indian/Alaska Native | 1 | 3 | 4 |
| Native Hawaiian/Pacific Islander | 1 | 2 | 3 |
| Unknown or not reported race/ethnicity | -- | 1 | 1 |
| Hispanic/Latino | 49 | 43 | 92 |
| Not Hispanic/Latino | 362 | 356 | 718 |
| Mean PANSS (*SD*) | (*n* = 412) | (*n* = 399) | (*n* = 811) |
| Positive Symptom Score | 18.5 (5.4) | 18.4 (5.8) | 18.5 (5.6) |
| Negative Symptom Score | 19.8 (6.4) | 19.7 (6.2) | 19.8 (6.3) |
| General Symptom Score | 36.7 (9.0) | 37.0 (9.5) | 36.9 (9.3) |
| Medication | (*n* = 411) | (*n* = 399) | (*n* = 810) |
| Olanzapine | 112 | 110 | 222 |
| Quetiapine | 39 | 49 | 88 |
| Risperidone | 99 | 87 | 186 |
| Ziprasidone | 22 | 22 | 44 |
| Haloperidol | 25 | 18 | 43 |
| Decanoate | 6 | 6 | 12 |
| Perphenazine | 3 | 10 | 13 |
| Other | 39 | 24 | 63 |
| All Other | 88 | 79 | 167 |
| None | 110 | 112 | 222 |

*Note.* Neuroleptic medications were taken on the day of baseline cognitive testing or two weeks prior. Other = participant received any other neuroleptic besides one of the neuroleptics listed above; All Other = participant received any other neuroleptics (olanzipine, quetiapine, and risperidone not included); None = participant did not receive neuroleptics. Hispanic/Latino was a separate variable, so individuals also chose between race options listed. Race and ethnicity descriptors reflect those used in the CATIE database.

**Table 3. Scores Included in Factors**

| CATIE Domains and Test scores | CFA Models | | | |
|---|---|---|---|---|
| | 1-factor | 5-factor | 6-factor | 7-factor |
| Processing Speed | | | | |
| Grooved Pegboard Trial 1 | 1 | 1 | 1 | 1 |
| Grooved Pegboard Trial 2 | 1 | 1 | 1 | 1 |
| WAIS-R Digit-Symbol Test number correct | 1 | 1 | 1 | 1 |
| COWAT 1st letter | 1 | 1 | 6 | 6 |
| COWAT 2nd letter | 1 | 1 | 6 | 6 |
| COWAT 3rd letter | 1 | 1 | 6 | 6 |
| Category Instances 1st category | 1 | 1 | 6 | 7 |
| Category Instances 2nd category | 1 | 1 | 6 | 7 |
| Category Instances 3rd category | 1 | 1 | 6 | 7 |
| Reasoning | | | | |
| WCST perseverative errors | 1 | 2 | 2 | 2 |
| WCST completed categories | 1 | 2 | 2 | 2 |
| WCST sorts in final condition | 1 | 2 | 2 | 2 |
| WISC-III Mazes total correct | 1 | 2 | 2 | 2 |
| Working Memory | | | | |
| Letter-Number Sequencing Test total correct | 1 | 3 | 3 | 3 |
| CTVWM mean errors 5 second delay | 1 | 3 | 3 | 3 |
| CTVWM mean errors 15 second delay | 1 | 3 | 3 | 3 |
| Verbal Memory | | | | |
| HVLT-R Trial 1 | 1 | 4 | 4 | 4 |
| HVLT-R Trial 2 | 1 | 4 | 4 | 4 |
| HVLT-R Trial 3 | 1 | 4 | 4 | 4 |
| Vigilance | | | | |
| CPT-IP d' condition 2 | 1 | 5 | 5 | 5 |
| CPT-IP d' condition 3 | 1 | 5 | 5 | 5 |
| CPT-IP d' condition 4 | 1 | 5 | 5 | 5 |

*Note.* Hierarchical and bifactor models kept these domains for single-level and specific factors, respectively, with the addition of the higher-order or global factor accordingly. WAIS-R = Wechsler Adult Intelligence Scale-Revised (WAIS-R) COWAT = Controlled Oral Word Association; WISC-III = Wechsler Intelligence Scale for Children, 3rd Ed. (WISC-III); WCST = Wisconsin Card Sort Test; CTVWM = Computerized Test of Visual Working Memory; HVLT-R = Hopkins Verbal Learning Test- Revised; CPT-IP d' = Conners' Continuous Performance Test- Identical Pairs; d' = number of correct responses minus false alarms.

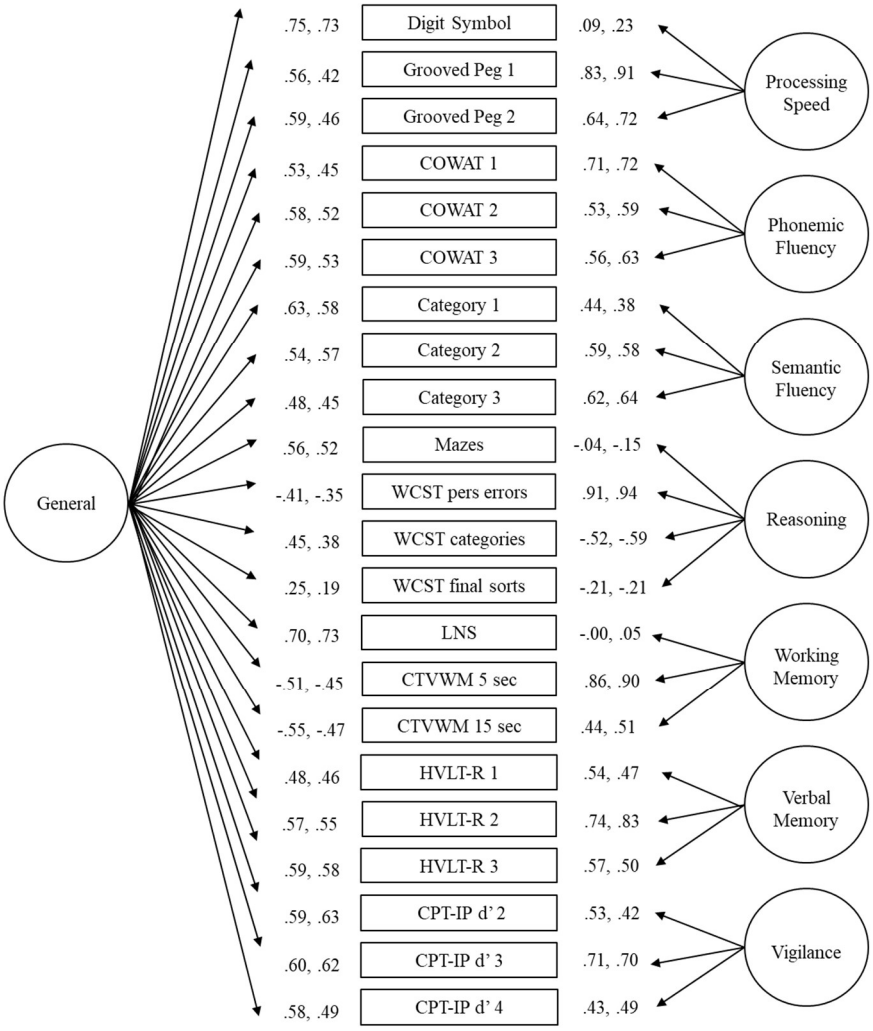
**Table 4. Results of Fit Indices Using Robust Methods with Standard Error Correction**

| Group | Models | $X^2$ (df) | CFI | RMSEA (90% CI) | AIC | BIC |
|---|---|---|---|---|---|---|
| Calibration | 1 | 2175.43(209) | 0.58 | 0.151 (0.145, 0.157) | 46241.69 | 46507.24 |
| | 5 | 1256.63 (199) | 0.78 | 0.113 (0.107, 0.119) | 45342.89 | 45648.68 |
| | H5 | 1467.43 (208) | 0.73 | 0.121 (0.115, 0.127) | 45535.70 | 45805.27 |
| | B5 | 589.02 (187) | 0.91 | 0.072 (0.066, 0.079) | 44699.29 | 45053.35 |
| | 6 | 746.80 (194) | 0.88 | 0.083 (0.077, 0.089) | 44843.06 | 45168.96 |
| | H6 | 1074.32 (208) | 0.82 | 0.100 (0.095, 0.106) | 45142.59 | 45412.16 |
| | B6 | 420.83 (189) | 0.95 | 0.054 (0.048, 0.061) | 44527.10 | 44873.11 |
| | 7 | 586.15 (188) | 0.92 | 0.072 (0.065, 0.078) | 44694.41 | 45044.45 |
| | H7 | 1030.11 (208) | 0.83 | 0.098 (0.092, 0.104) | 45098.38 | 45367.95 |
| | B7* | 385.10 (190) | 0.96 | 0.050 (0.043, 0.057) | 44489.37 | 44831.36 |
| Cross-validation | B7* | 293.91 (190) | 0.98 | 0.037 (0.028, 0.045) | 42726.56 | 43065.83 |

*Note.* CFI = comparative fit index. RMSEA = root mean-square error of approximation. RMSEA 90% CI = root mean-square error of approximation 90% confidence interval. AIC = Akaike's Information Criterion, BIC = Bayesian Information Criterion; model numbers represent the number of single-level factors; H = hierarchical with a single higher-order factor; B = bifactor with a

generalized factor, and numbers represent the number of specific factors. All of the bifactor seven models had significant chi-squared values at $p < .001$. * indicates the best fitting models.

**Figure 1. Bifactor Seven-Factor Model for the Calibration and Cross-Validation Samples**




*Note*. Numbers represent factor loadings for calibration (loading listed first) and cross-validation (loading listed second) groups. Digit Symbol = Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol Test; Grooved Peg (1 or 2) = Grooved Pegboard Test Trial (1 or 2); COWAT (1, 2, or 3) = Controlled Oral Word Association Test Trial 1, 2, or 3; Category (1, 2, or 3) = Category Test Trial 1, 2, or 3; Mazes = Wechsler Intelligence Scale for Children, 3rd Ed. (WISC-III) Mazes; WCST = Wisconsin Card Sort Test; per errors = perseverative errors; categories = number of categories administered; final sorts = number of sorts in the final

condition; LNS = Letter-Number Sequencing Test; CTVWM = Computerized Test of Visual Working Memory; 5 sec = mean errors during the five second delay; 15 sec = mean errors during the fifteen second delay; HVLT-R (1, 2, or 3) = Hopkins Verbal Learning Test- Revised Trial 1, 2, or 3; CPT-IP d' (2, 3, or 4) = Conners' Continuous Performance Test- Identical Pairs number of correctly identified targets on the two-, three-, or four- digit condition.

**Supplementary Materials**

**Table 1. Cognitive Tests within Each Domain**

| Domain | Test | Description | Scores |
|---|---|---|---|
| Processing Speed | Grooved Pegboard | Participant places pegs one at a time into a board with 25 randomly positioned slots using dominant hand for 45 seconds. This process is repeated for a second trial. | number of pegs placed dominant hand Trial 1<br>number of pegs placed dominant hand Trial 2 |
| | WAIS-R Digit-Symbol | Participant copies as many symbols as possible in 90 seconds when presented with the numeral associated with that symbol as denoted on a legend. | number of correct symbols |
| | COWAT | Participant verbally recalls as many words as possible that begin with a specific letter for 60 seconds. This process is repeated using a different letter per trial. | number of words recalled for 1st letter<br>number of words recalled for 2nd letter<br>number of words recalled for 3rd letter |
| | Category Instances | Participant verbally recalls as many words as possible that belong within a specific category for 60 seconds. This process is repeated using a different category per trial. | number of words recalled for 1st category<br>number of words recalled for 2nd category<br>number of words recalled for 3rd category |
| Reasoning | Computerized WCST | Participant indicates whether the stimuli on a card are within the same category as the original stimuli presented for a given sort (set of cards). | perseverative errors (participant hit the space bar either too slowly for one presentation of the stimulus or so quickly for its subsequent stimulus that the subsequent stimulus was likely not perceived)<br>number of completed categories |

| | | | |
|---|---|---|---|
| | | | number of sorts in the final condition |
| | WISC-III Mazes | Participant completes 10 mazes which involve tracing the correct path from a stick figure placed in the center of each maze to the opening on the outside of the maze. | completion time in seconds |
| Working Memory | Letter-Number Sequencing Test | Participant immediately recalls a sequence of numbers and letters in a specific order after being read the sequence of numbers and letters in a mixed order. This is repeated for 30 sequences. | number of correct sequences |
| | CTVWM | Participant stares at a fixation point in the center of the computer screen while a cue is presented for 150 milliseconds in one of 32 possible locations on the screen. Either no delay occurs or a 5 or 15 second delay occurs, during which the participant completes a distractor task involving identifying a target shape from a series of other shapes. Afterward, the fixation point appears again, and the participant must indicate where the cue was located. There are 8 trials for each delay type. | mean errors no delay (in millimeters between recalled cue location and actual cue location for each trial)<br><br>mean errors 5 second delay minus mean errors no delay<br><br>mean errors 15 second delay minus mean errors no delay |
| Verbal Memory | HVLT-R | Participant recalls as many words as possible after being read a list of 12 nouns. This is repeated for three trials with the same list of words. | number of words recalled on Trial 1<br><br>number of words recalled on Trial 2<br><br>number of words recalled on Trial 3 |

| | | | |
|---|---|---|---|
| Vigilance | CPT-IP | Participant is presented a two-digit number on a computer screen for condition 2 and lifts his/her finger after each stimulus presentation to indicate if the subsequent two-digit number presented is the same as the number seen previously. This is completed 150 times with different numbers. The participant then completes condition 3 which contains 150 trials of three-digit numbers and then completes condition 4 which contains 150 trials of four-digit numbers. | d' (number of target letters correctly identified) condition 2<br><br>d' condition 3<br><br>d' condition 4 |

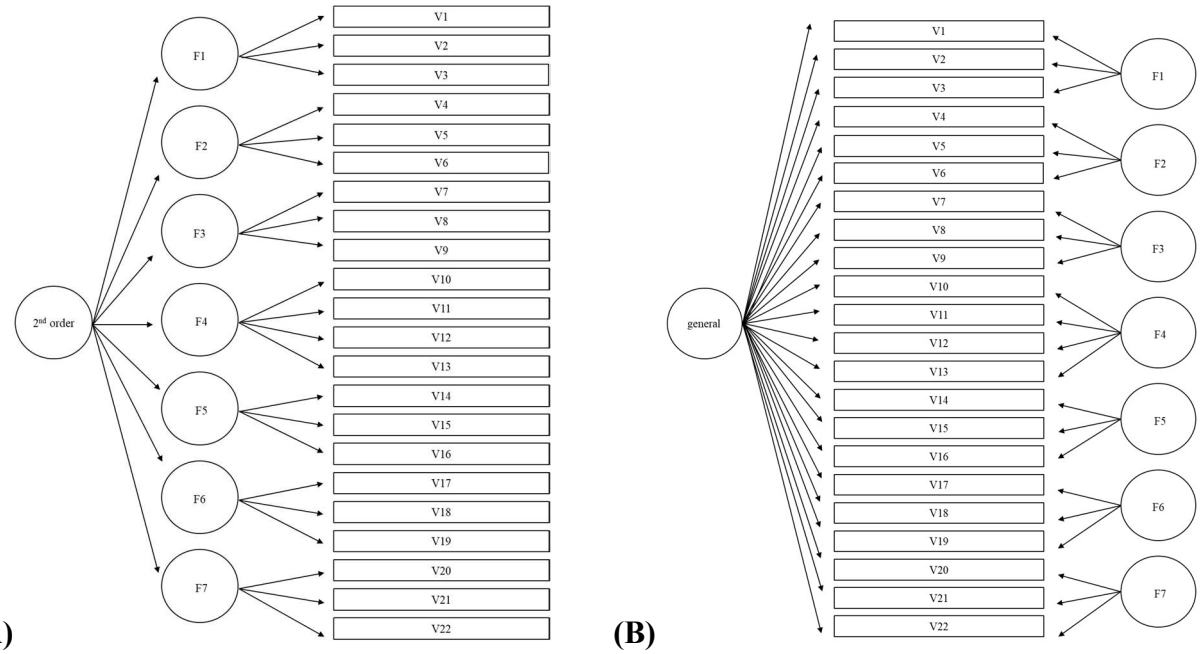
*Note.* Table information derived from Keefe et al. (2003, 2006).

**Table 2. Descriptive Statistics for Cognitive Tests (Raw Scores) in the Calibration, Cross-Validation, and Total Samples**

| Test | Calibration ($n$ = 413) Mean ($SD$) | Cross-validation ($n$ = 400) Mean ($SD$) | Total ($n$ = 813) Mean ($SD$) |
|---|---|---|---|
| Grooved Pegboard Trial 1 | 12.6 (3.7) | 12.6 (3.5) | 12.6 (3.6) |
| Grooved Pegboard: Trial 2 | 14.2 (3.8) | 14.1 (3.5) | 14.2 (3.7) |
| WAIS-R Digit Symbol Test | 40.7 (13.8) | 39.9 (12.9) | 40.3 (13.4) |
| COWAT 1st letter | 10.4 (4.0) | 10.3 (3.9) | 10.54 (4.0) |
| COWAT 2nd letter | 8.5 (3.8) | 8.4 (3.5) | 8.5 (3.7) |
| COWAT 3rd letter | 10.8 (4.4) | 10.6 (4.4) | 10.7 (4.4) |
| Category Instances 1st category | 14.5 (4.9) | 14.6 (4.4) | 14.6 (4.7) |
| Category Instances 2nd category | 10.5 (3.3) | 10.4 (3.4) | 10.5 (3.4) |
| Category Instances 3rd category | 8.8 (3.4) | 9.0 (3.2) | 8.9 (3.3) |
| WCST perseverative errors | 12.6 (9.9) | 13.1 (9.9) | 12.9 (9.9) |
| WCST completed categories | 2.3 (1.6) | 2.3 (1.6) | 2.3 (1.6) |
| WCST sorts in final condition | 2.2 (3.1) | 2.2 (2.9) | 2.2 (3.0) |
| WISC-III Mazes total correct | 18.8 (5.5) | 18.8 (5.5) | 18.8 (5.5) |
| Letter-Number Sequencing Test total correct | 11.2 (4.2) | 11.0 (4.2) | 11.1 (4.2) |
| CTVWM mean errors 5 second delay | 25.0 (14.5) | 25.0 (14.8) | 25.0 (14.7) |
| CTVWM mean errors 15 second delay | 26.8 (15.1) | 27.8 (16.1) | 27.3 (15.6) |
| HVLT-R Trial 1 | 5.1 (1.8) | 4.9 (1.6) | 5.0 (1.7) |
| HVLT-R Trial 2 | 6.8 (2.1) | 6.8 (2.0) | 6.8 (2.1) |
| HVLT-R Trial 3 | 7.9 (2.3) | 7.9 (2.3) | 7.9 (2.3) |
| CPT-IP: d′ condition 2 | 2.47 (1.05) | 2.50 (0.98) | 2.49 (1.02) |
| CPT-IP: d′ condition 3 | 1.85 (0.91) | 1.88 (0.86) | 1.87 (0.89) |
| CPT-IP: d′ condition 4 | 1.11 (0.86) | 1.02 (0.73) | 1.07 (0.80) |

*Note.* WAIS-R = Wechsler Adult Intelligence Scale-Revised (WAIS-R) COWAT = Controlled Oral Word Association; WISC-III = Wechsler Intelligence Scale for Children, 3rd Ed. (WISC-III); WCST = Wisconsin Card Sort Test; CTVWM = Computerized Test of Visual Working Memory; HVLT-R = Hopkins Verbal Learning Test- Revised; CPT-IP d' = Conners' Continuous Performance Test- Identical Pairs; d' = number of correct responses minus false alarms.

**Figure 1. Hierarchical Model Compared to Bifactor Model**




**(A)** **(B)**

*Note*. Adapted from Reise et al. (2010). Model A = Hierarchical model in which variables load on first-order factors which in turn load on a second-order factor; Model B = Bifactor model in which variables load on specific factors separately from their loadings on a general factor; F = factor; V = variable.

## Chapter III: Latent Structure of Cognitive Tests is Invariant in Men and Women with Schizophrenia

Note: Study II was submitted for publication to *Schizophrenia Research*.

