# THE NATURE AND FUNCTIONAL SIGNIFICANCE OF INTRA-INDIVIDUAL NEUROCOGNITIVE ABILITY ACROSS SERIOUS MENTAL ILLNESS DIAGNOSES

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Emily Anne Blanco

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THE NATURE AND FUNCTIONAL SIGNIFICANCE OF INTRA-INDIVIDUAL NEUROCOGNITIVE ABILITY ACROSS SERIOUS MENTAL ILLNESS DIAGNOSES

Emily Anne Blanco, Candidate for the Master of Arts Degree

University of Missouri-Kansas City, 2022

## ABSTRACT

Intra-individual performance variability (IIV) is defined as lawful, transient, within-person changes in cognitive performance. IIV has been found to predict functional and other crucial real-world outcomes among clinical populations with characteristic frontal lobe abnormalities. However, little is known about its significance among individuals with serious mental illness (SMI). Moreover, IIV's relationships to clinical, cognitive, diagnostic, and demographic variables in this population are yet uncertain. The aims of this study were (1) to characterize intra-individual neurocognitive performance variability among participants with serious mental illness (2) to examine possible differences in levels of IIV across diagnostic and educational groups, (3) and to explore its functional significance among participants with SMI, including its incremental validity to predict employment and living status outcomes, and performance on a test of grocery shopping skills. We completed a secondary analysis using data from 217 participants representing community-dwelling adults with either a psychotic disorder or an affective disorder diagnosis. We found that age, clinical symptoms, and overall cognitive ability were not significantly related to IIV among participants.

Psychotic and affective disorder groups evidenced similar levels of IIV, irrespective of positive and negative symptoms. IIV did not vary across groups with different levels of education. Further, IIV was not related to functional outcomes nor incrementally predictive of them, above and beyond overall cognitive ability. Future research may address limitations of the present study and explore interrelationships between IIV, cognitive effort, and disengaged lifestyle among individuals with SMI in the absence of relationships between IIV and our variables of interest.

# APPROVAL PAGE

The faculty listed below, appointed by the Dean of the College of Arts and Sciences have examined a thesis titled "The nature and functional significance of intra-individual neurocognitive ability across serious mental illness diagnoses" presented by Emily Anne Blanco, candidate for the Master of Arts degree, and certify that in their opinion it is worthy of acceptance.

<u>Supervisory Committee</u>

Melisa Rempfer, Ph.D., Committee Chair
Department of Psychology

Kym Bennett, Ph.D.
Department of Psychology

Jake Marszalek, Ph.D.
Department of Psychology

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# DEDICATION

I dedicate this manuscript to my family, friends and mentors, both past and present. I am so grateful to know you and to learn from you. Your unwavering confidence in me strengthens me in all things I do. This manuscript is for you.

# CHAPTER 1

# INTRODUCTION

Cognitive ability consistently correlates with everyday functional outcomes among individuals with serious mental illness (SMI) diagnoses, including schizophrenia-spectrum disorder, bipolar disorder, and major depressive disorder (Substance Abuse and Mental Health Services Administration, 2020). Cognitive ability refers to specific neurocognitive (e.g., verbal learning and memory, speed of processing, working memory) and social cognitive (e.g., emotion recognition, theory of mind) mental processes which assist the individual to encode and store important information, modulate emotional states, and initiate behavioral sequences in response to demands of the surrounding environment. Neurocognitive and social cognitive mental processes are typically captured using neuropsychological tasks or batteries, which theoretically measure cognitive functions related to specific structures or neural pathways in the brain. A substantial body of evidence has found that scores derived from performance on various neuropsychological tasks predict crucial real-world functional outcomes among individuals with SMI, including independent living skills (Rempfer et al., 2003), social and vocational functioning (Lepage et al., 2014; Green et al., 2006), self-management of illness-related challenges (Zhou et al., 2020), and mental health treatment utilization (Gooding et al., 2012; McGurk et al., 2004). Although there is evidence supporting the significance of cognitive ability on a variety of functional outcomes, a meta-analysis by Halverson and colleagues (2019) found that scores derived from performance on neuropsychological tasks are only weakly to moderately associated with dimensions of functioning and tend to predict a small amount of unique variance in real-world outcomes. More broadly, studies of predictors of everyday functional outcomes have stalled at accounting for about 50% or less of the variance in real-world functioning (Bowie et al., 2006, 2008, 2010; Harvey et al., 2011; Harvey et al., 2019). Accordingly, innovative and accessible measures capable of accounting for unexplained variance in real-world functional outcomes are crucial for refining therapeutic and remediation efforts to enhance community functioning among individuals with serious mental illness.