The first dissertation paper, "Bifactor model of cognition in schizophrenia: Evidence for general and specific abilities," estimated a number of competing models examining the latent constructs of cognitive abilities in schizophrenia (SZ). A number of bifactor and hierarchical models were estimated that addressed whether cognition in SZ was best conceptualized as composed of a number of different specific constructs, a general/global construct, or a combination of the two. A bifactor model that was not previously examined had the best fit in an initial calibration sample and was replicated within the cross-validation sample, which provided evidence supporting the validity of this complex model. It is important to understand the latent structure of cognitive abilities in SZ to compare cognitive subgroups of the disorder with the intention of linking those groups to specific disorder characteristics (symptom profiles, functional outcomes, etc.) to develop more targeted preventative efforts and treatment approaches. The findings of the first paper increase this understanding by demonstrating that cognition in SZ was not best characterized by specific factors or a general factor, but by a model incorporating a number of specific latent constructs with a general construct. Future directions for this work include further exploration as to whether a bifactor model can be replicated in SZ when using different tests that assess similar and different cognitive abilities. Subsequent studies should also explore generalizability of a bifactor model with other cognitive batteries for SZ and psychosis populations broadly, such as those with first episode psychosis and schizoaffective disorder compared to bipolar disorder with psychosis. Finally, the invariance of the bifactor model should be examined so that differences reported based on important demographic

characteristics (e.g., sex) and longitudinal changes in cognitive function with repeated assessment can be attributed to actual differences between groups or across time as opposed to measurement variance

The second paper examined invariance of the bifactor model between men and women with SZ. Cognitive differences based on binary sex are of interest in SZ, given differences in symptoms, onset, and premorbid functioning between men and women. However, cognitive test performance in SZ has continued to demonstrate mixed results as to whether differences between men and women are present, and if so, and the extent to which these differences might be attributable to variance in latent structure. The second dissertation paper, "Latent structure of cognitive tests is invariant in men and women with schizophrenia," first examined measurement invariance as a possible source that could explain the discrepancy between results of studies about cognition between men and women with SZ. Once the latent structure of cognition between men and women was found invariant at baseline and follow-up assessment, we assessed actual differences in cognition between men and women. Examination of invariance between the latent structure of cognitive abilities between men and women with SZ was important for better understanding and characterizing binary sex-based cognitive performance.

Latent structure of cognitive tests is invariant in men and women with schizophrenia

Megan L. Becker Wright[1], Anthony O. Ahmed[2], Kimberly A. Barchard[1], Stephen D. Benning[1], Samantha E. John[1,3], Daniel N. Allen[1]

[1]Department of Psychology, University of Nevada, Las Vegas, Las Vegas, NV

[2]Department of Psychiatry, Weill Cornell Medicine, White Plains, NY

[3]Department of Brain Health, University of Nevada, Las Vegas, Las Vegas, NV

*Address correspondence to: Daniel N. Allen, Ph.D., Department of Psychology, University of Nevada Las Vegas, 4505 Maryland Parkway, Las Vegas, NV 89154-5030. Phone: 702.895.0121. Fax: 702.895.0195. Email: daniel.allen@unlv.edu

Word count Abstract: 191

Word count body: 3,514

**Abstract**

Studies comparing the cognitive functioning of men and women with schizophrenia have produced conflicting results that could arise from sex-based differences in the latent structure of cognitive abilities. The current study used multigroup confirmatory factor analysis to examine invariance in latent structure of cognitive abilities between men and women with schizophrenia. Confirmatory factor analysis of an initial neurocognitive assessment (men $n$ = 612, women $n$ = 201) and cross-validation using second assessment (men $n$ = 549, women $n$ = 198) demonstrated that a bifactor seven-factor model fit the data best for both men and women. Invariance analyses further indicated this model was invariant across men and women at both assessments. Group comparisons indicated women had significantly higher scores for Semantic Fluency, Verbal Memory, and General Cognitive factors, whereas men exhibited better performance on the Vigilance factor. Results indicate that cognition in SZ is characterized by both a general cognitive factor and specific domains for both men and women. Invariance analysis provides evidence that cognitive differences between men and women do not result from sex-based differences in the latent structure of cognitive abilities. Current results also indicate small but statistically significant neurocognitive differences between men and women with SZ.

*Keywords:* schizophrenia, cognition, CATIE, factor analysis, invariance, sex differences

Student Contribution Statement: Megan Becker Wright's role on this manuscript included study conceptualization, data preparation, statistical analyses and interpretation, writing the first draft of the manuscript, and overseeing the revision process with coauthors.

## Introduction

Men and women with schizophrenia (SZ) differ across important disease and symptomatic domains (for review see Riecher-Rössler et al., 2018). Differences are seen in age of onset (Canuso and Pandina, 2007; Eranti et al., 2013; Häfner et al., 1989, 1994; Leung and Chue 2000; van der Werf et al., 2014), premorbid functioning (Allen et al., 2013; Ayesa-Arriola et al., 2020), course and outcome (Canuso and Pandina, 2007; Ochoa et al., 2012; Riecher-Rössler and Häfner, 2000), substance abuse (Abel et al., 2010; Ochoa et al., 2012), and affective symptoms (Ochoa et al., 2012). Men have demonstrated lower premorbid IQ compared to women (Alyward et al., 1984), and among those with SZ, some studies report sex differences on cognitive tests similar to those found in healthy adults (Bozikas et al., 2010; Halari et al., 2006). Among healthy adults, some evidence suggests that men perform better on visuospatial tasks, whereas women perform better on tests that measure verbal skills and memory (Halari et al., 2005; Ittig et al., 2015; Zanelli et al., 2013). Some studies also indicate healthy adult women have advantages in verbal memory and inhibition-switching compared to men (Riecher-Rössler et al., 2018; Vaskinn et al., 2011). For those with SZ, women generally perform better on processing speed and verbal memory tasks (Fond et al., 2018; Longenecker et al., 2010; Torniainen et al., 2011; Tsai et al., 2017), whereas men show some advantages on tests of vigilance/sustained attention, and perhaps working memory and problem solving (Fond et al., 2018; Mu et al., 2020). Women with later symptom onset may exhibit more severe visuospatial and problem solving deficits compared to men (Ayesa-Arriola et al., 2014; Buck et al., 2020; Ittig et al., 2015). However, these results are not consistent across studies. Notably, Fond et al. (2018) did not find differences in performance on phonemic fluency or problem solving between men and women with SZ. Others found similar working memory scores between men and

women with chronic SZ (Fond et al., 2018; Longenecker et al., 2010; Mu et al., 2020). Regarding general cognitive abilities, some studies indicate women may have higher global cognitive performance than men (Han et al., 2012), although this may depend on the number of domains and tests included within studies, as others find deficits in global cognitive scores for women (Fond et al., 2020), or a similar level of general deficit between men and women (Mu et al., 2020).

Methodological differences may explain some inconsistencies across studies (Keith et al., 2007; Pezutti et al., 2020). However, sex-based differences in the measurement properties of the cognitive tests might also contribute to inconsistent findings. Studies that report mean differences between men and women with SZ assume unbiased and invariant measurement, i.e., that the scales measure equivalent constructs in men and women. However, before attributing mean differences in performance on tests to differences in abilities, researchers must examine invariance in the latent structure of the tests to determine if the measurement of latent constructs is comparable between groups (Putnick & Bornstein, 2016). A number of studies of population-based normative samples for widely used tests (e.g., Wechsler Intelligence scales) conclude that some differences in performance between men and women appear to be real, whereas other appear to result from sex-based test measurement variance (e.g., Pezutti et al., 2020). Similarly, latent structure of cognitive abilities may be variant for men and women with SZ, which would contribute to inconsistent findings in the SZ literature. However, sex-based variance in measurement properties of cognitive tests has not been examined in SZ.

Therefore, the current study extends research findings regarding sex-based differences in cognition by examining whether the latent structure of cognition in SZ is invariant between men and women by applying multigroup confirmatory factor analysis (CFA) to neurocognitive data

collected as part of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study. Models were examined separately for men and women and included two assessments to determine stability of their latent structure. We expected that a bifactor seven-factor model (Becker et al., 2021) would fit the data better than other models. If the latent structure is invariant across sex, it is expected based on the literature that women will perform better on tests of processing speed (Fond et al., 2018; Longenecker et al., 2010; Torniainen et al., 2011), verbal memory (Fond et al., 2018; Longenecker et al., 2010; Tsai et al., 2017), and general cognitive ability (Han et al., 2012; Murillo-Garcia et al., 2020), whereas men were expected to score better scores on tests of vigilance (Mu et al., 2020).

## Method

*Participants*

The CATIE study included 1,493 people from 57 sites throughout the United States with a DSM-IV diagnosis of SZ who were between the ages of 18 and 65, able to take oral medication, demonstrated adequate decision making, and provide informed consent (Keefe et al, 2006; Stroup et al., 2003). Participants with two assessments were included in the current study. Neurocognitive data for assessment 1 was available for 1,425 participants (men $n$ = 1,060, women $n$ = 365) and 1,133 participants had data from assessment 2, conducted approximately two months after assessment 1 (men $n$ = 840, women $n$ = 293). Only individuals with complete cognitive data were included in analyses. Multivariate outliers were excluded based on Mahalonobis distance with $p < .001$, resulting in exclusion of 26 participants ($n$ = 22 men, $n$ = 4 women) at assessment 1 and 38 participants ($n$ = 26 men, $n$ = 7 women) at assessment 2. The final data set included 813 cases at assessment 1 (men $n$ = 612, women $n$ = 201), and 747 cases

at assessment 2 (men $n$ = 549, women $n$ = 198). This study used deidentified archival data and was deemed exempt by the local institutional review board for the protection of human subjects.

### *Measures*

The CATIE battery consists of numerous well-validated and reliable tests of Processing Speed, Reasoning, Working Memory, Verbal Memory, and Vigilance domains. Tests included in the multigroup CFA for this study are listed in Table 1 (Supplementary Materials). More detail about test battery and administration, staff training for adherence with standards for data collection, test scoring, and data editing and transmission is reported by Keefe et al. (2003). Following assessment 1, participants completed assessment 2 cognitive testing at scheduled study intervals.

### *Data Analysis*

Data were examined to determine if test scores met assumptions of CFA regarding normality, homoscedasticity, and linearity. The reaction time scores for the CPT and the no delay score for the visual working memory test were excluded because the violated these assumptions. Conventional standard errors were used to estimate CFA parameters. See Table 1 and Table 1 Supplementary Materials for group demographic and descriptive data, respectively.

Assessment 1 data was used to identify the best fitting model for men and women. Assessment 2 data was then used to cross-validate the findings from assessment 1. At assessment 1, first-order, hierarchical, and bifactor models were examined for men and women. Models are presented in Table 2 Supplementary Materials. First order models that were examined included one-, five-, six-, and seven-factor models. The one-factor model hypothesized all test scores loaded on one general cognitive factor. The five-factor model was based on Keefe et al. (2006) which reported a hierarchical model with five domains including Processing Speed, Reasoning,

Working Memory, Verbal Memory, and Vigilance for the CATIE cognitive data. A six-factor model separated Verbal Fluency measures from Processing Speed, based on studies that identified verbal fluency deficits in SZ (Tyberski et al., 2015). A final seven-factor model identified by Becker et al. (2021) further split phonemic and semantic fluency into separate constructs, according to research suggesting that those with SZ exhibit differential patterns of cognitive abilities across both components of verbal fluency (Ojeda et al., 2010; Piras et al., 2019). In contrast to first-order models, the hierarchical models include a general second order factor to examine whether a general cognitive construct accounts for the covariation among the specific first order factors. Hierarchical five-, six-, and seven-factor models were tested. Finally, bifactor five-, six-, and seven-factor models were also examined to determine whether there were separate latent contributions of general and specific factors. For assessment 2, the best fitting model identified in assessment 1 was then estimated in males and females.

*Mplus* version 5 using Maximum Likelihood as an estimator was used to estimate all models (Muthén and Muthén, 2007). Model fit was assessed using model chi-square, the Comparative Fit Index (CFI), Root Mean Squared Error of Approximation (RMSEA), and Bayesian Information Criterion (BIC). The chi-square provides a good indication of how well the hypothesized model fits the actual data (Hu and Bentler, 1999). Because chi-square may be significant even with good fitting models when sample size is large, the CFI, TLI, RMSEA, and BIC were also considered. The CFI was used to compare the independence model to the hypothesized model (Bentler, 1990), Tucker Lewis Index (TLI) values ≥. 95 were included as cutoffs for good model fit (Byrne, 2010; Browne and Cudeck, 1992), RMSEA to evaluate the fit between the hypothesized model and the population covariance matrix (Steiger, 1990), and the BIC to compare the relative fit of competing models. The BIC has a strict penalty for

overparameterized models than the other indices used for these analyses and was added to better estimate fit in larger models (Vrieze, 2012). Good model fit was indicated by CFI and TLI ≥ .95, and RMSEA ≤ .06 (Hu and Bentler, 1999). Lastly, relative fit was determined by lower BIC values (Dziak et al., 2020).

Following these analyses, multi-group CFA was used to assess measurement invariance between men and women at assessment 1 and 2. Configural, metric, scalar, and residual invariance were examined sequentially to allow for comparison of factorial invariance with successive and additive constraints (Byrne, 2008). Configural invariance was assessed to determine if the same items load on factors for men and women. Weak factorial invariance was examined using metric invariance to determine if factor loadings for the factor structures of men and women were similar (Horn and McArdle, 1992). Strong factorial invariance was assessed using scalar invariance to determine if both factor loadings and intercepts were the same. Strict factorial invariance was assessed using residual factorial invariance to determine if residual variances were the same. Change to the following goodness of fit indices with each step of analysis were used to evaluate model invariance: chi-square difference with $p < .05$, CFI and TLI decreases ≤ 0.010, and RMSEA increase ≤ 0.015 (Chen, 2007).

Following invariance analyses, standardized factor scores were extracted from assessment 1 data for each factor using *Mplus* version 5. Differences in factor scores between men and women were then examined for each factor. To determine if there were any group differences, a general linear modeling approach was used that included between-subjects effects (men, women) and within-subject effects (factor scores). Age and the PANSS negative symptom score were included as covariates, given that women were significantly older at assessment 1 ($p = .01$, Cohen's $d = 0.20$) and men had more severe negative symptoms ($p = .02$, Cohen's $d =$

0.18). Years of education and PANSS general and positive symptom scores were not significantly different between groups ($p$ = .74, .71, and .10, respectively). The percentage of men and women across neuroleptic type at assessment 1 or within two weeks prior were examined using chi-square; there was no statistically significant difference ($\chi^2(4) = 4.60$, $p = .33$), so neuroleptic type was not included as a covariate.

## Results

### *Model Fit Indices*

Table 2 shows the goodness of fit indices for men and women baseline models and the bifactor seven-factor model for men and women at assessment 1 and 2. The unidimensional one-, five-, six-, seven-factor, hierarchical five-, six-, seven-factor, and bifactor five-factor models did not result in good fit of assessment 1 data for either sex. The bifactor six-factor model had good fit for men at assessment 1, but not women. However, the bifactor seven-factor model provided good fit for both groups and was superior in fit for men relative to the bifactor six-factor model. Model fit remained good for the bifactor seven-factor model in both men and women at assessment 2. As expected, most of the assessment 1 test scores demonstrated strong loadings on their specific factors, with variable loadings on the general factor (see Figure 1). Notably, some tests (LNS, DS, Mazes) demonstrated relatively low loadings on their specific factors. Consistent with assessment 1, assessment 2 indicated that LNS, DS, and Mazes all showed higher factor loadings on the general factor and considerably low loadings on the specific factors.

### *Invariance Analyses*

Results of measurement invariance analyses are presented in Table 3, which includes estimates of measurement invariance for the bifactor seven-factor model in men and women at assessment 1 and at assessment 2. Overall, there were minor differences in fit statistics at

assessments 1 or 2 for the different levels of invariance that were examined. At assessment 1, estimates of configural invariance indicated CFI and TLI values of .96 and RMSEA of .045. Similar CFI and TLI values were obtained when testing for metric invariance. CFI and TLI values decreased slightly when testing for scalar invariance, but the change did not exceed .010, indicating invariance. CFI and TLI values were also stable when testing for residual invariance. At assessment 2, CFI and TLI values remained consistent at .95 and, together with consistent RMSEA values, demonstrated configural, metric, scalar, and residual invariance.

***Factor Score Comparisons for Women and Men***

Factor scores for men and women at assessment 1 for the eight cognitive factors are presented in Figure 2. Raw scores for each factor are presented (solid lines), as are estimated marginal means controlling for age and negative symptom differences between men and women (dashed lines). Results of the overall analysis with age and negative symptoms as covariates indicated a significant main effect for cognitive factor, $F(6.40,5147.25) = 22.32$, $p < .001$, partial $\eta^2 = .03$, but not sex, $F(1,804) = 3.75$, $p = .05$, partial $\eta^2 = .01$, with a significant sex by cognitive factor interaction, $F(6.40,5147.25) = 4.55$, $p < .001$, partial $\eta^2 = .01$. Negative symptoms were a significant predictor in the overall model, $F(1,840) = 33.17$, $p < .001$, partial $\eta^2 = .04$, whereas age was not, $F(1,840) = .41$, $p = .52$. As can be seen from Figure 2, the interaction effect was accounted for by women performing better than men on Semantic Fluency, $F(1,804) = 21.18$, $p < .001$, partial $\eta^2 = .03$, Verbal Memory, $F(1,804) = 6.89$, $p < .01$, partial $\eta^2 = .01$, and the General factor, $F(1,804) = 4.87$, $p < .05$, partial $\eta^2 = .01$. Men performed better on Vigilance, $F(1,804) = 7.63$, $p < .01$, partial $\eta^2 = .01$. There were no statistically significant differences between groups on Processing Speed, Phonemic Fluency, Reasoning, and Working Memory, $Fs(1, 804) < 0.72$, $ps > .88$ partial $\eta^2$s $< .00$. Univariate ANCOVAs with age and negative symptoms as covariates

confirmed this interpretation, with significant differences between groups on Semantic Fluency, $F(1,804) = 21.18$, $p < .001$, partial $\eta^2 = .03$, Verbal Memory, $F(1,804) = 6.89$, $p < .01$, partial $\eta^2 = .01$, Vigilance, $F(1,804) = 7.63$, $p < .01$, partial $\eta^2 = .01$, and General, $F(1,804) = 4.87$, $p < .05$, partial $\eta^2 = .01$ factors. There were no significant differences between groups on Processing Speed, Phonemic Fluency, Reasoning, and Working Memory, $Fs(1, 804) < 0.73$, $ps > .66$ partial $\eta^2s < .001$.

## Discussion

The purpose of this study was to determine whether the latent structure of cognitive abilities was invariant for women and men with SZ to further examine sex-based differences in cognitive abilities. Various competing models were examined, including first-order one-, five-, six-, and seven-factor models, hierarchical five-, six-, and seven-factor models with a general second-order factor, and bifactor five-, six-, and seven-factor models. A bifactor model with seven specific factors and one general factor provided the best fit for the latent structure of the CATIE cognitive data for both men and women. The results of this study are consistent with the model previously identified by Becker et al. (2021) using the CATIE data and extend those results by demonstrating that the bifactor model provides an excellent fit for men and women with SZ. The seven specific factors included Processing Speed, Phonemic Fluency, Semantic Fluency, Reasoning, Working Memory, Verbal Memory, and Vigilance. The distinction between this model and less complex five-factor models was the separation of the Processing Speed construct into Processing/Motor Speed, Phonemic Fluency, and Semantic Fluency constructs. Fit indices such as the BIC, suggested that increased complexity for the seven-factor bifactor model did not account for its optimal fit. Follow-up examination of standardized factor score differences revealed a significant interaction, where women performed significantly better than

men on Semantic Fluency, Verbal Memory, and on the overall General domain, and men performed better on Vigilance. However, differences on these factors were small (partial $\eta^2$s=.01-.03).

The impetus for examining the latent structure of cognitive abilities was based on numerous studies that demonstrated differences between the onset, presentation, and course of SZ in men and women, yet mixed evidence supporting sex-based cognitive differences. The extent to which these cognitive differences resulted from biases in the measurement properties of the tests, which could vary across men and women, had not previously been examined. Contrary to other well-documented important differences between women and men with SZ, the results of this study suggest that they have similar latent structure of cognitive abilities, indicating that any differences in their cognitive abilities are not accounted for by sex-based differences in the cognitive constructs assessed by the neuropsychological tests in the CATIE battery. These results were further strengthened by invariance between men and women at two different assessment times. Further, factor score differences between men and women were consistent with prior work suggesting that they differ across comparable tests of verbal memory (Fond et al., 2018; Longenecker et al., 2010; Tsai et al., 2017), vigilance (Mu et al., 2020) and general cognitive abilities (Han et al., 2012). Fewer studies of chronic SZ have included semantic fluency measures, although some reported comparable animal fluency scores between men and women with first-episode psychosis (Ayesa-Arriola et al., 2014; Danaher et al., 2018), a result that differs from the results of this study. The current study replicates previous research, which found similar performance for men and women with SZ in terms of processing speed (Mu et al., 2020), phonemic fluency (Fond et al., 2018), reasoning (Longenecker et al., 2010), and working memory (Longenecker et al., 2010; Mu et al., 2020) domains.

The identified latent structure may not fully characterize differences in cognition between men and women with SZ because the test battery did not evaluate some cognitive domains (e.g., visual memory, visuospatial skills), which could differ based on sex (Ayesa-Arriola et al., 2014). Also, some of the factors were estimated by multiple performance measures from a single test, due to the brevity of the CATIE battery. Our analyses indicated that the CATIE battery demonstrated invariance between men and women at assessments 1 and 2, which supports analyses that combine cognitive scores for both sexes. Therefore, further examination of men's and women's cognitive factor structures should include visuospatial tasks and more breadth of tests that examine verbal memory, executive function, and reaction time. Further, data for this study were collected from individuals with chronic SZ, so it remains unclear as to whether the bifactor seven-factor structure is invariant between men and women with psychosis broadly. The differences in performance between men and women with SZ identified on some factors were significant but small, which may explain why some studies identify differences and others do not.

These results are clinically relevant as they support measurement invariance for men and women with SZ, and thus indicate that the CATIE battery is appropriate for use with both sexes, such that scores can be interpreted in a similar manner. Given invariance of the latent structure of the CATIE battery between men and women, performance on any given test may best be attributed to actual abilities, albeit with small differences between groups, as opposed to measurement bias. Such findings are also critical when considering the utility of neuropsychological test scores in treatment outcome studies. Similarity in latent structure of cognitive abilities between men and women with SZ assures that changes in cognition may be

attributed to the independent variables of interest (e.g., intervention, changes in symptoms) as opposed to test bias.

Future research should examine the stability of latent cognitive structure of SZ with repeated assessment. While some differences in specific factors are expected based on the composition of the test battery, studies should examine whether this bifactor structure of cognitive abilities can also be identified with test batteries that incorporate different tests to understand the generalizability of these findings. However, the current results provide strong evidence for the invariance of the latent structure of cognitive abilities across men and women diagnosed with SZ.

## References


Abel, K. M., Drake, R., & Goldstein, J. M. (2010). Sex differences in schizophrenia. *International Review of Psychiatry*, *22*(5), 417–428. https://doi.org/10.3109/09540261.2010.515205

Allen, D. N., Strauss, G. P., Barchard, K. A., Vertinski, M., Carpenter, W. T., & Buchanan, R. W. (2013). Differences in developmental changes in academic and social premorbid adjustment between males and females with schizophrenia. *Schizophrenia Research*, *146*(1–3), 132–137. https://doi.org/10.1016/j.schres.2013.01.032

Ayesa-Arriola, R., de la Foz, V. O.-G., Setién-Suero, E., Ramírez-Bonilla, M. L., Suárez-Pinilla, P., Son, J. M., Vázquez-Bourgon, J., Juncal-Ruiz, M., Gómez-Revuelta, M., Tordesillas-Gutiérrez, D., & Crespo-Facorro, B. (2020). Understanding sex differences in long-term outcomes after a first episode of psychosis. *Npj Schizophrenia*, *6*(1), 33. https://doi.org/10.1038/s41537-020-00120-5

Ayesa-Arriola, R., Rodriguez-Sanchez, J. M., Gomez-Ruiz, E., Roiz-Santiáñez, R., Reeves, L. L., & Crespo-Facorro, B. (2014). No sex differences in neuropsychological performance in first episode psychosis patients. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *48*, 149–154. https://doi.org/10.1016/j.pnpbp.2013.09.009

Aylward, E., Walker, E., & Bettes, B. (1984). Intelligence in schizophrenia: Meta-analysis of the research. *Schizophrenia Bulletin*, *10*(3), 430–459. https://doi.org/10.1093/schbul/10.3.430

Becker, M. L., Ahmed, A. O., Benning, S. D., Barchard, K. A., John, S. E., & Allen, D. N. (2021). Bifactor model of cognition in schizophrenia: Evidence for general and specific abilities. *Journal of Psychiatric Research*, *136*, 132–139. https://doi.org/10.1016/j.jpsychires.2021.01.051

Bozikas, V. P., Kosmidis, M. H., Peltekis, A., Giannakou, M., Nimatoudis, I., Karavatos, A., Fokas, K., & Garyfallos, G. (2010). Sex differences in neuropsychological functioning among

schizophrenia patients. *Australian & New Zealand Journal of Psychiatry*, *44*(4), 333–341. https://doi.org/10.3109/00048670903489833

Browne, M. W., & Cudeck, R. (1992). Alternative ways of assessing model fit. *Sociological Methods & Research*, *21*(2), 230–258. https://doi.org/10.1177/0049124192021002005

Buck, G., Lavigne, K. M., Makowski, C., Joober, R., Malla, A., & Lepage, M. (2020). Sex differences in verbal memory predict functioning through negative symptoms in early psychosis. *Schizophrenia Bulletin*, *46*(6), 1587–1595. https://doi.org/10.1093/schbul/sbaa054

Byrne, B. M. (2008). Testing for multigroup equivalence of a measuring instrument: A walk through the process. *Psicothema*, 872-882.

Byrne, B. M. (2010). Structural equation modeling with AMOS: basic concepts, applications, and programming (multivariate applications series). *New York: Taylor & Francis Group*, *396*(1), 7384.

Canuso, C. M., & Pandina, G. (2007). Gender and schizophrenia. *Psychopharmacology Bulletin*, *40*(4), 178-190.

Chen, F. F. (2007). Sensitivity of goodness of fit indexes to lack of measurement invariance. *Structural Equation Modeling: A Multidisciplinary Journal*, *14*(3), 464–504. https://doi.org/10.1080/10705510701301834

Danaher, H., Allott, K., Killackey, E., Hester, R., & Cotton, S. (2018). An examination of sex differences in neurocognition and social cognition in first-episode psychosis. *Psychiatry Research*, *259*, 36–43. https://doi.org/10.1016/j.psychres.2017.09.053

Dziak, J. J., Coffman, D. L., Lanza, S. T., Li, R., & Jermiin, L. S. (2020). Sensitivity and specificity of information criteria. *Briefings in Bioinformatics*, *21*(2), 553–565. https://doi.org/10.1093/bib/bbz016

Eranti, S. V., MacCabe, J. H., Bundy, H., & Murray, R. M. (2013). Gender difference in age at onset of schizophrenia: A meta-analysis. *Psychological Medicine*, *43*(1), 155–167. https://doi.org/10.1017/S003329171200089X

Fond, G., Boyer, L., Leboyer, M., Godin, O., Llorca, P. M., Andrianarisoa, M., Berna, F., Brunel, L., Aouizerate, B., Capdevielle, D., Chereau, I., D'Amato, T., Dubertret, C., Dubreucq, J., Faget, C., Gabayet, F., Mallet, J., Misdrahi, D., Rey, R., … Zinetti-Bertschy, A. (2018). Influence of Venus and Mars in the cognitive sky of schizophrenia. Results from the first-step national FACE-SZ cohort. *Schizophrenia Research*, *195*, 357–365. https://doi.org/10.1016/j.schres.2017.09.027

Häfner, H., Maurer, K., Löffler, W., Fätkenheuer, B., Der Heiden, W. A., Riecher-Rössler, A., ... & Gattaz, W. F. (1994). The epidemiology of early schizophrenia: influence of age and gender on onset and early course. *The British Journal of Psychiatry*, *164*(S23), 29-38.

Häfner, H., Riecher, A., Maurer, K., Löffler, W., Munk-Jørgensen, P., & Strömgren, E. (1989). How does gender influence age at first hospitalization for schizophrenia? A transnational case register study. *Psychological Medicine*, *19*(4), 903–918. https://doi.org/10.1017/S0033291700005626

Halari, R., Hines, M., Kumari, V., Mehrotra, R., Wheeler, M., Ng, V., & Sharma, T. (2005). Sex differences and individual differences in cognitive performance and their relationship to endogenous gonadal hormones and gonadotropins. *Behavioral Neuroscience*, *119*(1), 104–117. https://doi.org/10.1037/0735-7044.119.1.104

Halari, R., Mehrotra, R., Sharma, T., Ng, V., & Kumari, V. (2006). Cognitive impairment but preservation of sexual dimorphism in cognitive abilities in chronic schizophrenia. *Psychiatry Research*, *141*(2), 129–139. https://doi.org/10.1016/j.psychres.2005.07.021

Han, M., Huang, X.-F., Chen, D. C., Xiu, M. H., Hui, L., Liu, H., Kosten, T. R., & Zhang, X. Y. (2012). Gender differences in cognitive function of patients with chronic schizophrenia.

*Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *39*(2), 358–363. https://doi.org/10.1016/j.pnpbp.2012.07.010

Horn, J. L., & Mcardle, J. J. (1992). A practical and theoretical guide to measurement invariance in aging research. *Experimental Aging Research*, *18*(3), 117–144. https://doi.org/10.1080/03610739208253916

Hu, L., & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling: A Multidisciplinary Journal*, *6*(1), 1–55. https://doi.org/10.1080/10705519909540118

Ittig, S., Studerus, E., Papmeyer, M., Uttinger, M., Koranyi, S., Ramyead, A., & Riecher-Rössler, A. (2015). Sex differences in cognitive functioning in at-risk mental state for psychosis, first episode psychosis and healthy control subjects. *European Psychiatry*, *30*(2), 242–250. https://doi.org/10.1016/j.eurpsy.2014.11.006

Keefe, R. S. E., Bilder, R. M., Harvey, P. D., Davis, S. M., Palmer, B. W., Gold, J. M., Meltzer, H. Y., Green, M. F., Miller, D. D., Canive, J. M., Adler, L. W., Manschreck, T. C., Swartz, M., Rosenheck, R., Perkins, D. O., Walker, T. M., Stroup, T. S., McEvoy, J. P., & Lieberman, J. A. (2006). Baseline neurocognitive deficits in the catie schizophrenia trial. *Neuropsychopharmacology*, *31*(9), 2033–2046. https://doi.org/10.1038/sj.npp.1301072

Keefe, R. S. E., Mohs, R. C., Bilder, R. M., Harvey, P. D., Green, M. F., Meltzer, H. Y., Gold, J. M., & Sano, M. (2003). Neurocognitive assessment in the clinical antipsychotic trials of intervention effectiveness (Catie) project schizophrenia trial: Development, methodology, and rationale. *Schizophrenia Bulletin*, *29*(1), 45–55. https://doi.org/10.1093/oxfordjournals.schbul.a006990

Keith, T. Z., Reynolds, M. R., Patel, P. G., & Ridley, K. P. (2008). Sex differences in latent cognitive abilities ages 6 to 59: Evidence from the Woodcock–Johnson III tests of cognitive abilities. *Intelligence*, *36*(6), 502–525. https://doi.org/10.1016/j.intell.2007.11.001

Leung M.D., Dr. A., & Chue M. R. C. Psych., Dr. P. (2000). Sex differences in schizophrenia, a review of the literature. *Acta Psychiatrica Scandinavica*, *101*(401), 3–38. https://doi.org/10.1111/j.0065-1591.2000.0ap25.x

Longenecker, J., Dickinson, D., Weinberger, D. R., & Elvevåg, B. (2010). Cognitive differences between men and women: A comparison of patients with schizophrenia and healthy volunteers. *Schizophrenia Research*, *120*(1–3), 234–235. https://doi.org/10.1016/j.schres.2009.12.009

Mu, L., Liang, J., Wang, H., Chen, D., Xiu, M., & Zhang, X. Y. (2020). Sex differences in association between clinical correlates and cognitive impairment in patients with chronic schizophrenia. *Journal of Psychiatric Research*, *131*, 194–202. https://doi.org/10.1016/j.jpsychires.2020.09.003

Murillo-García, N., Setién-Suero, E., Pardo-de-Santayana, G., Murillo-García, M., Pelayo-Terán, J. M., Crespo-Facorro, B., & Ayesa-Arriola, R. (2021). Entire duration of active psychosis and neurocognitive performance in FIRST-EPISODE NON-AFFECTIVE psychosis. *Early Intervention in Psychiatry*, *15*(5), 1266–1275. https://doi.org/10.1111/eip.13077

Muthen, L. K., & Muthen, B. O. (2007). Mplus (version 5.0)[computer software]. *Los Angeles, CA: Author*. https://www.statmodel.com/index.shtml

Ochoa, S., Usall, J., Cobo, J., Labad, X., & Kulkarni, J. (2012). Gender differences in schizophrenia and first-episode psychosis: A comprehensive literature review. *Schizophrenia Research and Treatment*, *2012*, 1–9. https://doi.org/10.1155/2012/916198

Ojeda, N., Sánchez, P., Peña, J., Elizagárate, E., Yoller, A. B., Larumbe, J., Gutiérrez, M., Casais, L., & Ezcurra, J. (2010). Verbal fluency in schizophrenia: Does cognitive performance reflect the

same underlying mechanisms in patients and healthy controls? *Journal of Nervous & Mental Disease*, *198*(4), 286–291. https://doi.org/10.1097/NMD.0b013e3181d61748

Pezzuti, L., Tommasi, M., Saggino, A., Dawe, J., & Lauriola, M. (2020). Gender differences and measurement bias in the assessment of adult intelligence: Evidence from the Italian WAIS-IV and WAIS-R standardizations. *Intelligence*, *79*, 101436. https://doi.org/10.1016/j.intell.2020.101436

Piras, F., Piras, F., Banaj, N., Ciullo, V., Vecchio, D., Edden, R. A. E., & Spalletta, G. (2019). Cerebellar GABAergic correlates of cognition-mediated verbal fluency in physiology and schizophrenia. *Acta Psychiatrica Scandinavica*, *139*(6), 582–594. https://doi.org/10.1111/acps.13027

Putnick, D. L., & Bornstein, M. H. (2016). Measurement invariance conventions and reporting: The state of the art and future directions for psychological research. *Developmental Review*, *41*, 71–90. https://doi.org/10.1016/j.dr.2016.06.004

Riecher-Rössler, A., Butler, S., & Kulkarni, J. (2018). Sex and gender differences in schizophrenic psychoses—A critical review. *Archives of Women's Mental Health*, *21*(6), 627–648. https://doi.org/10.1007/s00737-018-0847-9

Riecher-Rössler, A., & Häfner, H. (2000). Gender aspects in schizophrenia: Bridging the border between social and biological psychiatry: Gender aspects in schizophrenia. *Acta Psychiatrica Scandinavica*, *102*, 58–62. https://doi.org/10.1034/j.1600-0447.2000.00011.x

Steiger, J. H. (1980). Statistically based tests for the number of common factors. In *the annual meeting of the Psychometric Society. Iowa City, IA. 1980*.

Stroup, T. S., McEvoy, J. P., Swartz, M. S., Byerly, M. J., Glick, I. D., Canive, J. M., McGee, M. F., Simpson, G. M., Stevens, M. C., & Lieberman, J. A. (2003). The national institute of mental

health clinical antipsychotic trials of intervention effectiveness (Catie) project: Schizophrenia trial design and protocol development. *Schizophrenia Bulletin*, *29*(1), 15–31. https://doi.org/10.1093/oxfordjournals.schbul.a006986

Torniainen, M., Suvisaari, J., Partonen, T., Castaneda, A. E., Kuha, A., Perälä, J., Saarni, S., Lönnqvist, J., & Tuulio-Henriksson, A. (2011). Sex differences in cognition among persons with schizophrenia and healthy first-degree relatives. *Psychiatry Research*, *188*(1), 7–12. https://doi.org/10.1016/j.psychres.2010.11.009

Tsai, P.-C., McDowd, J., Tang, T.-C., & Su, C.-Y. (2012). Processing speed mediates gender differences in memory in schizophrenia. *The Clinical Neuropsychologist*, *26*(4), 626–640. https://doi.org/10.1080/13854046.2012.678887

Tyburski, E., Sokołowski, A., Chęć, M., Pełka-Wysiecka, J., & Samochowiec, A. (2015). Neuropsychological characteristics of verbal and non-verbal fluency in schizophrenia patients. *Archives of Psychiatric Nursing*, *29*(1), 33–38. https://doi.org/10.1016/j.apnu.2014.09.009

van der Werf, M., Hanssen, M., Köhler, S., Verkaaik, M., Verhey, F. R., RISE Investigators, van Winkel, R., van Os, J., & Allardyce, J. (2014). Systematic review and collaborative recalculation of 133 693 incident cases of schizophrenia. *Psychological Medicine*, *44*(1), 9–16. https://doi.org/10.1017/S0033291712002796

Vaskinn, A., Sundet, K., Simonsen, C., Hellvin, T., Melle, I., & Andreassen, O. A. (2011). Sex differences in neuropsychological performance and social functioning in schizophrenia and bipolar disorder. *Neuropsychology*, *25*(4), 499–510. https://doi.org/10.1037/a0022677

Vrieze, S. I. (2012). Model selection and psychological theory: A discussion of the differences between the Akaike information criterion (Aic) and the Bayesian information criterion (Bic). *Psychological Methods*, *17*(2), 228–243. https://doi.org/10.1037/a0027127

Zanelli, J., Morgan, K., Dazzan, P., Morgan, C., Russo, M., Pilecka, I., Fearon, P., Demjaha, A., Doody, G. A., Jones, P. B., Murray, R. M., & Reichenberg, A. (2013). Gender differences in neuropsychological performance across psychotic disorders – a multi-centre population based case-control study. *PLoS ONE*, *8*(10), e77318. https://doi.org/10.1371/journal.pone.0077318

**Table 1. Assessment 1 Demographics**

| | Men | Women | Total |
|---|---|---|---|
| Mean age in years (*SD*) | (*n* = 609) | (*n* = 201) | (*n* = 810) |
| | 38.1 (10.9) | 40.2 (9.8) | 39.1 (10.4) |
| Mean education in years (*SD*) | (n = 604) | (*n* = 200) | (*n* = 804) |
| | 11.7 (3.4) | 11.8 (3.8) | 11.8 (3.6) |
| Race | (*n* = 609) | (*n* = 200) | (*n* = 809) |
| White/Caucasian | 397 | 112 | 509 |
| Black/African American | 183 | 73 | 256 |
| Asian | 12 | 7 | 19 |
| More than one race | 12 | 5 | 17 |
| American Indian/Alaska Native | 1 | 3 | 4 |
| Native Hawaiian/Pacific Islander | 3 | 0 | 3 |
| Unknown or not reported race/ethnicity | 1 | 0 | 1 |
| Ethnicity | 73 | 19 | 92 |
| Hispanic/Latino | | | |
| Not Hispanic/Latino | 536 | 182 | 718 |
| Mean PANSS (*SD*) | (*n* = 611) | (*n* = 200) | (*n* = 811) |
| Positive Symptom Score | 18.6 (5.6) | 17.9 (5.5) | 18.3 (5.6) |
| Negative Symptom Score | 20.0 (6.3) | 18.9 (6.4) | 19.5 (6.4) |
| General Symptom Score | 36.8 (9.2) | 37.1 (9.5) | 37.0 (9.4) |
| Medication | (*n* = 450) | (*n* = 158) | (*n* = 608) |
| Olanzapine | 176 | 46 | 222 |
| Quetiapine | 58 | 30 | 88 |
| Risperidone | 137 | 49 | 186 |
| Ziprasidone | 28 | 16 | 44 |
| Haloperidol | 33 | 10 | 43 |
| Decanoate | 11 | 1 | 12 |
| Perphenazine | 7 | 6 | 13 |
| Other | 42 | 21 | 63 |
| All Other | 114 | 53 | 167 |
| None | 171 | 51 | 222 |

*Note*. Table adapted from Becker et al. (2021). Neuroleptic medications were taken on the day of assessment 1 testing or two weeks prior. Other = participant received any other neuroleptic besides of the neuroleptics listed above; All Other = participant received any other neuroleptics (olanzapine, quetiapine, and risperidone not included); None = participant did not receive neuroleptics.