## Introducing the Intra-individual Variability Perspective

Researchers are making strides to understand the nature of cognitive variability among individuals with serious mental illness. Studies focusing on cognitive variability are frequently concerned with inter-individual variability, or meaningful differences in cognitive ability between individuals with serious mental illness, either within or across diagnostic groups. Many studies in the existing literature aggregate scores of participants to derive and compare measures of central tendency, such as average performance, on neuropsychological tasks (e.g., Afshari et al., 2020; Bo et al., 2018). Researchers typically use these methods with the goal of minimizing error on neurocognitive functioning estimation derived from the sum of true tests scores and error to deduce an ideally reliable and representative measure of functioning, as assumed by classical test theory. Implicit in this perspective is the idea that within-person performance variability is random error variance and a nuisance variable rather than a variable with significance for characterizing neuropsychological functioning (Nesselroade & Salthouse, 2004). From this perspective, error variance is viewed as “noise” in the statistical process.

However, some researchers have challenged this perspective by attending to error variance as a possible source of meaningful information about within-person performance variability (Hillborn et al., 2009; Nesselroade & Salthouse, 2004; Ram et al., 2005). These researchers view error variance as being indicative of *intra-individual variability* (IIV), defined as lawful, transient, within-person changes in performance, typically indexed using trial-by-trial fluctuations on a reaction-time task, or variation in cognitive performance (Li et al., 2004; MacDonald, 2006). Specifically, proponents of this perspective suggest that when intra-individual variability in performance is small, mean-level differences are capable of providing valuable predictive information (MacDonald et al., 2006; Nesselroade & Salthouse, 2004). However, when intra-individual variability in performance is larger, it may represent *systematic* as opposed to random error variance. From this standpoint, scores on neuropsychological tasks derived from a single measurement occasion may be flawed estimates of performance and inter-individual differences (Hultsch et al., 2004; Nesselroade & Salthouse, 2004). Stated more simply, when within-person performance variability is large, it may drive apparent between-person variance, particularly when a variable used for grouping participants is associated with increased within-person variance (Hill et al., 2013). From an intra-individual perspective, error variance is viewed as “signal” with significance in its own right (Salthouse et al., 2011).

# CHAPTER 2

# REVIEW OF THE LITERATURE

## The Concept of Intra-individual Performance Variability

Intra-individual performance variability has been conceptualized as an important marker of nervous system integrity with significance for a number of clinical populations (Hultsch et al., 2004; MacDonald et al., 2009). Greater fluctuation in behavioral performance represents increased intra-individual variability, and is presumed to be secondary to neural "noise" or variation in neural firing, which is conceptualized to provide a consistent background to our perceptual, motor, and cognitive processing (MacDonald et al., 2006). IIV can also be viewed from a developmental perspective, as it has been found to normatively take on a U-shaped trajectory across the lifespan, with performance variability relatively greater during early and later life (MacDonald et al., 2006; Williams et al., 2005). Decreased intra-individual performance variability from childhood into adolescence and early adulthood are hypothesized to be the result of adaptive neurodevelopmental changes including synaptic pruning, reductions in gray-matter density, and increased white matter maturity and connectivity, which together increase neural efficiency and decrease neural noise (MacDonald et al., 2006; MacDonald et al., 2009). Aging research has played an instrumental role in substantiating the functional significance of greater intra-individual performance as an early marker of pathology, given findings that relatively greater IIV among older individuals is linked with poorer cognitive outcomes, greater subsequent cognitive decline (Christensen et al., 1999; Li & Lindenberger, 1998), and even death (MacDonald et al., 2008). Greater intra-individual performance variability is hypothesized to reflect compromised neural integrity of the frontal lobes in particular, given converging evidence of greater intra-individual performance variability among participants with frontal lobe lesions relative to non-frontal lesions (Stuss et al., 2003), sustained focal damage to the prefrontal cortex (Stuss et al., 1989), frontal lobe dementia (Murtha et al., 2002), and neurodevelopmental disorders with characteristic frontal lobe abnormalities, like attention-hyperactivity disorder (Leth-Steensen et al., 2000), and schizophrenia (Schwartz et al., 1989). Although there are multiple theories as to what greater intra-individual variability precisely reflects at the level of cognition (Bunce et al., 2004; Li et al., 2001; Schmiedek et al., 2007; West et al., 2002), researchers have proposed that it reflects impairment of the executive control function subserved by the frontal lobes, which are instrumental in sustaining top-down attentional control during neuropsychological and other goal-directed tasks (Bellgrove et al., 2004; Bunce et al., 2004; West, 2002). Greater intra-individual variability may therefore broadly reflect a lesser ability for performance consistency due to reduced maintenance of concentration on task-relevant stimuli and inattention to task-irrelevant stimuli necessary to meet certain task demands.