**Table 2. Results of Fit Indices for Men and Women with SZ**

| Assessment | Model | $\chi 2$ (df) | CFI | RMSEA (90% CI) | TLI | BIC |
|---|---|---|---|---|---|---|
| Assessment 1 | | | | | | |
| Men | 1 | 3121.60 (209) | .57 | .151 (.146, .156) | .52 | 68496.27 |
| | 5 | 1881.49 (199) | .75 | .118 (.113, .122) | .71 | 67320.33 |
| | H5 | 2158.88 (208) | .71 | .124 (.119, .129) | .68 | 67539.97 |
| | B5 | 855.55 (187) | .90 | .076 (.071, .082) | .88 | 66371.39 |
| | 6 | 1135.83 (194) | .86 | .089 (.084, .094) | .83 | 66606.76 |
| | H6 | 1599.39 (208) | .79 | .105 (.100, .109) | .77 | 66980.48 |
| | B6 | 492.26 (188) | .96 | .051 (.046, .057) | .94 | 66001.69 |
| | 7 | 876.43 (188) | .90 | .077 (.072, .083) | .87 | 66385.86 |
| | H7 | 1561.13 (208) | .80 | .103 (.098, .108) | .78 | 66942.22 |
| | B7* | 381.88 (188) | .97 | .041 (.035, .047) | .97 | 65891.30 |
| Women | 1 | 1187.57 (209) | .54 | .153 (.144, .161) | .49 | 22588.79 |
| | 5 | 756.88 (199) | .74 | .118 (.109, .127) | .70 | 22211.13 |
| | H5 | 860.67 (208) | .69 | .125 (.116, .134) | .66 | 22267.19 |
| | B5 | 376.30 (188) | .91 | .071 (.060, .081) | .89 | 21888.89 |
| | 6 | 461.45 (194) | .88 | .083 (.073, .093) | .85 | 21942.21 |
| | H6 | 652.36 (208) | .79 | .103 (.094, .112) | .77 | 22058.88 |
| | B6 | 344.96 (188) | .93 | .064 (.054, .075) | .91 | 21857.54 |
| | 7 | 367.37 (188) | .92 | .069 (.058, .079) | .90 | 21879.95 |
| | H7 | 673.11 (208) | .78 | .105 (.097, .114) | .76 | 22079.62 |
| | B7* | 314.94 (188) | .94 | .058 (.047, .069) | .93 | 21827.52 |
| Assessment 2 | | | | | | |
| Men | B7* | 457.71 (189) | .96 | .051 (.045, .057) | .95 | 58736.24 |
| Women | B7* | 303.95 (188) | .95 | .056 (.044, .067) | .94 | 21341.65 |

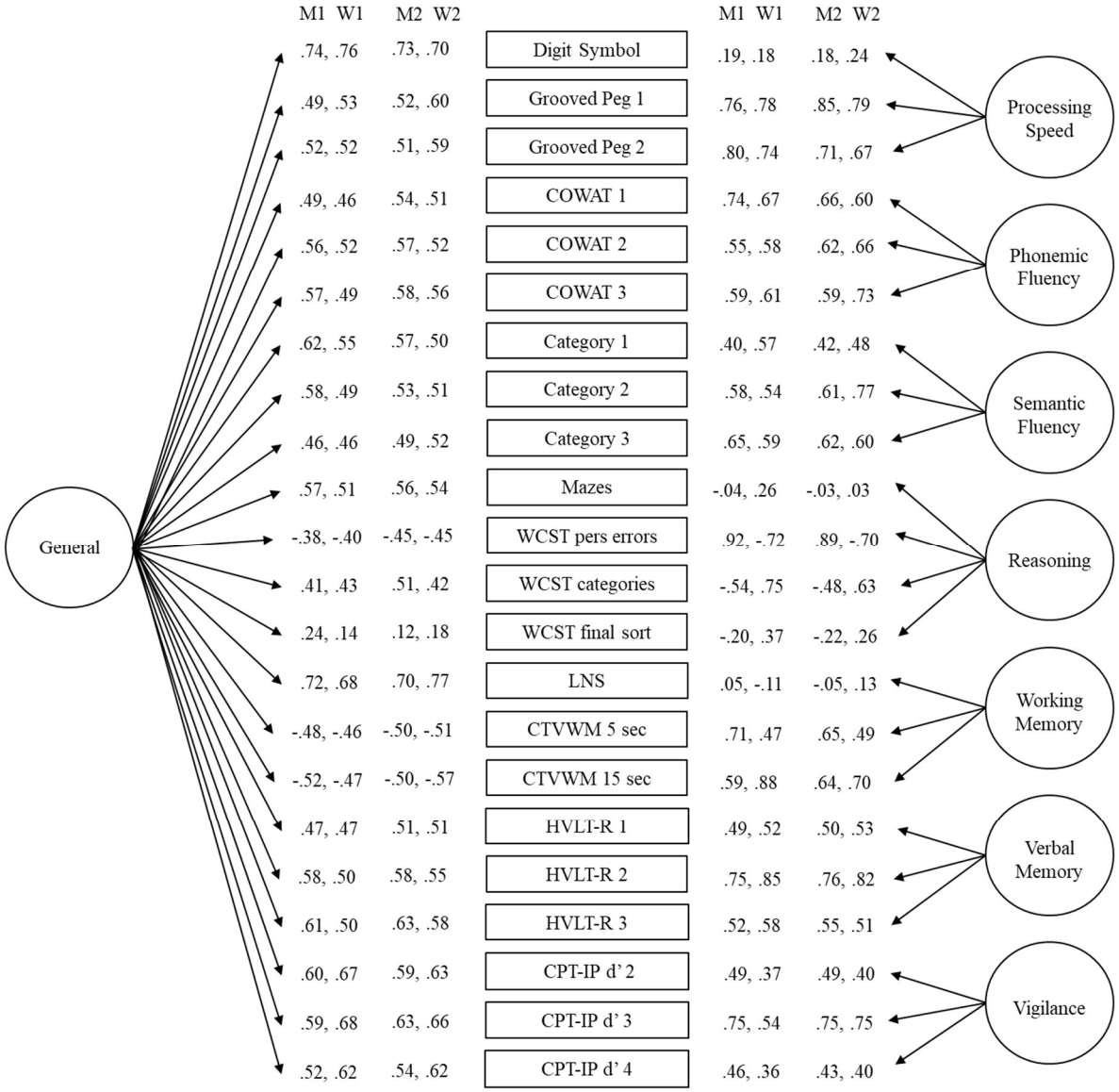
*Note.* Model numbers represent the number of single-level factors; H = hierarchical with g as the higher order factor; B = bifactor with g as the global factor and numbers represent the number of specific factors. All of the bifactor seven-factor models had significant chi-squared values at $p <$ .001. * indicates that best fitting models.

**Table 3. Measurement Invariance of the Bifactor Seven-Factor Model**

| Invariance Level | Chi-Square $\chi^2$ (df) | Chi-Square Difference Test $\chi^2$(df) | CFI | CFI Change | TLI | TLI Change | RMSEA | RMSEA Change | BIC |
|---|---|---|---|---|---|---|---|---|---|
| Assessment 1 | | | | | | | | | |
| Configural | $\chi^2(201)=368.87$, $p<.001$ | - | .960 | - | .956 | - | .045 | - | 87865.11 |
| Metric | $\chi^2(209)=371.54$, $p<.001$ | $\chi^2(32)=38.83$, $p=.19$ | .962 | -.002 | .959 | -.003 | .044 | .001 | 87657.33 |
| Scalar | $\chi^2(212)=413.39$, $p<.001$ | $\chi^2(19)=91.45$, $p<.001$ | .953 | .009 | .949 | .010 | .048 | -.004 | 87632.02 |
| Residual | $\chi^2(215)=403.89$, $p<.001$ | $\chi^2(10)=19.77$, $p<.05$ | .956 | -.003 | .953 | -.004 | .046 | .002 | 87550.55 |
| Assessment 2 | | | | | | | | | |
| Configural | $\chi^2(196)=393.76$, $p<.001$ | - | .951 | - | .946 | - | .052 | - | 80213.42 |
| Metric | $\chi^2(202)=386.55$, $p<.001$ | $\chi^2(30)=30.15$, $p=0.46$ | .954 | -.003 | .951 | -.005 | .049 | .003 | 80002.13 |
| Scalar | $\chi^2(202)=410.22$, $p<.001$ | $\chi^2(19)=73.23$, $p<.001$ | .948 | .006 | .945 | .006 | .053 | -.004 | 79953.53 |
| Residual | $\chi^2(205)=409.13$, $p<.001$ | $\chi^2(9)=34.90$, $p<.001$ | .949 | -.001 | .947 | -.002 | .052 | .001 | 79905.57 |

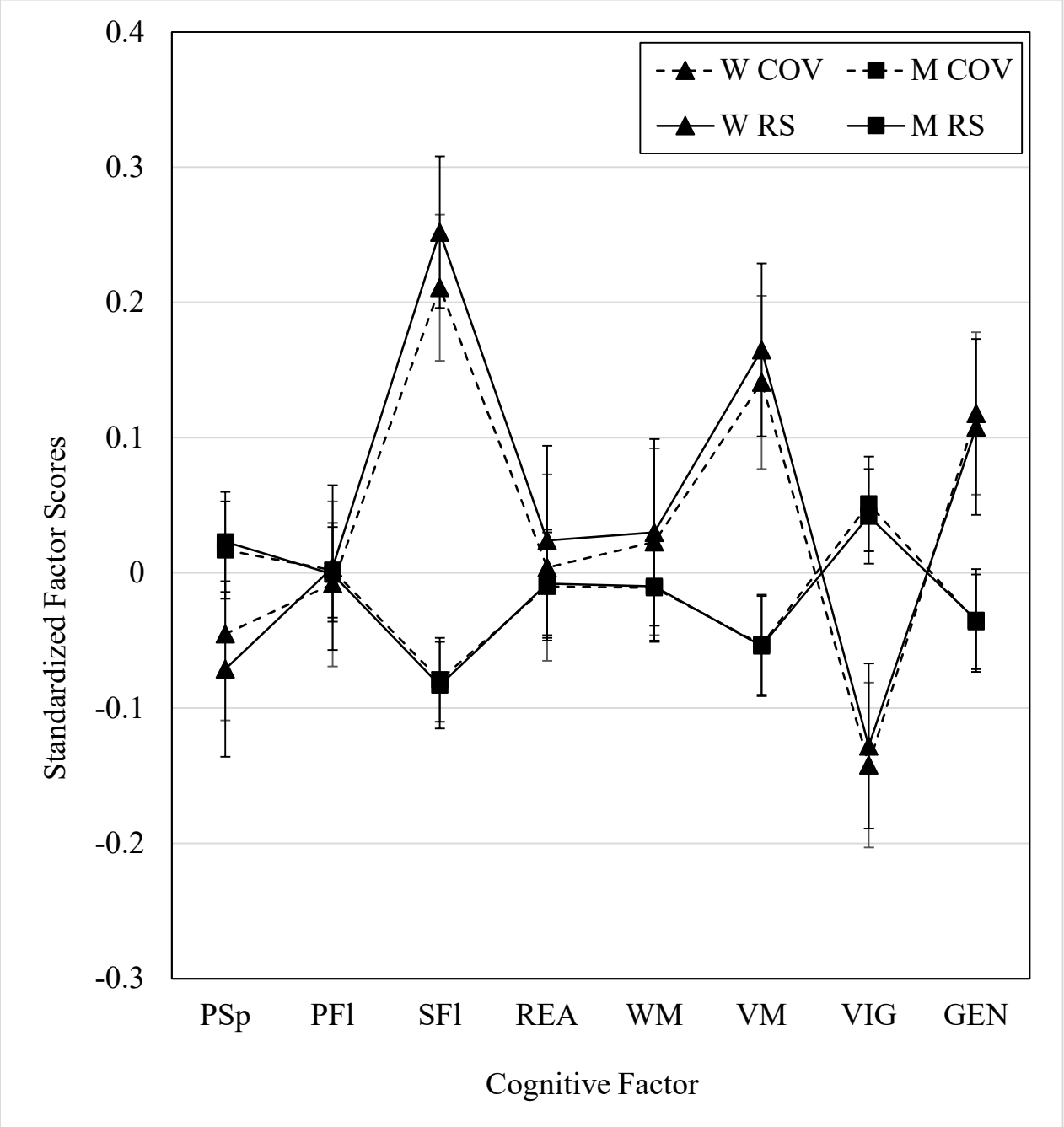
Note. Chi-square for the baseline model in the Assessment 1 data: $\chi^2(226) = 4{,}475.27$, $p < .001$. Chi-square for the baseline model in the Assessment 2 data: $\chi^2(215) = 4{,}250.86$, $p < .001$.

**Figure 1. Bifactor Seven-factor Model Loadings for Men (M) and Women (W) at Assessments 1 and 2**




*Note*. See Table 3 in Supplementary Materials for definitions of variables.

**Figure 2. Specific and General Standardized Factor Scores for Men (M) and Women (W)**




*Note*. W=Women; M=Men; RS=Raw Scores, COV=raw scores with age and negative symptoms covaried. Error bars represent standard errors. PSp=Processing Speed, PFl=Phonemic Fluency, SFl=Semantic Fluency, REA=Reasoning, WM=Working Memory, VM=Verbal Memory, VIG=Vigilance, and GEN=General.

**Supplementary Materials**

**for**

# Latent structure of cognitive tests is invariant in men and women with schizophrenia

Megan L. Becker Wright[1]

Anthony O. Ahmed[2]

Kimberly A. Barchard[1]

Stephen D. Benning[1]

Samantha E. John[1]

Daniel N. Allen[1]

1. Department of Psychology, University of Nevada, Las Vegas, Las Vegas, NV

2. Department of Psychiatry, Weill Cornell Medicine, White Plains, NY

*Address correspondence to: Daniel N. Allen, Ph.D., Department of Psychology, University of Nevada Las Vegas, 4505 Maryland Parkway, Las Vegas, NV 89154. Phone: 702.895.0121. Fax: 702.895.0195. Email: daniel.allen@unlv.edu

**Supplementary Materials**

**Table 1. Descriptive Statistics**

| Test Score | Assessment 1 Mean (*SD*) | | Assessment 2 Mean (*SD*) | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| Grooved Pegboard Trial 1 | 12.6 (3.6) | 12.5 (3.8) | 12.9 (3.7) | 12.8 (3.9) |
| Grooved Pegboard: Trial 2 | 14.1 (3.6) | 14.1 (3.9) | 14.1 (3.8) | 14.2 (3.9) |
| WAIS-R Digit Symbol Test | 39.2 (13.3) | 43.6 (13.0) | 39.9 (13.1) | 44.9 (13.3) |
| COWAT 1st letter | 10.2 (4.0) | 10.7 (3.8) | 10.2 (4.0) | 10.8 (4.0) |
| COWAT 2nd letter | 8.4 (3.7) | 8.6 (3.5) | 8.1 (3.7) | 8.7 (3.5) |
| COWAT 3rd letter | 10.6 (4.5) | 10.8 (4.0) | 10.3 (4.2) | 10.9 (4.2) |
| Category Instances 1st category | 14.5 (4.8) | 14.6 (4.3) | 14.5 (4.8) | 14.8 (4.2) |
| Category Instances 2nd category | 10.2 (3.2) | 11.4 (3.5) | 10.2 (3.4) | 11.8 (3.3) |
| Category Instances 3rd category | 8.5 (3.2) | 10.2 (3.3) | 8.7 (3.4) | 10.5 (3.6) |
| WCST perseverative errors | 12.9 (10.0) | 12.7 (9.9) | 10.9 (8.0) | 10.5 (8.3) |
| WCST completed categories | 2.3 (1.6) | 2.3 (1.6) | 2.5 (1.7) | 2.5 (1.7) |
| WCST additional cards in final category | 2.2 (3.0) | 2.4 (3.2) | 2.0 (2.8) | 2.1 (2.8) |
| WISC-III Mazes total correct | 19.2 (5.5) | 17.6 (5.2) | 19.5 (5.3) | 17.6 (5.4) |
| Letter-Number Sequencing Test total correct | 10.9 (4.3) | 11.5 (3.9) | 11.6 (4.2) | 12.1 (3.8) |
| CTVWM mean errors 5 second delay | 25.1 (15.3) | 24.7 (12.4) | 24.6 (15.3) | 25.0 (13.9) |
| CTVWM mean errors 15 second delay | 27.2 (16.0) | 27.4 (14.6) | 27.4 (16.6) | 28.1 (17.9) |
| HVLT-R Trial 1 | 4.9 (1.7) | 5.5 (1.8) | 5.0 (1.7) | 5.4 (1.8) |
| HVLT-R Trial 2 | 6.6 (2.0) | 7.1 (2.2) | 6.8 (2.1) | 7.5 (2.1) |
| HVLT-R Trial 3 | 7.7 (2.3) | 8.4 (2.3) | 7.9 (2.3) | 8.5 (2.3) |
| CPT-IP: d′ condition 2 | 2.51 (1.00) | 2.41 (1.07) | 2.69 (0.97) | 2.65 (1.06) |
| CPT-IP: d′ condition 3 | 1.87 (0.90) | 1.85 (0.86) | 2.10 (0.96) | 1.93 (0.90) |
| CPT-IP: d′ condition 4 | 1.09 (0.82) | 1.00 (0.76) | 1.18 (0.80) | 1.06 (0.75) |

*Note:* Assessment 1 (men $n = 612$, women $n = 201$), Assessment 2 (men $n = 549$, women $n = 198$)

**Table 2. Scores Included in Factors**

| CATIE Domains and Test scores | CFA Models | | | |
|---|---|---|---|---|
| | 1-factor | 5-factor | 6-factor | 7-factor |
| Processing Speed | | | | |
| Grooved Pegboard Trial 1 | 1 | 1 | 1 | 1 |
| Grooved Pegboard Trial 2 | 1 | 1 | 1 | 1 |
| WAIS-R Digit-Symbol Test number correct | 1 | 1 | 1 | 1 |
| COWAT 1st letter | 1 | 1 | 6 | 6 |
| COWAT 2nd letter | 1 | 1 | 6 | 6 |
| COWAT 3rd letter | 1 | 1 | 6 | 6 |
| Category Instances 1st category | 1 | 1 | 6 | 7 |
| Category Instances 2nd category | 1 | 1 | 6 | 7 |
| Category Instances 3rd category | 1 | 1 | 6 | 7 |
| Reasoning | | | | |
| WCST perseverative errors | 1 | 2 | 2 | 2 |
| WCST completed categories | 1 | 2 | 2 | 2 |
| WCST additional cards in final category | 1 | 2 | 2 | 2 |
| WISC-III Mazes total correct | 1 | 2 | 2 | 2 |
| Working Memory | | | | |
| Letter-Number Sequencing Test total correct | 1 | 3 | 3 | 3 |
| CTVWM mean errors 5 second delay | 1 | 3 | 3 | 3 |
| CTVWM mean errors 15 second delay | 1 | 3 | 3 | 3 |
| Verbal Memory | | | | |
| HVLT-R Trial 1 | 1 | 4 | 4 | 4 |
| HVLT-R Trial 2 | 1 | 4 | 4 | 4 |
| HVLT-R Trial 3 | 1 | 4 | 4 | 4 |
| Vigilance | | | | |
| CPT-IP d' condition 2 | 1 | 5 | 5 | 5 |
| CPT-IP d' condition 3 | 1 | 5 | 5 | 5 |
| CPT-IP d' condition 4 | 1 | 5 | 5 | 5 |

*Note.* Table was adapted from Becker et al. (2021). Hierarchical and bifactor models kept these domains for single-level and specific factors, respectively with the addition of g (including all variables) as the higher-order or global factor accordingly. WAIS-R = Wechsler Adult Intelligence Scale-Revised (WAIS-R) COWAT = Controlled Oral Word Association; WISC-III = Wechsler Intelligence Scale for Children, 3rd Ed. (WISC-III); WCST = Wisconsin Card Sorting Test; CTVWM = Computerized Test of Visual Working Memory; HVLT-R = Hopkins

Verbal Learning Test- Revised; CPT-IP d' = Conners' Continuous Performance Test- Identical Pairs number of correctly identified targets

**Table 3. Definitions of Variables**

| Abbreviation | Test Score |
|---|---|
| Digit Symbol | Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol Test |
| Grooved Peg (1 or 2) | Grooved Pegboard Test Trial (1 or 2) |
| COWAT (1, 2, or 3) | Controlled Oral Word Association Test Trial 1, 2, or 3 |
| Category (1, 2, or 3) | Category Test Trial 1, 2, or 3 |
| Mazes | Wechsler Intelligence Scale for Children, 3rd Ed. (WISC-III) Mazes |
| WCST | Wisconsin Card Sorting Test |
| per errors | perseverative errors |
| categories | number of categories administered |
| final sort | number of additional consecutive cards in the final category |
| LNS | Letter-Number Sequencing Test |
| CTVWM | Computerized Test of Visual Working Memory |
| 5 sec | mean errors during the five second delay |
| 15 sec | mean errors during the 15 second delay |
| HVLT-R (1, 2, or 3) | Hopkins Verbal Learning Test- Revised Trial 1, 2, or 3 |
| CPT-IP d' (2, 3, or 4) | Conners' Continuous Performance Test- Identical Pairs number of correctly identified targets on the two-, three-, or four- digit condition |

## Chapter IV: Longitudinal Stability of the Latent Structure of Cognition in Schizophrenia

Note: Study III was submitted to *European Psychiatry*.

The second dissertation paper, "Latent structure of cognitive tests is invariant in men and women with schizophrenia," examined the latent structure of cognitive abilities in men and women with SZ to determine if measurement variance between these groups could underlie the variability observed in studies comparing cognitive performance in men and women. The results from this paper indicated that a bifactor seven-factor structure best fit the latent structure of cognitive abilities for both men and women with SZ. This bifactor model achieved strict factorial invariance, which further suggests that the latent structure between men and women with SZ is the same despite known differences in onset, symptoms, disorder course, and other important variables between men and women. Given that the factor structure was invariant, differences in the latent structure do not appear to account for differences in cognitive test performance between men and women with SZ. Future work should include tests that assess other domains such as visuospatial skills, that have documented sex differences among healthy adults. Such work would help determine if sex difference in SZ are consistent with what is found in the general population or are more consistent with neurodevelopmental abnormality that may contribute to symptoms and course of the disorder. Additional work would also benefit from inclusion of gender diverse individuals with SZ.

Following this work, the third dissertation paper, "Stability of bifactor structure of cognition in schizophrenia with repeated assessment," further examined the stability of the latent structure of cognition in SZ. It was critical to examine the latent structure longitudinally because neuropsychological tests are often used to examine changes in cognitive abilities over time, which could indicate improvement or decline in function. These analyses will elucidate whether

potential practice effects, changes in symptoms or medications, and other influences alter the constructs the tests measure when repeatedly administered over an extended period of time. Such information is critical when drawing conclusions from treatment outcome studies that incorporate neuropsychological measures to examine changes in cognition rather than measurement error.

**Longitudinal stability of the latent structure of cognition in schizophrenia**

Megan L. Becker Wright[1], Anthony O. Ahmed[2], Samantha E. John[1,3], Kimberly A. Barchard[1], Stephen D. Benning[1], and Daniel N. Allen[1]

[1]Department of Psychology, University of Nevada, Las Vegas, Las Vegas, NV

[2]Department of Psychiatry, Weill Cornell Medicine, White Plains, NY

[3]Department of Brain Health, University of Nevada, Las Vegas, Las Vegas, NV

*Address correspondence to: Daniel N. Allen, Ph.D., Department of Psychology, University of Nevada Las Vegas, 4505 Maryland Parkway, Las Vegas, NV 89154-5030. Phone: 702.895.0121. Fax: 702.895.0195. Email: daniel.allen@unlv.edu

**Abstract**

Neurocognitive tests are now commonly used in treatment outcome studies of schizophrenia (SZ) spectrum disorders to determine if treatment is impacting cognitive abilities. In these applications, longitudinal measurement invariance of the neurocognitive tests is essential to ensure that changes in test scores over time are not simply the result of changes in the measurement properties of the tests caused by repeated administrations. However, this critical issue has not been rigorously examined. To investigate measurement invariance of neurocognitive tests in SZ, the current study examined neurocognitive test performance across four repeated assessments that were collected as part of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). Confirmatory factor analysis was conducted to identify whether first-order or bifactor models provided the best fit to the data for all four assessments, and invariance analysis was used to examine change in the latent structure of cognition across repeated assessments. Results lend support for a stable bifactor model characterized by both a global cognitive factor and specific cognitive domains. These findings allow longitudinal changes in cognitive abilities as a result of treatment or other relevant variables to be more confidently attributed to actual changes in cognition and thus demonstrate that neurocognitive tests are well suited for longitudinal investigation of cognitive changes in SZ.

*Keywords:* schizophrenia, cognition, CATIE, factor analysis, repeated assessment

Student Contribution Statement: Megan Becker Wright's role on this manuscript included study conceptualization, data preparation, statistical analyses and interpretation, writing the first draft of the manuscript, and overseeing the revision process with coauthors.

## Introduction

Cognitive deficits in schizophrenia (SZ) are common and predict important outcomes, which has prompted their examination in treatment trials designed to ameliorate SZ symptoms. One basic issue that requires further investigation is whether the latent structure of cognitive abilities remains stable across repeated assessment. In treatment outcome trails, longitudinal cognitive changes could be associated with the effects of novel interventions, exposure-related practice effects that change the nature of the cognitive constructs assessed by the tests, changes in positive or negative symptoms that might interfere with a patient's ability to perform optimally, or numerous other factors (Herold et al., 2020; Moritz et al. 2021; Okasha et al., 2020; Rodriguez-Toscano et al., 2020). The extent to which longitudinal changes in cognitive test scores may reflect measurement error that results from repeated assessments is important to determine if cognitive tests are to be confidently used to assess changes in cognition in randomized controlled trials of novel interventions, developmental studies of age-related changes, or other conditions where longitudinal changes in cognition are central to assessment objectives. However, the longitudinal stability of the latent structure of specific and general neurocognitive abilities in SZ has not been rigorously evaluated.

An exploratory factor analysis of the neurocognitive data from the Comparison of Atypicals in First Episode SZ (CAFE) study found support for the longitudinal stability of a one factor model of neurocognition over a 12-week assessment period (Hill et al., 2008). Similarly, over an 18-week assessment period, invariance analysis provided support for a model consisting of one latent construct reflecting performance on neurocognitive and functional performance measures for individuals with SZ (Harvey et al., 2013). In both studies, one factor was identified, and the latent structure of the neurocognitive test scores did not appear to change in response to

antipsychotic medication treatment. These findings provide preliminary support for the stability of a generalized neurocognitive factor, but do not provide much insight into whether latent models that include more specific neurocognitive abilities identified as important features of SZ (e.g., attention, executive functions, memory) would demonstrate similar stability over time. The stability of specific factors is relevant because some studies support a unitary factor (Dickinson et al., 2004; 2006; Harvey et al., 2013; Hill et al., 2008), whereas other factor analytic studies identify separable and specific cognitive domains including processing speed, executive function, working memory, verbal memory, and attention/vigilance domains (Burton et al., 2013; Becker Wright et al., 2021; Gladsjo et al., 2004; Keefe et al., 2006; Ojeda et al., 2012; McCleery et al., 2015; Nuechterlein et al., 2004). Some studies also identify crystalized verbal abilities, visual learning and memory, and social cognition when measures for these abilities are included in the batteries (Burton et al., 2013; Gladsjo et al., 2004; Ojeda et al., 2012; McCleery et al., 2015; Nuechterlein et al., 2004). Becker et al. (2021) recently examined whether the latent structure of neurocognition in SZ might be best characterized by models that include general and specific latent constructs, including hierarchical and bifactor models. Confirmatory factor analysis (CFA) of the CATIE data set indicated a bifactor model with one general factor and seven specific factors provided the best fit of the data. That model demonstrated better fit than multidimensional first-order and hierarchical models and is consistent with idea that cognition in SZ may manifest with both specific and generalized deficits. This model also provided the best fit when males and females were examined separately, and it evidenced strict factorial invariance, which further suggests that measurement variance does not appear to account for differences in levels of cognitive performance sometimes reported between males and females (Ayesa-Arriola et al., 2014; Bozikas et al., 2010; Buck et al., 2020; Halari et al., 2006; Fond et

al., 2018; Longenecker et al., 2010; Mu et al., 2020; Ittig et al., 2015; Torniainen et al., 2011; Tsai et al., 2017).

This study was conducted to follow up the results reported by Becker et al. (2021) by determining whether the bifactor latent structure of cognitive tests identified in that study would demonstrate longitudinal invariance across four assessments spanning 18 months. The analyses were conducted on the neurocognitive data collected as part of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study to identify a best fitting model using CFA to compare first-order and bifactor models. Invariance analyses were then conducted for the best fitting model to examine longitudinal measurement invariance.

## Method

### *Participants*

Participants in the current study were selected from the CATIE database, which consisted of 1,493 participants from 57 sites across the United States with a DSM-IV diagnosis of SZ. Individuals in the database were between 18 and 65 years old, were able to take oral medication, had adequate decision making, and provided informed consent (Keefe et al., 2006; Stroup et al., 2003). Of the 839 participants who had complete neurocognitive baseline data, only those who had complete data at all four assessment timepoints were included in the current student, which resulted in a sample of 211 participants. Multivariate outliers were identified using a Mahalanobis distance cut-off of $p < .001$, and based on these analyses, a total of six participants were excluded from the dataset, resulting in a final sample of 205. Demographic and clinical data for this sample of 205 participants at baseline assessment is presented in Table 1.

### *Measures*

The CATIE battery was comprised of tests for the following domains: Processing Speed, Reasoning, Working Memory, Verbal Memory, and Vigilance. The specific tests within the battery included: WRAT-III Reading Test (Wilkinson, 1993), Controlled Oral Word Association Test (COWAT; Benton and Hamscher, 1978), Category Instances (Benton and Hamscher, 1978), Wechsler Intelligence Scale for Children Revised-Third Edition (WISC-III) Mazes (Wechsler, 1991), Hopkins Verbal Learning Test (HVLT-R; Brandt, 1991), Face Emotion Discrimination Task (FEDT; Kerr and Neale, 1993), Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol (Wechsler, 1974), Letter-Number Span Test (Gold et al., 1997), Grooved Pegboard (Lafayette Instrument Company, 1989), Computerized Continuous Performance Test-Identical Pairs (CPT-IP; Cornblatt et al., 1988), Computerized Test of Visuospatial Working Memory (CTVWM; Hershey et al., 1999) and a computerized, 64-card version of the Wisconsin Card Sorting Test (WCST; Heaton et al., 1993). FEDT scores were excluded from analyses for two reasons: First, previous work demonstrated that social cognition is separate from other subdomains of neurocognition (Allen et al., 2007), and second, CATIE FEDT scores are considered unacceptably skewed, per the report of Keefe et al. (2006).

***Procedures***

Neurocognitive tests were administered by CATIE staff, who were trained in data collection, editing, and transmission by the National Institute of Mental Health Neurocognitive Assessment Training Unit. Training included specific consideration for testing those with SZ to help ensure reliable data collection (Keefe et al., 2003). The National Institute of Mental Health Neurocognitive Assessment Training Unit audited test scores for accuracy. Participants repeated cognitive testing at approximately two, six, and 18 months following a baseline assessment or a change in medication. Some participants had additional assessments for a variety of reasons

(switching study medications) but only four assessments were used in the current study in order to maximize sample size.

***Data Analysis***

Cognitive data from the first four consecutive assessments was used to ensure that any practice effects based on test exposure would be similar across participants. The four assessment points included baseline assessment and follow-up assessments occurring approximately two, six, and 18 months after the baseline assessment and following study neuroleptic induction (see Keefe et al., 2003, for more detail about the CATIE study phases and design). Descriptive statistics for the test-retest intervals are provided in Table 2. Cognitive data met the assumptions of CFA regarding normality, homoscedasticity, and linearity, so parameter estimates were produced with conventional standard errors.

Factor models were completed using *Mplus* version 5 using Maximum Likelihood as an estimator (Muthén and Muthén, 2007). Fit was assessed using model chi-square and additional goodness of fit indices due to the sensitivity of chi-square to sample size. These additional analyses included comparative fit index (CFI) to examine differences between the independence model and the hypothesized model (Bentler, 1990), root mean squared error of approximation (RMSEA) to evaluate fit between the hypothesized model and the population covariance matrix (Steiger, 1980), and Bayesian information criterion (BIC) to compare the fit between the models tested. BIC was examined due to its stricter penalty for overparameterized models compared to other relative fit indices (e.g., Akaike information criterion; Vrieze, 2012). Model fit was considered good according to the following thresholds: CFI and TLI $\geq .95$, RMSEA $\leq .06$ (Hu & Bentler, 1999), and lower BIC values (Dziak et al., 2020). Acceptable fit included CFI and TLI $\geq .90$ and RMSEA $\leq .08$.

Models evaluated in the current study are presented in Table 3. A one-factor model was evaluated as an informed baseline model that hypothesized all test scores loaded on one general neurocognitive factor. The five-factor model evaluated was used as a comparison model and was based on the report of Keefe et al. (2006) and included Processing Speed, Reasoning, Working Memory, Verbal Memory, and Vigilance factors. A single-level model was included in this paper given that it had better fit than hierarchical baseline models in recent work (Becker et al., 2021). The seven-factor model split phonemic and semantic fluency into separate constructs, based on research suggesting that these two fluency measures are differentially sensitive to cerebral dysfunction in SZ (Piras et al., 2019).

After examining factor structure, multi-group CFA was used to assess longitudinal measurement invariance across the four repeated assessments. As recommended by Byrne (2008), invariance was assessed at configural, metric, scalar, and residual levels, to allow determination of weak, strong, or strict factorial invariance. Configural invariance measures whether the same items load on the same factors at each assessment. Metric invariance assesses the equivalence of factor loadings across the repeated assessment (Horn and McArdle, 1992) which provides evidence for weak factorial invariance. Scalar invariance was used to assess whether loadings for each test score on each factor remained the same with repeated assessment, which would provide evidence for strong factorial invariance. Finally, residual factorial invariance examines the equivalence of residual variances across assessment, which provides evidence for strict factorial invariance. Models were considered invariant with repeated assessment if chi-square (chi-square difference with $p > .05$) and if differences in fit indices did not exceed the following thresholds: CFI difference $\leq 0.010$, TLI difference $\leq 0.010$, and RMSEA difference $\leq 0.015$ (Chen, 2007).

## Results

### *Model Fit Indices*

Table 4 contains the goodness of fit indices for the single-level one-factor, five-factor, and bifactor seven-factor models for all four assessments. The single-level one- and five-factor models had consistently poor fit for each assessment. However, the bifactor seven-factor model demonstrated good fit for the first and fourth assessment, with acceptable fit for the second and third assessments. Thus, the bifactor seven-factor model fit the data best for each assessment. Factor loadings for the bifactor seven-factor model are presented in Table 5. Digit Symbol, Mazes, and LNS had relatively low loadings on their specific factors and high loadings with the general factor across all four assessments.

### *Invariance Analyses*

Invariance analyses are presented for all four assessments for the one-factor, five-factor, and bifactor seven-factor models in Table 6. For the bifactor seven-factor model, CFI, TLI, and RMSEA values remained stable, indicating metric invariance. CFI and TLI values decreased slightly in models with assumed scalar invariance, and RMSEA increased minimally; however, these changes in fit indices were small enough to indicate that the models were invariant. Lastly, CFI, TLI, and RMSEA values remained stable across assessments when testing for residual invariance. In conclusion, all four assessments were found to have configural, metric, scalar, and residual invariance.

### *Secondary Analyses*

To determine whether missing data was influencing the current results, the fit of the bifactor seven-factor structure that was identified in the sample of 205 participants was compared to the fit of the model for the remainder of the baseline sample of participants who did

not have complete neurocognitive data at all four assessments. After adjusting for univariate outliers and deleting multivariate outliers, this comparison sample included 621 participants. Invariance analyses comparing the 205 participants who were included to the 621 participants who were not indicated that the latent structure did not differ between those who had all four assessments compared to those who did not. Fit indices indicated that the bifactor seven-factor structure provided good fit for both samples (Supplementary Materials Table 1). Invariance analyses conducted using the bifactor seven-factor model for both samples also found that CFI, TLI, and RMSEA values were stable between samples (Supplementary Materials Table 2). CFI decreased slightly with examination of scalar invariance; however, this did not exceed the change thresholds specified previously. Thus, the latent structure for the sample used to examine longitudinal stability did not appear to differ from the rest of participants included in the baseline sample.

## Discussion

The purpose of this study was to determine whether the latent structure of cognitive abilities remained stable across four longitudinal assessments collected over a 65-week period. Various competing models were examined, including a one-factor, a five-factor, and bifactor seven-factor model. The bifactor seven-factor model provided the best fit for the CATIE data at all four assessments, and consisted of seven specific factors (Processing Speed, Phonemic Fluency, Semantic Fluency, Reasoning, Working Memory, Verbal Memory, and Vigilance) and a generalized factor. These findings are consistent with our previous work that identified and validated a bifactor seven-factor model for the CATIE baseline data (Becker et al., 2021). It was critical to examine the latent structure of cognitive abilities across repeated assessments because a number of aspects might influence test performance over time, such as changes in symptoms

and medications, which may in turn alter the cognitive factor structure. Potential changes in factor structure would limit conclusions that might be drawn from changes in test performance over time, such as in outcome studies that use cognitive data to examine the efficacy of various treatments for SZ, given that those studies often span months or years. This study is the first to examine longitudinal invariance of a complex model of cognition in SZ. Results provide strong evidence for the stability of the latent structure of cognitive abilities with repeated assessment in individuals diagnosed with SZ. The results also suggest that the stability of the latent structure is robust, given that a significant amount of time passed (approximately 16.5 months) between baseline testing and the fourth assessment, and given that extraneous factors (e.g., medication, psychiatric symptoms, health status) may impact performance on cognitive tests (Herold, Duval, & Schröder, 2020; Moritz et al. 2021; Okasha et al., 2020). This finding suggests that cognitive tests that are commonly utilized in SZ batteries measure the same latent constructs with repeated assessments (and over time). The stability in cognitive factor structure identified here allows changes in cognition to be more confidently attributed to variables of interest as opposed to measurement variance of the cognitive tests. Invariance was present despite induction of medication and other changes in disorder manifestations or health-related characteristics (e.g., symptoms, side-effects) that inevitably occur in longitudinal evaluations.

The current results present multiple important considerations for research. These results suggest that expected changes in test scores are not introducing measurement variance. Thus, factor scores derived from the latent constructs identified here will be useful for longitudinal cognitive evaluations that document cognitive changes in SZ as a result of intervention, disease progression, and other important clinical factors. It is the case that depending on the test characteristics, prior exposure to a test may operate on test scores in different ways. Although

not directly examined in the current study, the results suggest that the measurement properties of these cognitive tests remain invariant regardless of changes in test scores that result from prior exposure or practice effects.

Regarding clinical implications, the results of the current study corroborate previous findings that various neuropsychological profiles are found in SZ and provide support for conclusions drawn from reliable change indices. For example, some people with SZ have relatively well-preserved cognitive abilities with good separation of domains similar to healthy adults, whereas others have generalized deficits across multiple domains, and others show a mix of generalized and/or specific deficits (Becker et al., 2021). These findings regarding invariance of factor structure with repeated assessment are also relevant for repeated clinical evaluations because reliable change indices assume measurement invariance; specifically, that the latent structure of cognition does not change over time except with the induction of neurological insult. Thus, changes in performance over time are attributed to decline in cognitive functioning. Furthermore, these results provide strong support that the latent structure is invariant at the group level.

This study is limited in several respects. Individuals included in these analyses were drawn from a larger group, and the substantial reduction in available cases with repeated assessment is likely due to the considerable attrition reported within the CATIE study following an 18-month course, which raises concern for generalizability (Rosenheck et al., 2006; Volavka et al., 2014). However, this bifactor model was demonstrated to fit in the larger sample (Becker et al., 2021), when participants were split into male and female groups (Becker Wright et al., under review), and when compared to the participants at baseline who were not included in the current longitudinal analyses, which provides evidence that results found in this group

generalize. Another important consideration is that the factors identified in this study were limited to some degree by the neuropsychological tests that were included in the assessment battery. A more extensive neuropsychological test battery is expected to identify other factors that were not identified here. Furthermore, the CATIE battery also includes multiple scores derived from single tests, which raises concerns about method variance contributing to the overall model fit, making it difficult to determine how well the measures assess the cognitive constructs of interest (Becker et al., 2021).

Future studies should investigate the generalizability of the bifactor seven-factor structure, examine the stability of factor structure with varying durations, and compare subgroups of SZ profiles over time. Generalizability of the bifactor structure would be improved by inclusion of more diverse ethnoracial samples of individuals with SZ and with related populations (e.g., psychosis broadly). Additionally, alternative batteries should be examined that include different tests and their respective scores within each domain to examine whether a bifactor structure is truly replicable or at least partially attributed to method variance. Studies may examine whether the bifactor seven-factor structure is consistent with repeated assessment and over longer durations given the lifespan course of SZ. Future work may also examine intraindividual profile comparisons within subgroups of cognitive performance (such as by using general or specific factor scores) to determine if there is variability in cognition for certain cognitive subgroups of SZ with repeated assessment or over time. This study provides support for consistency of the latent structure of cognition in SZ with repeated assessment and supports the use of neuropsychological data to examine longitudinal changes in cognition in treatment outcome studies and other circumstances where changes in cognitive function are anticipated.

## Acknowledgments

Data and/or research tools used in the preparation of this manuscript were obtained from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) for Schizophrenia database from the National Institute of Mental Health (NIMH) Data Archive (NDA). NDA is a collaborative informatics system created by the National Institutes of Health to provide a national resource to support and accelerate research in mental health. *[NIMH Data Archive DOI: 10.15154/1519583]*. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or of the Submitters submitting original data to NDA.

## Financial Support

The authors did not receive funding for this research.

## Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting or reporting this research. This study was used to partially fulfill dissertation requirements for the lead author, Megan Becker Wright.

## References


Allen, D. N., Strauss, G. P., Donohue, B., & van Kammen, D. P. (2007). Factor analytic support for social cognition as a separable cognitive domain in schizophrenia. *Schizophrenia Research*, *93*(1–3), 325–333. https://doi.org/10.1016/j.schres.2007.02.008

Ayesa-Arriola, R., Rodriguez-Sanchez, J. M., Gomez-Ruiz, E., Roiz-Santiáñez, R., Reeves, L. L., & Crespo-Facorro, B. (2014). No sex differences in neuropsychological performance in first episode psychosis patients. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *48*, 149–154. https://doi.org/10.1016/j.pnpbp.2013.09.009

Becker, M. L., Ahmed, A. O., Benning, S. D., Barchard, K. A., John, S. E., Allen, D. N. Bifactor model of cognition in schizophrenia: Evidence for general and specific abilities. Journal of Psychiatric Research 2021; 136: 132-139. https://doi.org/10.1016/j.jpsychires.2021.01.051.

Bentler, P. M. (1990). Comparative fit indexes in structural models. *Psychological Bulletin*, *107*(2), 238–246. https://doi.org/10.1037/0033-2909.107.2.238

Benton, A. L., & Hamscher, K. (1978). Multilingual Aphasia Examination Manual (revised) Iowa City. *IA: University of Iowa*.

Bozikas, V. P., Kosmidis, M. H., Peltekis, A., Giannakou, M., Nimatoudis, I., Karavatos, A., Fokas, K., & Garyfallos, G. (2010). Sex differences in neuropsychological functioning among schizophrenia patients. *Australian & New Zealand Journal of Psychiatry*, *44*(4), 333–341. https://doi.org/10.3109/00048670903489833

Brandt, J. (1991). The Hopkins Verbal Learning Test: Development of a new memory test with six equivalent forms. *The Clinical Neuropsychologist*, *5*(2), 125-142.