## IIV Theory and Measurement

Intra-individual variability is specifically concerned with the amount of *deviation* within an individual's performance rather than an individual's average performance (Hillborn et al., 2009; Hultsch et al., 2002). Intra-individual variability can be indexed using various methodologies, including measures of *inconsistency* of performance across trials of a single cognitive task at various timepoints (e.g., test/retest performance) or within a single testing session (e.g., reaction time tasks), or *dispersion* of performance across different cognitive domains within a single testing session (e.g., neuropsychological task performance). The terminology of dispersion has been used interchangeably with inconsistency in the reaction time literature when intra-individual variability in reaction time is measured during a single testing session (e.g., Kaiser et al., 2008). Such interchangeability in terminology may be a generalization of evidence finding that these constructs are correlated, suggesting that individuals who exhibit more intra-individual variability within a cognitive task also demonstrate more intra-individual variability between cognitive tasks (Hillborn et al., 2009; Hultsch et al., 2002).

Compared to across-trial intra-individual variability, across-domain intra-individual variability is thought to approach performance variability in a more general way, given that it is derived from measures of performance across different cognitive domains. Across-domain IIV therefore indexes a broader dimension of individual difference than across trial intra-individual variability derived from repeated performance on a single cognitive task (Cole et al., 2011). Additionally, across-domain IIV holds the benefit of being able to be derived using a number of datasets which include participant or client performance on neuropsychological tasks. For instance, assessments commonly used to index across-trial intraindividual variability in reaction time, like the Go/Nogo task, may require use of a computerized format and demand additional knowledge and skill to administer. By contrast, clinical researchers and practitioners with training and access to common paper-and-pencil neuropsychological batteries including multiple neuropsychological tasks (e.g. the Wechsler Adult Intelligence Scale, the MATRICS Consensus Cognitive Battery) can derive an across-domain intra-individual variability score. For these reasons, across-domain intra-individual variability may represent an accessible way to index and incorporate information regarding intra-individual performance variability into their assessment of an individual's cognitive functioning.

Across-domain intra-individual variability is similar to the concept of subtest scatter (Wechsler, 1958) in neuropsychological performance, proposed by some researchers to be a useful diagnostic tool to identify individuals with schizophrenia (Cole et al., 2011). While some researchers have found no reliable scatter patterns distinguishing participants with schizophrenia from other participants without a psychotic disorder (Garfield et al., 1948), other researchers (Olch, 1948; Trehub & Scherer, 1958) have reported scatter across subtests to be predictive of a schizophrenia diagnosis. However, quantitative measurement of subtest scatter has been inconsistent, reflecting a lack of reliability in the definition of scatter (Juni & Trobliger, 2009). The use of a standardized way of calculating intrasubject scatter offered by the intra-individual variability perspective may assist researchers with building a body of evidence as to the significance of deviation within individual performance across cognitive domains.