Byrne, B. (2008). Testing for multigroup equivalence of a measurement instrument: A walkthrough process. *Psicothema, 20*, 872-882.

Buck, G., Lavigne, K. M., Makowski, C., Joober, R., Malla, A., & Lepage, M. (2020). Sex differences in verbal memory predict functioning through negative symptoms in early psychosis. *Schizophrenia Bulletin*, *46*(6), 1587–1595. https://doi.org/10.1093/schbul/sbaa054

Burton, C. Z., Vella, L., Harvey, P. D., Patterson, T. L., Heaton, R. K., & Twamley, E. W. (2013). Factor structure of the matrics consensus cognitive battery (Mccb) in schizophrenia. *Schizophrenia Research*, *146*(1–3), 244–248. https://doi.org/10.1016/j.schres.2013.02.026

Chen F. F. (2007). Sensitivity of Goodness of Fit Indexes to Lack of Measurement Invariance. *Structural Equation Modeling: A Multidisciplinary Journal, 14*(3): 464–504. https://doi.org/10.1080/10705510701301834

Cornblatt, B. A., Risch, N. J., Faris, G., Friedman, D., & Erlenmeyer-Kimling, L. (1988). The continuous performance test, identical pairs version (Cpt-ip): I. new findings about sustained attention in normal families. *Psychiatry Research*, *26*(2), 223–238. https://doi.org/10.1016/0165-1781(88)90076-5

Dickinson, D., Iannone, V. N., Wilk, C. M., & Gold, J. M. (2004). General and specific cognitive deficits in schizophrenia. *Biological Psychiatry*, *55*(8), 826–833. https://doi.org/10.1016/j.biopsych.2003.12.010

Dickinson, D., Ragland, J., Calkins, M., Gold, J., & Gur, R. (2006). A comparison of cognitive structure in schizophrenia patients and healthy controls using confirmatory factor analysis. *Schizophrenia Research*, *85*(1–3), 20–29. https://doi.org/10.1016/j.schres.2006.03.003

Fond, G., Boyer, L., Leboyer, M., Godin, O., Llorca, P. M., Andrianarisoa, M., Berna, F., Brunel, L., Aouizerate, B., Capdevielle, D., Chereau, I., D'Amato, T., Dubertret, C., Dubreucq, J., Faget, C., Gabayet, F., Mallet, J., Misdrahi, D., Rey, R., … Zinetti-Bertschy, A. (2018). Influence of Venus

and Mars in the cognitive sky of schizophrenia. Results from the first-step national FACE-SZ cohort. *Schizophrenia Research*, *195*, 357–365. https://doi.org/10.1016/j.schres.2017.09.027

Gladsjo, J. A., McAdams, L. A., Palmer, B. W., Moore, D. J., Jeste, D. V., & Heaton, R. K. (2004). A six-factor model of cognition in schizophrenia and related psychotic disorders: Relationships with clinical symptoms and functional capacity. *Schizophrenia Bulletin*, *30*(4), 739–754. https://doi.org/10.1093/oxfordjournals.schbul.a007127

Gold, J. M. (1997). Auditory working memory and wisconsin card sorting test performance in schizophrenia. *Archives of General Psychiatry*, *54*(2), 159. https://doi.org/10.1001/archpsyc.1997.01830140071013

Halari, R., Mehrotra, R., Sharma, T., Ng, V., & Kumari, V. (2006). Cognitive impairment but preservation of sexual dimorphism in cognitive abilities in chronic schizophrenia. *Psychiatry Research*, *141*(2), 129–139. https://doi.org/10.1016/j.psychres.2005.07.021

Harvey, P. D., Raykov, T., Twamley, E. W., Vella, L., Heaton, R. K., & Patterson, T. L. (2013). Factor structure of neurocognition and functional capacity in schizophrenia: A multidimensional examination of temporal stability. *Journal of the International Neuropsychological Society*, *19*(6), 656–663. https://doi.org/10.1017/S1355617713000179

Heaton, R. K., Chelune, G. J., Talley, J. L., Kay, G. G., & Curtiss, G. (1993). *Wisconsin Card Sorting Test (WCST): Manual: Revised and Expanded*. Psychological Assessment Resources (PAR).

Herold, C. J., Duval, C. Z., & Schröder, J. (2020). Neurological soft signs and cognition in the late course of chronic schizophrenia: A longitudinal study. *European Archives of Psychiatry and Clinical Neuroscience*. https://doi.org/10.1007/s00406-020-01138-7

Hershey, T., Selke, G., Fucetola, R., Newcomer, J.W. (1999). Spatial long-term memory but not working memory decreases over time in schizophrenia. [Abstract]. Society for Neuroscience 25, 572. Part l

Hill, S. K., Sweeney, J. A., Hamer, R. M., Keefe, R. S. E., Perkins, D. O., Gu, H., Mcevoy, J. P., & Lieberman, J. A. (2008). Efficiency of the CATIE and BACS neuropsychological batteries in assessing cognitive effects of antipsychotic treatments in schizophrenia. *Journal of the International Neuropsychological Society*, *14*(02). https://doi.org/10.1017/S1355617708080570

Horn, J. L., & McArdle, J. J. (1992). A practical and theoretical guide to measurement invariance in aging research. *Experimental Aging Research*, *18*(3), 117-144.

Hu, L. T., & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling: a Multidisciplinary Journal*, *6*(1), 1-55.

Instrument, L. (1989). Grooved pegboard: instruction/owner's manual. *Lafayette Instrument*.

Ittig, S., Studerus, E., Papmeyer, M., Uttinger, M., Koranyi, S., Ramyead, A., & Riecher-Rössler, A. (2015). Sex differences in cognitive functioning in at-risk mental state for psychosis, first episode psychosis and healthy control subjects. *European Psychiatry*, *30*(2), 242–250. https://doi.org/10.1016/j.eurpsy.2014.11.006

Keefe, R. S. E., Bilder, R. M., Harvey, P. D., Davis, S. M., Palmer, B. W., Gold, J. M., Meltzer, H. Y., Green, M. F., Miller, D. D., Canive, J. M., Adler, L. W., Manschreck, T. C., Swartz, M., Rosenheck, R., Perkins, D. O., Walker, T. M., Stroup, T. S., McEvoy, J. P., & Lieberman, J. A. (2006). Baseline neurocognitive deficits in the catie schizophrenia trial. *Neuropsychopharmacology*, *31*(9), 2033–2046. https://doi.org/10.1038/sj.npp.1301072

Keefe, R. S. E., Mohs, R. C., Bilder, R. M., Harvey, P. D., Green, M. F., Meltzer, H. Y., Gold, J. M., & Sano, M. (2003). Neurocognitive assessment in the clinical antipsychotic trials of intervention effectiveness (Catie) project schizophrenia trial: Development, methodology, and rationale. *Schizophrenia Bulletin*, *29*(1), 45–55. https://doi.org/10.1093/oxfordjournals.schbul.a006990

Kerr, S.L., Neale, J.M. (1993). Emotion perception in schizophrenia: specific deficit or further evidence of generalized poor performance? *Journal of Abnormal Psychology, 102* (2), 312–318. https://doi.org/10.1037/0021-843X.102.2.312.

Lafayette Instrument Company. (1989). *Grooved Pegboard instruction manual, model 32025.* Lafayette, IN: Lafayette Instrument Company.

Longenecker, J., Dickinson, D., Weinberger, D. R., & Elvevåg, B. (2010). Cognitive differences between men and women: A comparison of patients with schizophrenia and healthy volunteers. *Schizophrenia Research*, *120*(1–3), 234–235. https://doi.org/10.1016/j.schres.2009.12.009

McCleery, A., Ventura, J., Kern, R. S., Subotnik, K. L., Gretchen-Doorly, D., Green, M. F., Hellemann, G. S., & Nuechterlein, K. H. (2014). Cognitive functioning in first-episode schizophrenia: Matrics consensus cognitive battery (Mccb) profile of impairment. *Schizophrenia Research*, *157*(1–3), 33–39. https://doi.org/10.1016/j.schres.2014.04.039

Moritz, S., Silverstein, S. M., Beblo, T., Özaslan, Z., Zink, M., & Gallinat, J. (2021). Much of the neurocognitive impairment in schizophrenia is due to factors other than schizophrenia itself: implications for research and treatment. *Schizophrenia Bulletin Open*, *2*(1), sgaa034.

Múthen, L. K., & Múthen, B. O. (2007). Mplus (version 5.0)[computer software]. *Los Angeles, CA: Author*. https://www.statmodel.com/index.shtml

Mu, L., Liang, J., Wang, H., Chen, D., Xiu, M., & Zhang, X. Y. (2020). Sex differences in association between clinical correlates and cognitive impairment in patients with chronic schizophrenia. *Journal of Psychiatric Research*, *131*, 194–202. https://doi.org/10.1016/j.jpsychires.2020.09.003

Nuechterlein, K. H., Barch, D. M., Gold, J. M., Goldberg, T. E., Green, M. F., & Heaton, R. K. (2004). Identification of separable cognitive factors in schizophrenia. *Schizophrenia Research*, *72*(1), 29–39. https://doi.org/10.1016/j.schres.2004.09.007

Ojeda, N., Peña, J., Schretlen, D. J., Sánchez, P., Aretouli, E., Elizagárate, E., Ezcurra, J., & Gutiérrez, M. (2012). Hierarchical structure of the cognitive processes in schizophrenia: The fundamental role of processing speed. *Schizophrenia Research*, *135*(1–3), 72–78. https://doi.org/10.1016/j.schres.2011.12.004

Okasha, T. A., Hussein, H., Shorub, E., Nagi, H., Moustafa, A. A., & El-Serafi, D. (2020). Cognitive dysfunction among inpatients and outpatients with schizophrenia: relationship to positive and negative symptoms. *Middle East Current Psychiatry*, *27*(1), 1-7.

Piras, F., Piras, F., Banaj, N., Ciullo, V., Vecchio, D., Edden, R. A. E., & Spalletta, G. (2019). Cerebellar GABAergic correlates of cognition-mediated verbal fluency in physiology and schizophrenia. *Acta Psychiatrica Scandinavica*, *139*(6), 582–594. https://doi.org/10.1111/acps.13027

Rodriguez-Toscano E., López G., Mayoral M., Lewis S., Lees J., Drake R., Arango C., Rapado-Castro M. (2020). A longitudinal comparison of two neurocognitive test batteries in patients with schizophrenia and healthy volunteers: Time effects on neuropsychological performance and their relation to functional outcome. *Schizophrenia Research, 216*: 347-356. https://doi.org/10.1016/j.schres.2019.11.018

Rosenheck, R. A., Leslie, D. L., Sindelar, J., Miller, E. A., Lin, H., Stroup, T. S., ... & Lieberman, J. (2006). Cost-effectiveness of second-generation antipsychotics and perphenazine in a randomized trial of treatment for chronic schizophrenia. *American Journal of Psychiatry*, *163*(12), 2080-2089.

Steiger, J. H. (1980). Statistically based tests for the number of common factors. In *The Annual Meeting of the Psychometric Society. Iowa City, IA. 1980*.

Stroup, T. S., McEvoy, J. P., Swartz, M. S., Byerly, M. J., Glick, I. D., Canive, J. M., McGee, M. F., Simpson, G. M., Stevens, M. C., & Lieberman, J. A. (2003). The national institute of mental health clinical antipsychotic trials of intervention effectiveness (Catie) project: Schizophrenia trial design and protocol development. *Schizophrenia Bulletin*, *29*(1), 15–31. https://doi.org/10.1093/oxfordjournals.schbul.a006986

Tabachnick, B. G., & Fidell, L. S. (2013). *Using multivariate statistics.* Upper Saddle River, NJ: Pearson Education, Inc.

Torniainen, M., Suvisaari, J., Partonen, T., Castaneda, A. E., Kuha, A., Perälä, J., Saarni, S., Lönnqvist, J., & Tuulio-Henriksson, A. (2011). Sex differences in cognition among persons with schizophrenia and healthy first-degree relatives. *Psychiatry Research*, *188*(1), 7–12. https://doi.org/10.1016/j.psychres.2010.11.009

Tsai, P.-C., McDowd, J., Tang, T.-C., & Su, C.-Y. (2012). Processing speed mediates gender differences in memory in schizophrenia. *The Clinical Neuropsychologist*, *26*(4), 626–640. https://doi.org/10.1080/13854046.2012.678887

Volavka, J., Czobor, P., Citrome, L., & Van Dorn, R. A. (2014). Effectiveness of antipsychotic drugs against hostility in patients with schizophrenia in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study. *CNS Spectrums*, *19*(5), 374-381.

Wechsler, D., 1974. Wechsler Adult Intelligence Scale—Revised. Psychological Corporation., San Antonio, Texas

Wechsler, D. (1991). Manual for the Wechsler Intelligence Scale for Children 3rd ed Psychological Corporation. *San Antonio, TX*.

Wilkinson, G. S. (1993). WRAT-3: Wide Range Achievement Test Administration Manual. Wide Range. *Inc, Wilmington, DE*.

**Table 1. Baseline Demographics**

| Demographic Type | A1 |
|---|---|
| | *n* = 205 |
| Mean age in years (*SD*) | 39.1 (10.6) |
| | *n* = 205 |
| Mean education in years (*SD*) | 12.1 (3.0) |
| | *n* = 205 |
| % Male | 72.7 |
| % Race | *n* = 204 |
| White/Caucasian | 73.0 |
| Black/African American | 21.1 |
| Asian | 3.4 |
| More than one race | 1.5 |
| American Indian/Alaska Native | .98 |
| Native Hawaiian/Pacific Islander | 0 |
| % Ethnicity | *n* = 205 |
| Hispanic/Latino | 26 |
| Not Hispanic/Latino | 179 |
| Mean PANSS (*SD*) | *n* = 205 |
| Positive Symptom Score | 17.2 (5.2) |
| Negative Symptom Score | 19.6 (6.5) |
| General Symptom Score | 35.4 (8.9) |
| Medication | *n* = 205 |
| Olanzapine | 74 |
| Quetiapine | 20 |
| Risperidone | 55 |

| | |
|---|---|
| Ziprasidone | 11 |
| Haloperidol | 10 |
| Decanoate | 1 |
| Perphenazine | 4 |
| Other | 12 |
| All Other | 36 |
| None | 35 |

*Note*. A = Assessment 1. Table was adapted from Becker et al. (2021). Race and ethnicity descriptors reflect those used in the CATIE database. Hispanic/Latino was a separate variable, so individuals also chose between race options listed. Neuroleptic medications were taken on the day of baseline testing or two weeks prior. Other = participant received any other neuroleptic besides of the neuroleptics listed above; All Other = participant received any other neuroleptics (olanzapine, quetiapine, and risperidone not included); None = participant did not receive neuroleptics.

**Table 2. Descriptive Statistics**

| Test Score | A1<br>Mean (SD) | A2<br>Mean (SD) | A3<br>Mean (SD) | A4<br>Mean (SD) |
|---|---|---|---|---|
| | | *n* = 205 | *n* = 205 | *n* = 205 |
| Test-retest interval from baseline (weeks) | - | 8.7 (2.3) | 24.6 (4.6) | 65.4 (15.9) |
| Grooved Pegboard Trial 1 | 12.77 (3.84) | 13.67 (3.58) | 13.79 (3.64) | 13.98 (4.12) |
| Grooved Pegboard: Trial 2 | 14.29 (3.74) | 14.84 (3.64) | 15.01 (3.66) | 15.04 (3.88) |
| WAIS-R Digit Symbol Test | 41.15 (12.57) | 44.01 (12.88) | 44.76 (13.93) | 45.58 (14.70) |
| COWAT 1st letter | 10.38 (4.12) | 10.54 (4.07) | 10.75 (4.06) | 11.28 (4.45) |
| COWAT 2nd letter | 8.63 (3.72) | 8.31 (3.58) | 8.43 (3.80) | 8.89 (3.77) |
| COWAT 3rd letter | 10.74 (4.58) | 10.76 (4.48) | 10.70 (4.39) | 11.07 (4.48) |
| Category Instances 1st category | 14.80 (4.69) | 14.88 (4.70) | 14.89 (4.88) | 15.10 (4.73) |
| Category Instances 2nd category | 10.50 (3.20) | 10.90 (3.55) | 10.80 (3.30) | 11.00 (3.44) |
| Category Instances 3rd category | 9.23 (3.37) | 9.24 (3.39) | 9.65 (3.45) | 9.47 (3.39) |
| WCST perseverative errors | 11.80 (9.03) | 9.94 (7.16) | 10.11 (8.35) | 10.22 (8.35) |
| WCST completed categories | 2.42 (1.66) | 2.60 (1.77) | 2.81 (1.87) | 2.80 (1.84) |
| WCST additional cards in final category | 2.42 (3.18) | 2.11 (2.94) | 2.34 (2.95) | 2.43 (2.96) |
| WISC-III Mazes total correct | 19.78 (4.74) | 19.96 (4.92) | 20.41 (4.75) | 20.39 (4.74) |
| Letter-Number Sequencing Test total correct | 11.38 (4.09) | 12.28 (4.02) | 12.25 (3.99) | 12.42 (4.43) |
| CTVWM mean errors 5 second delay | 23.24 (12.19) | 21.45 (10.94) | 21.47 (10.78) | 21.31 (11.36) |
| CTVWM mean errors 15 second delay | 25.14 (12.59) | 24.27 (12.66) | 24.14 (13.16) | 24.75 (13.35) |
| HVLT-R Trial 1 | 5.05 (1.75) | 5.24 (1.85) | 5.32 (1.91) | 5.26 (1.80) |
| HVLT-R Trial 2 | 7.03 (2.07) | 7.07 (2.16) | 7.14 (2.07) | 7.21 (2.26) |
| HVLT-R Trial 3 | 8.18 (2.31) | 8.22 (2.28) | 8.37 (2.22) | 8.31 (2.40) |

| | | | | |
|---|---|---|---|---|
| CPT-IP: d′ condition 2 | 2.72 (0.96) | 2.93 (0.88) | 2.98 (0.89) | 2.97 (0.89) |
| CPT-IP: d′ condition 3 | 2.03 (0.84) | 2.27 (0.96) | 2.33 (0.89) | 2.23 (0.96) |
| CPT-IP: d′ condition 4 | 1.13 (0.82) | 1.29 (0.81) | 1.32 (0.83) | 1.37 (0.82) |

*Note.* $n = 205$ for all test scores. A1 = Assessment 1, A2 = Assessment 2, A3 = Assessment 3, A4 = Assessment 4.

**Table 3. Scores Included in Factors**

| CATIE Domains and Test scores | 1-factor | 5-factor | 7-factor |
|---|---|---|---|
| Processing Speed | | | |
| Grooved Pegboard Trial 1 | 1 | 1 | 1 |
| Grooved Pegboard Trial 2 | 1 | 1 | 1 |
| WAIS-R Digit-Symbol Test number correct | 1 | 1 | 1 |
| COWAT 1st letter | 1 | 1 | 6 |
| COWAT 2nd letter | 1 | 1 | 6 |
| COWAT 3rd letter | 1 | 1 | 6 |
| Category Instances 1st category | 1 | 1 | 7 |
| Category Instances 2nd category | 1 | 1 | 7 |
| Category Instances 3rd category | 1 | 1 | 7 |
| Reasoning | | | |
| WCST perseverative errors | 1 | 2 | 2 |
| WCST completed categories | 1 | 2 | 2 |
| WCST additional cards in final category | 1 | 2 | 2 |
| WISC-III Mazes total correct | 1 | 2 | 2 |
| Working Memory | | | |
| Letter-Number Sequencing Test total correct | 1 | 3 | 3 |
| CTVWM mean errors 5 second delay | 1 | 3 | 3 |
| CTVWM mean errors 15 second delay | 1 | 3 | 3 |
| Verbal Memory | | | |
| HVLT-R Trial 1 | 1 | 4 | 4 |
| HVLT-R Trial 2 | 1 | 4 | 4 |
| HVLT-R Trial 3 | 1 | 4 | 4 |
| Vigilance | | | |
| CPT-IP d' 2 | 1 | 5 | 5 |
| CPT-IP d' 3 | 1 | 5 | 5 |
| CPT-IP d' 4 | 1 | 5 | 5 |

*Note.* Table was adapted from Becker et al. (2021). The bifactor seven-factor model kept these domains for specific factors, with the addition of g (including all variables) as the global factor. WAIS-R = Wechsler Adult Intelligence Scale-Revised (WAIS-R) COWAT = Controlled Oral Word Association; WISC-III = Wechsler Intelligence Scale for Children, 3rd Ed. (WISC-III); WCST = Wisconsin Card Sort Test; CTVWM = Computerized Test of Visual Working Memory; HVLT-R = Hopkins Verbal Learning Test- Revised; CPT-IP d' = Conners' Continuous Performance Test-Identical Pairs number of correctly identified targets for conditions 2-4.

**Table 4. Fit Indices of the Factor Models for Each Assessment**

| Assessment | Model | χ2 (df) | CFI | TLI | RMSEA (90% CI) | BIC |
|---|---|---|---|---|---|---|
| 1 | 1 | 1192.67 (209) | .558 | .512 | .152 (.143, .160) | 22906.82 |
| | 5 | 749.41 (199) | .753 | .713 | .116 (.107, .125) | 22516.79 |
| | B7* | 285.00 (188) | .956 | .946 | .050 (.038, .062) | 22110.93 |
| 2 | 1 | 1345.51 (209) | .544 | .496 | .163 (.155, .171) | 22695.64 |
| | 5 | 817.28 (199) | .752 | .712 | .123 (.114, .132) | 22220.64 |
| | B7* | 316.97 (189) | .949 | .937 | .057 (.046, .068) | 21773.55 |
| 3 | 1 | 1297.92 (209) | .548 | .500 | .159 (.151, .168) | 22831.11 |
| | 5 | 798.44 (199) | .751 | .711 | .121 (.112, .130) | 22384.86 |
| | B7* | 330.58 (189) | .941 | .928 | .060 (.049, .071) | 21970.23 |
| 4 | 1 | 1216.88 (209) | .581 | .537 | .153 (.145, .162) | 23019.70 |
| | 5 | 731.15 (199) | .779 | .743 | .114 (.105, .123) | 22587.19 |
| | B7* | 272.50 (189) | .965 | .958 | .046 (.034, .058) | 22181.78 |

*Note.* For each of the four assessments, $n = 205$. CFI = comparative fit index. RMSEA = root mean-square error of approximation. RMSEA 90% CI = root mean-square error of approximation 90% confidence interval. BIC = Bayesian information criterion. Model numbers represent the number of single-level factors; 5 = five first-order factors; B7 = bifactor model with one global factor and 7 specific factors. Each of the bifactor seven-factor models had significant chi-squared values at $p < .001$. * indicates that best fitting models.

**Table 5. Factor Loadings for the Bifactor Seven-factor Model at Four Assessments**

| Factor | General factor loadings | | | | Specific factor loadings | | | |
|---|---|---|---|---|---|---|---|---|
| Test Score | A1 | A2 | A3 | A4 | A1 | A2 | A3 | A4 |
| Processing Speed | | | | | | | | |
| Digit Symbol | .70 | .71 | .72 | .74 | .22 | .20 | .26 | .24 |
| Grooved Peg 1 | .55 | .52 | .49 | .54 | .78 | .79 | .77 | .80 |
| Grooved Peg 2 | .54 | .48 | .49 | .56 | .74 | .80 | .84 | .72 |
| Phonemic Fluency | | | | | | | | |
| COWAT 1 | .51 | .53 | .57 | .53 | .73 | .62 | .67 | .66 |
| COWAT 2 | .62 | .52 | .67 | .60 | .52 | .65 | .39 | .56 |
| COWAT 3 | .56 | .58 | .62 | .65 | .59 | .67 | .58 | .53 |
| Semantic Fluency | | | | | | | | |
| Category 1 | .62 | .52 | .60 | .64 | .45 | .49 | .40 | .40 |
| Category 2 | .54 | .54 | .52 | .59 | .61 | .67 | .61 | .56 |
| Category 3 | .42 | .45 | .50 | .49 | .67 | .71 | .66 | .66 |
| Reasoning | | | | | | | | |
| Mazes | .45 | .53 | .45 | .43 | .13 | .10 | -.14 | .05 |
| WCST pers errors | -.42 | -.59 | -.42 | -.50 | -.71 | -.69 | .91 | -.80 |
| WCST categories | .44 | .53 | .46 | .50 | .66 | .54 | -.55 | .58 |
| WCST final sort | .17 | .19 | .27 | .16 | .17 | .27 | -.18 | .25 |
| Working Memory | | | | | | | | |
| LNS | .71 | .76 | .77 | .71 | -.05 | .08 | -.08 | -.09 |
| CTVWM 5 sec | -.49 | -.49 | -.39 | -.40 | .74 | .38 | .92 | .92 |
| CTVWM 15 sec | -.48 | -.62 | -.43 | -.44 | .51 | .79 | .39 | .47 |
| Verbal Memory | | | | | | | | |
| HVLT-R 1 | .51 | .51 | .51 | .49 | .47 | .52 | .59 | .55 |
| HVLT-R 2 | .59 | .58 | .55 | .58 | .81 | .76 | .76 | .67 |
| HVLT-R 3 | .52 | .64 | .61 | .61 | .51 | .52 | .57 | .63 |
| Vigilance | | | | | | | | |
| CPT-IP d' 2 | .58 | .56 | .57 | .59 | .45 | .49 | .45 | .47 |
| CPT-IP d' 3 | .63 | .62 | .61 | .66 | .73 | .79 | .77 | .75 |
| CPT-IP d' 4 | .57 | .58 | .63 | .64 | .38 | .40 | .38 | .36 |

*Note.* Factor loadings are presented for both general and specific factors for each of the four assessments ($n$ = 205). A1-4 = Assessment number. Digit Symbol = Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol Test; Grooved Peg (1 or 2) = Grooved Pegboard Test Trial (1 or 2); COWAT (1, 2, or 3) = Controlled Oral Word Association Test Trial 1, 2, or 3; Category (1, 2, or 3) = Category Test Trial 1, 2, or 3; Mazes = Wechsler Intelligence Scale for

Children, 3rd Ed. (WISC-III) Mazes; WCST = Wisconsin Card Sort Test; per errors = perseverative errors; categories = number of categories administered; final sort = number of additional consecutive cards in the final category; LNS = Letter-Number Sequencing Test; CTVWM = Computerized Test of Visual Working Memory; 5 sec = mean errors during the five second delay; 15 sec = mean errors during the fifteen second delay; HVLT-R (1, 2, or 3) = Hopkins Verbal Learning Test- Revised Trial 1, 2, or 3; CPT-IP d' (condition 2, 3, or 4) = Conners' Continuous Performance Test-Identical Pairs number of correctly identified targets on the two-, three-, or four-digit condition.

**Table 6. Measurement Invariance Estimates at Four Assessments**

| **1-Factor Model** | **Chi-Square** $\chi^2$ (df) | **Chi-Square Difference Test** $\chi^2$(df) | **CFI** | **CFI Change** | **TLI** | **TLI Change** | **RMSEA** | **RMSEA Change** | **BIC** |
|---|---|---|---|---|---|---|---|---|---|
| Invariance Threshold | | | | **≤ -.010** | | **≤ -.010** | | **≤ .015** | |
| Configural | $\chi^2(180)= 374.16$, $p < .001$ | - | .729 | - | .726 | - | .073 | - | 86135.38 |
| Metric | $\chi^2(181)= 372.46$, $p <.001$ | $\chi^2(40)=34.66$, $p =.7091$ | .733 | .004 | .732 | .006 | .072 | -.001 | 85853.90 |
| Scalar | $\chi^2(181)=371.75$, $p < .001$ | $\chi^2(63)=114.69$, $p < .001$ | .734 | .001 | .733 | .001 | .072 | .000 | 85633.07 |
| Residual | $\chi^2(181)= 369.27$, $p < .001$ | $X^2(47)=62.31$, $p = .0666$ | .738 | .004 | .736 | .003 | .071 | -.001 | 85376.23 |
| **Five-Factor Model** | | | | | | | | | |
| Configural | $\chi^2(180)= 305.83$, $p < .001$ | - | .825 | - | .823 | - | .058 | - | 85428.54 |
| Metric | $\chi^2(180)= 304.31$, $p < .001$ | $\chi^2(39)= 44.56$, $p = .2492$ | .827 | .002 | .825 | .002 | .058 | .000 | 85215.05 |
| Scalar | $\chi^2(180)= 363.51$, $p < .001$ | $\chi^2(57)= 1259.45$, $p < .001$ | .744 | -.083 | .741 | -.084 | .071 | .013 | 86171.21 |
| Residual | $\chi^2(181)= 362.12$, $p < .001$ | $\chi^2(47)=51.11$, $p = .3155$ | .748 | .004 | .746 | .005 | .070 | -.001 | 85898.69 |
| | | | | | | | | | |
| **Bifactor 7-Factor Model** | | | | | | | | | |
| Configural | $\chi^2(179)= 242.06$, $p < .001$ | - | .912 | - | .911 | - | .041 | - | 85350.08 |
| Metric | $\chi^2(180)= 243.11$, $p < .001$ | $\chi^2(70)= 90.97$, $p = .0469$ | .912 | .000 | .911 | .000 | .041 | .000 | 84832.98 |
| Scalar | $\chi^2(180)= 246.38$, $p < .001$ | $\chi^2(66)= 149.76$, $p < .001$ | .907 | -.005 | .906 | -.005 | .042 | .001 | 84631.42 |
| Residual | $\chi^2(181)= 248.06$, $p < .001$ | $\chi^2(46)= 66.95$, $p = .0234$ | .907 | .000 | .906 | .000 | .043 | .001 | 84391.85 |
| | | | | | | | | | |

*Note.* CFI = Confirmatory fit index; TLI = Tucker Lewis index; RMSEA = root mean square error of approximation; BIC = Bayesian information criterion. Chi-square for the baseline model: $\chi^2(182) = 899.53$, $p < .0001$. Values represent fit indices and their change over four repeated assessments for a one-factor, five-factor, and bifactor seven-factor model.

**Supplementary Materials**

**for**

# Longitudinal stability of the latent structure of cognition in schizophrenia

Megan L. Becker Wright[1]

Anthony O. Ahmed[2]

Samantha E. John[1]

Kimberly A. Barchard[1]

Stephen D. Benning[1]

Daniel N. Allen[1]

1. Department of Psychology, University of Nevada, Las Vegas, Las Vegas, NV

2. Department of Psychiatry, Weill Cornell Medicine, White Plains, NY

*Address correspondence to: Daniel N. Allen, Ph.D., Department of Psychology, University of Nevada Las Vegas, 4505 Maryland Parkway, Las Vegas, NV 89154. Phone: 702.895.0121. Fax: 702.895.0195. Email: daniel.allen@unlv.edu

**Supplementary Materials**

**Table 1. Model Fit Statistics for the Repeated Assessment Sample Compared to the Other Baseline Participants**

| Sample | Model | χ2 (df) | CFI | TLI | RMSEA (90% CI) | BIC |
|---|---|---|---|---|---|---|
| 205 | B7 | 285.00 (188) | .956 | .946 | .050 (.038, .062) | 22110.93 |
| 621 | B7 | 421.31 (188) | .965 | .957 | .045 (.039, .050) | 67288.54 |

*Note.* CFI = Confirmatory fit index; TLI = Tucker Lewis index; RMSEA = root mean square error of approximation; BIC = Bayesian information criterion. B7 = bifactor model with one global factor and 7 specific factors. Each of the bifactor seven-factor models had significant chi-squared values at $p < .001$. Repeated assessment sample ($n = 205$) and the rest of the baseline participants ($n = 621$).

**Table 2. Invariance Analysis for the Repeated Assessment Sample Compared to the Other Baseline Participants**

| **Bifactor 7-Factor Model** | **Chi-Square** $\chi^2$ (df) | **Chi-Square Difference Test** $\chi^2$(df) | **CFI** | **CFI Change** | **TLI** | **TLI Change** | **RMSEA** | **RMSEA Change** | **BIC** |
|---|---|---|---|---|---|---|---|---|---|
| | | | | **≤ -.010** | | **≤ -.010** | | **≤ .015** | |
| Configural | $\chi^2(208)= 391.95$, $p < .001$ | - | .958 | - | .953 | - | .046 | - | 89545.56 |
| Metric | $\chi^2(214)= 384.72$, $p < .001$ | $\chi^2(31)= 28.46$, $p = .598$ | .961 | .003 | .958 | .005 | .044 | -.002 | 89337.53 |
| Scalar | $\chi^2(219)= 393.60$, $p < .001$ | $\chi^2(20)= 35.90$, $p = .016$ | .960 | -.001 | .958 | .000 | .044 | .000 | 89229.10 |
| Residual | $\chi^2(221)= 393.78$, $p < .001$ | $\chi^2(17)= 25.78$, $p = .079$ | .961 | .001 | .959 | .001 | .044 | .000 | 89133.42 |
| | | | | | | | | | |

*Note.* CFI = Confirmatory fit index; TLI = Tucker Lewis index; RMSEA = root mean square error of approximation; BIC = Bayesian information criterion. Chi-square for the baseline model: $\chi^2(231) = 4622.19$, $p < .001$. Repeated assessment sample ($n = 205$) and the rest of the baseline participants ($n = 621$).

## Chapter V: Conclusion

This series of studies was undertaken to achieve three goals including 1) determining whether a first order, hierarchical or bifactor models best characterized the latent structure of cognitive abilities in SZ, 2) determine whether the latent structure of cognitive abilities in SZ was invariant between men and women, and 3) determine if the latent structure was stable over time with repeated assessment. The major findings for each aim were as follows: the first dissertation paper, "Bifactor model of cognition in schizophrenia: Evidence for general and specific abilities," found that a bifactor seven-factor model best fit cognitive data in SZ and that this model was replicated in a cross-validation sample. The second paper, "Latent structure of cognitive tests is invariant in men and women with schizophrenia," concluded that a bifactor seven-factor model characterized the latent structure of cognitive abilities in men and women with SZ. Further, this structure was invariant, and women performed better than men on Semantic Fluency, Verbal Memory, and General cognition, whereas men had better Vigilance scores. However, men and women with SZ performed similarly on Processing Speed, Phonemic Fluency, Reasoning, and Working Memory measures. Results of the third paper "Stability of bifactor structure of cognition in schizophrenia with repeated assessment," indicated that a bifactor seven-factor model of cognition in SZ was invariant over four repeated assessments conducted over 16.5 months.

The results from these studies contributed to existing literature by introducing a bifactor model of cognition in SZ, providing evidence that measurement invariance is not an underlying cause of discrepancies in cognitive differences in men and women with SZ, and support longitudinal administration of cognitive tests because the latent structure (bifactor model) remains invariant with repeated assessment. Specifically, a bifactor model had not previously

been tested in SZ and may characterize the latent structure of cognitive abilities better than previous models that concluded SZ is characterized by a general deficit or hierarchical models, as these models cannot allow for the examination of how individual scores contribute to a general factor. Importantly, the results of this study imply that cognitive tests in SZ might be best selected and interpreted with scores that capture specific areas of cognition and general cognitive abilities. Thus, data collected in evaluations can be used to target specific deficits for treatment targets, as with cognitive remediation, and allow for the examination of a more generalized deficit across domains that might be associated with functional outcomes and other important domains.

Given the heterogeneity of cognitive performance in SZ, it was important to examine whether the latent structure of cognitive abilities was the same for men and women due to mixed evidence about performance between these groups across cognitive domains. The second paper added to literature on differences between men and women by providing evidence that the measurement of cognitive tests is invariant between these groups and thus is not a likely explanation for discrepancies in cognitive performance previously reported for men and women with SZ. Further, the results suggest that men and women with SZ differ across some aspects of cognitive functioning, but that performance across many domains is comparable. This work directly relates to the importance of test selection for men and women with SZ, as it suggests that the CATIE battery is appropriate for use with men and women with SZ because the tests likely consistently measure the same constructs in both groups. Regarding the observed differences in cognitive performance between men and women, findings in this area warrant replication and extension to include other cognitive domains where sex-based differences have been identified in the normal population.

The final study further contributes to extant knowledge by demonstrating that the latent structure, specifically a bifactor structure, remains stable with repeated assessment over the course of 16.5 months. Although cognitive tests are often used for longitudinal assessment, previous research with SZ has not examined longitudinal invariance in the latent structure of complex models like the bifactor model, over multiple follow-up assessments, nor over the duration examined in this third paper. These findings are important for drawing conclusions from repeated cognitive evaluations in SZ and suggest that because test measurement remains invariant over time, change in scores may be attributed to actual change performance (i.e., reliable change), rather than error that could result from changes in the measurement of test constructs with repeated assessment. With this known, the accuracy of clinical decision making based on reliable change can be more confidently assured.

Future directions based on these works should examine whether a bifactor model generalizes to other samples of individuals with SZ, such as ones that include more ethnoracially diverse sample or other groups with psychosis. Studies should include additional measures of the cognitive domains with fewer scores derived from the same measure, which would increase divergent validity and add incrementally to the robust assessment of aspects of each cognitive domain. Additional exploration as to whether a bifactor model can be replicated despite including fewer or more cognitive domains (specific factors) to better understand the scores related to the general deficit in SZ when considering more practical (shorter) or comprehensive (longer) batteries.

Subsequent studies of cognition in men and women with SZ should include tests that assess additional domains with identified differences in healthy men and women. Also, more studies are needed that compare cognitive differences in men and women with SZ to men and

women without the disorder to determine what differences may be unique to those with SZ as opposed to more typically replicated differences in healthy men and women. Importantly, more research is needed to better understand cognition in SZ in sex and gender diverse individuals. Further, additional investigation is necessary to determine what factors contribute to these differences and the extent that any consistent differences in cognitive performance between men and women with SZ are related to other heterogenous characteristics of the disorder (symptoms, disorder onset, premorbid abilities in men and women). Lastly, future work should examine ethnoracial differences in the latent structure of cognitive abilities in SZ to better understand if test measurement is similar or different between groups and what sociocultural factors could underlie such differences if present.

Finally, future work would benefit from determining whether a bifactor structure remains stable over longer periods of time. Additional studies would benefit from examining changes in symptom level data and medication over time with repeated assessment to understand the extent to which these factors vary, despite likely stable test measurement with repeated assessment. In conclusion, these papers provide evidence that the latent structure of cognition in SZ is stable and support the use of neuropsychological testing within this population for assessing cognitive abilities and change in cognitive performance with repeated assessment. Thus, results from these studies provide strong support for the use of neuropsychological tests within SZ treatment outcome studies.

# Appendix A. IRB Exemption Letter

UNLV

**UNLV Social/Behavioral IRB - Administrative Review**
**Notice of Excluded Activity**

| | |
|---|---|
| **DATE:** | February 5, 2020 |
| **TO:** | Daniel Allen, Ph.D. |
| **FROM:** | UNLV Social/Behavioral IRB |
| **PROTOCOL TITLE:** | [1547808-1] Stability of Neurocognitive Abilities in Heterogeneous Subgroups of Schizophrenia |
| **SUBMISSION TYPE:** | New Project |
| **ACTION:** | EXCLUDED - NOT HUMAN SUBJECTS RESEARCH |
| **REVIEW DATE:** | February 5, 2020 |
| **REVIEW TYPE:** | Administrative Review |

Thank you for your submission of New Project materials for this protocol. This memorandum is notification that the protocol referenced above has been reviewed as indicated in Federal regulatory statutes 45CFR46.

The UNLV Social/Behavioral IRB has determined this protocol does not meet the definition of human subjects research under the purview of the IRB according to federal regulations. It is not in need of further review or approval by the IRB.

We will retain a copy of this correspondence with our records.

*Any* changes to the excluded activity may cause this protocol to require a different level of IRB review. Should any changes need to be made, please submit a Modification Form.

If you have questions, please contact the Office of Research Integrity - Human Subjects at IRB@unlv.edu or call 702-895-2794. Please include your protocol title and IRBNet ID in all correspondence.

Office of Research Integrity - Human Subjects
4505 Maryland Parkway . Box 451047 . Las Vegas, Nevada 89154-1047
(702) 895-2794 . FAX: (702) 895-0805 . IRB@unlv.edu

## Appendix B. Use of Previously Published Material

Study I was published in the *Journal of Psychiatric Research*, Study II was submitted to *Schizophrenia Research,* and Study III was submitted to *European Psychiatry*. Elsevier allows replication of published works by the author within the publication of a dissertation manuscript along with the link to the original article. For reference to the published article, visit the link below:

Becker, M. L., Ahmed, A. O., Benning, S. D., Barchard, K. A., John, S. E., & Allen, D. N. (2021). Bifactor model of cognition in schizophrenia: Evidence for general and specific abilities. *Journal of Psychiatric Research*, *136*, 132-139. https://doi.org/10.1016/j.jpsychires.2021.01.051.

**Curriculum Vitae**

Megan L. Becker Wright
beckermegan0@gmail.com

## Education

2022 — University of Nevada, Las Vegas (UNLV)
Ph.D. Clinical Psychology, Neuropsychology Major Area of Study
Dissertation: Stability of Neurocognitive Abilities in Heterogeneous Subgroups of Schizophrenia
Dissertation Advisor: Daniel Allen, Ph.D.
Defense Passed: 10/21/21

2016 — California State University (CSU), San Bernardino
M.A. General/Experimental Psychology
Thesis: Effects of Repeated Aripiprazole Treatment on the cAMP and Akt Pathways in the Dorsal Striatum of Preadolescent and Adult Rats
Thesis Advisor: Sanders McDougall, Ph.D.

2013 — California State University (CSU), Channel Islands
B.A. Psychology, Cum Laude, Psychology Program Honors

2011 — Santa Barbara City College
A.A. Behavioral Science
A.A. Liberal Arts, emphasis in Science and Mathematics

## Clinical Experience

2021-current — **APA-Accredited Doctoral Internship at Henry Ford Hospital Division of Neuropsychology- will be completed 6/30/22**
Adult Neuropsychology Doctoral Intern
Supervisors: Adrianna Zec, Psy.D., ABPP-CN, Brent Funk, Psy.D., ABPP-CN

- Initial intakes, test administration, scoring, report writing, and feedback for outpatient neuropsychological evaluations of adults and geriatric adults with neurological and psychiatric conditions, caseload of 2-3 evaluations weekly
    - primary referral sources are from neurology and neurosurgery and most common populations include stroke and vascular disease, movement disorders, dementia, traumatic brain injury, and epilepsy
- Cognitive remediation and tandem caregiver support sessions for post-ICU patients and their caregivers

2020 - 2021 — **Cure 4 the Kids Foundation**

Multidisciplinary Pediatric Oncology Specialty Clinic
Clinical practicum IV
Supervisor: Danielle Bello, Ph.D., ABPP-CN

- Test administration, scoring, and report writing for neuropsychological evaluations with children and adolescents with cancer (leukemia, lymphomas, and solid tumors) or in remission
- Brief interventions with adolescents and young adults related to mood symptoms, adjustment, or anxiety with medical procedures

2019 - 2020 **Cleveland Clinic Foundation, Lou Ruvo Center for Brain Health**
Multidisciplinary Dementia Specialty Clinic
Clinical practicum III
Supervisors: Jessica Caldwell, Ph.D., ABPP-CN & Justin Miller, Ph.D., ABPP-CN

- Test administration, scoring, and report writing for neuropsychological evaluations with geriatric adults with Alzheimer's disease, Parkinson's disease, Lewy Body dementia, vascular dementia, primary progressive aphasia, and alcohol-related dementias

2019 - 2020 **UNLV Academic Success Center,** Las Vegas, NV
Multidisciplinary Department/School Clinic
Graduate Assistantship
Supervisor: Michelle Paul, Ph.D.

- Test administration, scoring, and report writing for psychodiagnostic and neuropsychological evaluations for students with various psychiatric and neurological conditions in need of academic accommodations at UNLV Academic Success Center and Disability Resource Center (DRC), including consultations for accommodations with DRC Document Review Team

2018 - 2019 **Center for Applied Neuroscience,** Las Vegas, NV
Neuropsychology Private practice
Clinical practicum II
Supervisors: Thomas Kinsora, Ph.D. and Sharon Jones-Forrester, Ph.D.

- Test administration, scoring, and report writing for neuropsychological evaluations with geriatric, adult, and child patients for medical and civil/criminal forensic referrals with varying neurological and psychiatric conditions

2017 - 2018 **UNLV The PRACTICE,** Las Vegas, NV
Multidisciplinary Community Mental Health Center/University Training Clinic
Clinical practicum I

Supervisors: Stephen D. Benning, Ph.D. (assessment), Kristen M. Culbert, Ph.D. (individual therapy), Noelle Lefforge, Ph.D. (intakes and group therapy), and Michelle G. Paul, Ph.D. (PRACTICE director)

- Initial intakes- scored and interpreted symptom inventories and initial outcome tracking data, presented intakes in grand rounds, and provided clients with feedback regarding treatment recommendations
- Psychological assessment- test administration, scoring, and report writing for psychodiagnostic evaluations for adults with various psychiatric conditions
- Individual Psychotherapy- caseload of four clients, with weekly 50-minute sessions with individuals who had psychiatric conditions
- Group psychotherapy- adult cognitive behavioral therapy (CBT) group facilitator with Catherine Isaza, Psy.D., weekly for 1.5 hour sessions

**Clinical Supervision of Other Doctoral Students**

2019 - 2020 **UNLV Academic Success Center,** Las Vegas, NV
Multidisciplinary Department/School Clinic
Graduate Assistantship
Supervisor: Michelle Paul, Ph.D.
Tiered supervision with weekly one-hour supervision of an advanced clinical psychology doctoral student in test administration, scoring, and report writing for neuropsychological or psychodiagnostic evaluations with students in need of academic accommodations

**Research Experience**

2019 - 2020 **Cleveland Clinic Foundation- Lou Ruvo Center for Brain Health**
Primary Investigator: Justin Miller, Ph.D., ABPP-CN
Role: Co-investigator
Lead data analysis examining learning on cognitive measures in Parkinson's and Alzheimer's diseases using the National Institute of Health (NIH) Center of Biomedical Research Excellence (COBRE) dataset

2016 - current **Neuropsychology Research Program Laboratory,** University of Nevada, Las Vegas
Primary Investigator: Daniel Allen, Ph.D.
Role: Co-investigator
Lead data collection and manuscript preparation for the validation of a novel brief social cognition measure and analysis of neuropsychological testing data (dissertation) for the National Institute of Mental Health (NIMH) Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) database

2013 - 2016 **Behavioral Psychopharmacology Laboratory,** CSU, San Bernardino

NIMH grant number: MH102930
Primary Investigator: Sanders McDougall, Ph.D.
Additional Supervisor: Cynthia Crawford, Ph.D.
Role: Graduate Research Assistant
Lead data collection and analysis on a study that assessed the second-messenger systems responsible for the effects of aripiprazole (Abilify) across development, also examined the ontogeny of serotonin and dopamine pathways that mediate behavioral sensitization in preweanling rats

2012 - 2013 **Clinical/Developmental Psychology Laboratory,** CSU, Channel Islands
Primary Investigator: Harley Baker, Ph.D.
Role: Undergraduate Research Assistant
Responsible for helping generate and design a study on defense mechanisms and perception of God among self-identified Christians of various religious denominations

2012 **Social Psychology Laboratory,** CSU, Channel Islands
Supervisor: Virgil Adams, Ph.D.
Role: Undergraduate Research Assistant
Independent Project: "Hope and Understanding of Government in Relation to Tea Party Affiliation"
Responsible for the design of a portion of a survey that assessed the political efficacy and trust in government in the 2012 Presidential Election

**Peer Reviewed Publications**

1. **Becker, M. L.**, Maietta, J. E., Strong, M. N., Kuwabara, H. C., Kinsora, T. F., Ross, S. R., & Allen, D. N. (2021). Spanish and English language-based differences in cognitive performance and symptom reporting on ImPACT baseline concussion assessment. *Journal of Pediatric Neuropsychology*.

2. **Becker, M. L.**, Ahmed, A. O., Benning, S. D., Barchard, K. A., John, S. E., & Allen, D. N. (2021). Bifactor model of cognition in schizophrenia: Evidence for general and specific abilities. *Journal of Psychiatric Research*, *136*, 132-139. doi.org/10.1016/j.jpsychires.2021.01.051

3. Ringdahl, E. N., **Becker, M. L.**, Hussey, J. E., Thaler, N. S., Vogel, S. J., Cross, C., Mayfield, J., & Allen, D. N. (2018). Executive function profiles in pediatric traumatic brain injury. *Developmental Neuropsychology, 44*(2), 172-188.

4. Parke, E. M., **Becker, M. L.**, Graves, S. J., Baily, A. R., Paul, M. G., Freeman, A. J., & Allen, D. N. (2018). Social cognition in children with attention-deficit/hyperactivity disorder. *Journal of Attention Disorders*, http://doi.org/10.1177/1087054718816157.

**Published Book Chapters and Encyclopedia Entries**

Allen, D. N., & **Becker, M. L.** (2019). Clinical Interviewing. In G. Goldstein, D. N. Allen, & J. DeLuca, & (Ed)., *Handbook of Psychological Assessment* (4th Ed). Oxford: Elsevier Science.

Allen, D. N., **Becker, M. L.** (2019). Diagnostic and Symptom Interviews for Adults. In G. Goldstein, D. N. Allen, & J. DeLuca (Eds)., *Handbook of Psychological Assessment* (4th Ed). Oxford: Elsevier Science.

**Becker, M.**, Allen, D. N. (2017). Agitated Behavior Scale. In J. Kreutzer, J. DeLuca, B. Caplan, & S. Bush (Eds), *Encyclopedia of Clinical Neuropsychology, 2nd edition*. Springer Publishing Company: New York. ISBN: 978-3-319-56782-2. https://doi.org/10.1007/978-3-319-56782-2_165-3

**Becker, M.**, Allen, D. N. (2017). Galveston Orientation & Amnesia Test (GOAT). In J. Kreutzer, J. DeLuca, B. Caplan, & S. Bush (Eds), *Encyclopedia of Clinical Neuropsychology, 2nd edition*. Springer Publishing Company: New York. ISBN: 978-3-319-56782-2. https://doi.org/10.1007/978-3-319-56782-2_184-3

**Becker, M.**, Allen, D. N. (2017). COGNISTAT. In J. Kreutzer, J. DeLuca, B. Caplan, & S. Bush (Eds), *Encyclopedia of Clinical Neuropsychology, 2nd edition*. Springer Publishing Company: New York. ISBN: 978-3-319-56782-2. https://doi.org/10.1007/978-3-319-56782-2_170-2

**Becker, M.**, & Allen, D. N. (2017). Brief Cognitive Rating Scale. In J. Kreutzer, J. DeLuca, B. Caplan, & S. Bush (Eds), *Encyclopedia of Clinical Neuropsychology, 2nd edition*. Springer Publishing Company: New York. ISBN: 978-3-319-56782-2. https://doi.org/10.1007/978-3-319-56782-2_168-3

**Manuscripts Submitted or in Preparation**

**Becker, M. L.**, Ahmed, A. O., Barchard, K. A., Benning, S. D., John, S. E., & Allen, D. N. (2022). *The latent structure of cognitive tests is invariant in men and women with schizophrenia*. [Manuscript submitted for publication]. Department of Psychology, University of Nevada, Las Vegas.

**Becker, M. L**., Ahmed, A. O., John, S. E., Barchard, K. A., Benning, S. D., & Allen, D. N. (2022). *Longitudinal stability of the latent structure of cognition in schizophrenia*. [Manuscript submitted for publication]. Department of Psychology, University of Nevada, Las Vegas.

## Oral Presentations and Symposia

**Becker, M. L.,** Meza Perez, C., Galante, M., & Paul, M. G. (2018, October). Cognitive behavioral therapy: Lecture series for University of Nevada, Las Vegas Psychiatry Residents. [Symposium]. Las Vegas, NV.

Teranishi Martinez, C., & **Becker, M. L.** (2013, May). Media as a teaching tool in psychology classes. [Symposium]. EduSoCal Annual Conference. Camarillo, CA.

**Becker, M. L.,** & Adams, V. (2012, November). Hope and understanding of government in relation to tea party affiliation. [Symposium]. Southern California Conference for Undergraduate Research 2nd Annual Conference. Camarillo, CA.

## Conference Presentations and Published Abstracts

**Becker, M. L.,** Caldwell, J. Z. K., Ritter, A. R., Mishra, V. R., Cummings, J. L., & Miller, J. B. (2021, February). *Early and late list learning in Parkinson's and Alzheimer's diseases*. [Poster presentation]. 49th Annual Conference of the International Neuropsychological Society, San Diego, CA.

**Becker, M. L.,** Ahmed, A. O., Benning, S. D., Barchard, K. A., John, S. E., & Allen, D. N. (2021, February). *Bifactor structure of cognition in schizophrenia*. [Poster presentation]. 49th Annual Conference of the International Neuropsychological Society, San Diego, CA.

**Becker, M. L.,** & Allen, D. N. (2019, November). *Is the latent structure of neurocognitive domains invariant across males and females with schizophrenia?* [Poster presentation]. 39th Annual Conference of the National Academy of Neuropsychology, San Diego, CA.

Vertinski, M., Zenisek, R. P., **Becker, M. L.**, Paul, N. B., Frantom, M. B., Foreman, R., Call, E., Boyd, J. E., & Allen, D. N. (2018, August). *Examining the cortisol stress response in schizophrenia*. [Poster presentation]. 126th American Psychological Association Annual Convention, San Francisco, CA.

**Becker, M. L.**, Zenisek, R. P., Paul, N. B., Vertinski, M., Frantom, M. B., Call, E. T., & Allen, D. N. (2017, October). *Performance on a novel brief measure for social cognition in individuals with schizophrenia.* [Poster presentation]. 37th Annual Conference of the National Academy of Neuropsychology, Boston, MA.

Hussey, J. E., **Becker, M. L.**, Call, E., Juarez, N., Kinsora, T., Ross, S., & Allen, D. N. (2017, October). *Effects of native language on ImPACT baseline scores.* [Poster presentation]. 37th Annual Conference of the National Academy of Neuropsychology, Boston, MA.

Paul, N. B., Zenisek, R. P., **Becker, M. L.**, Gomez, R. I., Strong, M., Chaleunsouck, R. A., & Allen, D. N. (2017, October). *Psychometric evaluation of a new brief test of social cognitive abilities (BTSCA)*. [Poster presentation]. 37th Annual Conference of the National Academy of Neuropsychology, Boston, MA.

**Becker, M. L.**, Real, V., Hardin, A., Crawford, C. A., & McDougall, S. A. (2016, November). *Effects of repeated aripiprazole treatment on $D2^{High}$ receptors and the Akt-GSK3β signaling pathway in preadolescent and adult rats.* [Poster presentation]. Annual meeting of the Society for Neuroscience, San Diego.

Harmony, Z. R., Stone, M. J., **Becker, M. L.**, Rudberg, K. N., Moran, A. E., Macedo, E., & McDougall, S. A. (2015, October). *Effects of a histone deactylase inhibitor on the induction of one-trial methamphetamine- and cocaine-induced behavioral sensitization in preweanling rats.* [Poster presentation]. Annual meeting of the Society for Neuroscience, Chicago.

Stone, M. J., **Becker, M. L.**, Mortola, J. A., & McDougall, S. A. (2014, November). *Cocaine induced behavioral sensitization in pre-weanling rats.* [Poster presentation]. Annual meeting of the Society for Neuroscience, Washington, D.C.

Baker, H. E., Ayala, R. M., **Becker, M. L.**, & Hanzelik, C. (2013, April). *God images: depression and defense mechanism correlates.* [Poster presentation]. Annual meeting of the Western Psychological Association. Reno, NV.

## Grants

2015 - 2016 **Research Initiative for Scientific Enhancement (RISE)**
National Institute of Health (NIH)
Grant number: R25GM100829
Primary Investigator: Cynthia Crawford, Ph.D.
Role: Teaching Assistant

2013 - 2016 **Ontogeny of Caudate-Putamen Functioning: Behavioral Relevance**
National Institute of Mental Health (NIMH)
Grant number: MH102930
Primary Investigator: Sanders McDougall, Ph.D.
Role: Research Assistant

## Teaching Experience

2020 - 2021 **Introduction to Psychology** (100 level online course), UNLV
Instructor of Record for two online courses per semester

2018 - 2019 **Introduction to Psychology** (100 level course), UNLV
Instructor of Record for two courses per semester

2015 - 2016 **Biological Psychology Adjunct Support Class** (300 level course), CSU, San Bernardino
Teaching Associate and Instructor of Record
NIH grant number: R25GM100829
Primary Instructor: Cari Goetz, Ph.D.

Spring 2014 **Introduction to Counseling Theory,** CSU, San Bernardino
Teaching Assistant
Instructor: Kindra Edmondson, M.F.T.
Guest Lectures: Family Systems Therapy (two-part series)

Spring 2013 **Behavioral Neuroscience,** CSU, Channel Islands
Teaching Assistant
Instructor: Beatrice de Oca, Ph.D.

## Leadership

2019 - 2021 **Clinical Student Committee Representative**, UNLV
Doctoral cohort representative on a student-lead committee for the 2019-2020 and 2020-2021 academic years to advocate for training, financial, social, and other departmental concerns of psychology doctoral students

2016 - 2020 **Outreach Undergraduate Mentoring Program (OUMP) Mentor**, UNLV
Graduate mentor for undergraduate students from traditionally underrepresented groups in graduate programs through individual bi-weekly or monthly mentorship in applying to graduate school and career goals

2015 - 2016 **Neuroscience Club President,** CSU San Bernardino
Faculty Advisors: Matthew Quinlan, Ph.D. and Cari Goetz, Ph. D.
Collaborated with club officers and faculty advisors to inform students about graduate school and career opportunities, organized attendance of research symposiums, and participated in community outreach and education

2012 - 2013 **Psi Chi President,** CSU Channel Islands Chapter of the International Honor Society
Faculty Advisor: Christy Teranishi Martinez, Ph.D.

Collaborated with club officers and faculty advisors, regulated membership, and oversaw all meetings, induction ceremonies, and philanthropic activities

2012 - 2013 **Student Advisory Board,** University Committee, CSU Channel Islands
Faculty Advisor: William G. Sawyer, Ph.D.
Participated on a board comprised of campus club presidents and vice presidents to promote student engagement in campus activities

**Professional Service**

2020 - current **Ad Hoc Reviewer**

Peer reviewer of manuscripts submitted for publication to neuropsychology and psychiatry journals

2020 - 2021 **Inclusion, Diversity, Equity, Access, and Solutions (IDEAS) Committee**, UNLV
Contributed input and reform in collaboration with UNLV students and faculty to advocate for social justice efforts aimed at increasing inclusion, diversity, and equity within the UNLV Psychology Department and greater UNLV community

2020 **Interdisciplinary Training for Medical Technicians at Cleveland Clinic Foundation- Lou Ruvo Center for Brain Health**
Developed a curriculum and conducted trainings for new medical technicians administering cognitive screeners [i.e., Montreal Cognitive Assessment (MoCA) and Mini Mental Status Exam (MMSE)] that addressed administration and quality data collection for research and clinic purposes

2020 **Interdisciplinary Education for Neuropsychology Trainees at Cleveland Clinic Foundation- Lou Ruvo Center for Brain Health**
Facilitated educational opportunities for neuropsychology trainees via shadowing various departments (neurology including cognitive, movement disorder, and multiple sclerosis specialists, music therapy, physical therapy, and occupational therapy)

2019 - 2020 **Doctoral Student Consultant for Disability Resource Center**, UNLV
Reviewed students' external psychological reports and documentation for academic accommodations bi-weekly, and provided accommodation and referral recommendations

2019 **National Academy of Neuropsychology (NAN) Annual Conference Volunteer**
Tracked neuropsychologists' CE credits and monitored conference symposia

2017 - 2019 **Interprofessional Education and Practice (IPEP) Seminar Volunteer**, UNLV
(2017-2018) Aided in running a poverty simulation activity and participated in interdisciplinary discussions and case conceptualizations with nursing, physical therapy, dental, and social work students, and (2019) multidisciplinary group facilitator leading treatment team for interdisciplinary case vignettes

**Volunteer Experience**

2014 - 2016 **VA Loma Linda Health Care System**
Escorted patients that need ambulatory assistance getting to appointments in the hospital, waited with patients at their appointments, and assisted the hospital staff primarily on the mental health/rehabilitation floor

2012 **Child Abuse Listening and Mediation (CALM),** Santa Barbara, CA
Caregiver for children who were abused or at risk while their parents attended therapy sessions

2011 **Hearts Adaptive Riding,** Santa Barbara, CA
Facilitated horseback riding lessons for veterans and children who had experienced trauma or had other mental or physical disabilities

2011 **Learning and Behavioral Center,** Tarzana, CA
Individual behavioral therapy (applied behavior analysis) with children with autism spectrum disorder or ADHD

**Scholarships**

2020 **Donald Carns Scholarship**
Competitive scholarship awarded to UNLV doctoral students for research projects

2019, 2020 **Summer Doctoral Research Fellowship**
Competitive scholarship awarded to approximately 20 UNLV doctoral students for summer research projects

2018 **Dearmin Trust Honorary Fund Scholarship**
Santa Barbara Scholarship Foundation
Competitive private scholarship awarded for graduate tuition

2017, 2018 **College of Liberal Arts (COLA) University of Nevada, Las Vegas Summer Stipend**
Competitive stipend awarded to five Clinical Psychology Ph.D. students for summer research projects

| | |
|---|---|
| 2013, 2014, 2015, 2016, 2017, 2019, 2020 | **Burnand-Partridge Foundation Scholarship**<br>Santa Barbara Scholarship Foundation<br>Competitive private scholarship awarded for graduate tuition |
| 2012 | **Orfalea Scholarship**<br>Santa Barbara Scholarship Foundation<br>Competitive private scholarship awarded for undergraduate tuition |
| 2011 | **Herbert and Gertrude Latkin Trust Scholarship**<br>Santa Barbara Scholarship Foundation<br>Competitive private scholarship awarded for undergraduate tuition |
| 2010 | **Women's Service Club of Goleta Scholarship**<br>Santa Barbara Scholarship Foundation<br>Competitive private scholarship awarded for undergraduate tuition |

**Affiliations**

| | |
|---|---|
| 2013 - current | American Psychological Association Division 40, Student Member |
| 2020 - current | International Neuropsychological Society, Student Member |
| 2016 - current | National Academy of Neuropsychology, Student Member |
| 2019 - current | Hispanic Neuropsychological Society, Student Member |
| 2012 | Psi Chi International Honor Society Member |
| 2012 | Gamma Beta Phi National Honor Society Member |
| 2011 | Phi Theta Kappa National Honor Society Member |

***References are available upon request.***