## IIV as a Predictor of Outcomes and Functioning

Intra-individual performance variability is thought to be a construct that is psychometrically separable from the cognitive construct used to the measure the performance (Ram et al., 2005) with the ability to provide incremental information beyond measures of central tendency (Dixon et al., 2007). Accordingly, researchers have used measures of intra-individual variability to predict a range of outcomes above mean or global cognitive performance in multiple clinical populations. For example, greater IIV has been found to be a better predictor of cognitive decline among individuals of advanced age than baseline mean cognitive functioning (Kliegel & Sliwinski, 2004), and medication adherence over the course of six months above mean-level change in cognitive performance among adults with human immunodeficiency virus (HIV) (Thaler et al., 2015). Further, intra-individual variability has been found to be associated with physical health-related quality of life among individuals with West Nile Virus independent of IQ (Sheppard et al., 2018). Measures of intra-individual variability may therefore offer additional value beyond overall cognitive ability to predict crucial outcomes among clinical and aging populations. Additionally, IIV has been used to predict a range of every-day outcomes across clinical groups irrespective of the consideration of its incremental or mean-independent value. For example, it has been found that unemployed individuals with hepatitis C evidence significantly higher dispersion scores compared to employed individuals with a hepatitis C diagnosis (Morgan et al., 2012). Further, it has been found that intra-individual variability significantly predicts health-related quality of life among veterans with a remote history of mild traumatic brain injury (Merritt et al., 2021). Intra-individual variability has also been found to be related to mental health quality of life among healthy, community dwelling adults (Bauermeister & Bunce, 2015). Thus, existing evidence suggests that IIV is predictive of crucial functional and real-world outcomes across a range of clinical populations.

### IIV as a Predictor of Functioning in Participants with Serious Mental Illness

Despite discoveries as to the significance of intra-individual variability to predict a range of outcomes, a noticeable lack of attention has been paid to the functional significance of intra-individual variability among individuals with serious mental illness. Importantly, however, Wexler and Nicholls (2004) found an association between intra-individual variation on a reaction time task and complexity, quality and hours of work among 17 individuals with schizophrenia spectrum disorders, suggesting that greater cognitive consistency may be related to greater work performance. Rentrop (2010) later followed up to study the specific relationship between reaction time variability and work performance among 28 participants with schizophrenia who were interviewed by a work therapist who rated participants' work capabilities. They found reaction time variability to be associated with work capability. Cole and colleagues (2011) then used an across-domain neuropsychological performance variability paradigm to index IIV among individuals with schizophrenia, their unaffected siblings and health controls, and found a modest association between IIV and a Global Assessment of Functioning score in the entire sample, but not in when these groups were considered separately. To our knowledge, no studies have explored the functional significance of greater intra-individual variability among other forms of serious mental illness, like bipolar disorder or major depressive disorder, despite the suggestion IIV may be a core feature of these disorders (Gallagher et al., 2015). Although the above-referenced studies represent important first steps in exploring the real-world significance of intra-individual variability among individuals with serious mental illness, the sample sizes included in some of these studies are small, include only participants with schizophrenia, and use indirect measures of work performance (e.g. a rating of work capability by a therapist). Additionally, a majority of studies used a reaction time paradigm to index intra-individual variability by evaluating fluctuations in a participant's ability to use simple mental operations to rapidly signal perception of stimuli, such as the sound of a tone. It is therefore unclear whether larger sample sizes, intra-individual cognitive variability indexed more broadly using across-domain neuropsychological performance, or other measures of work performance (i.e. employment status) may be related to work ability across serious mental illness diagnoses. Further, the relationship of intra-individual performance variability to other types of functional outcomes among individuals with serious mental illness remains unstudied.

## Clinical Symptom Correlates of Intra-individual Variability

Although performance variability may be relevant to the study of cognitive functioning among individuals diagnosed with serious mental illness, it is yet unclear whether or not clinical features contribute to intra-individual variability. The majority of studies on intra-individual performance variability among individuals with serious mental illness use reaction time (RT) tasks to estimate intra-individual variability. Several studies have specifically reported a simple measure of dispersion using reaction time tasks and explored its relationship with clinical symptomology (Kaiser et al., 2008; O'Gráda, 2009; Pellizer & Stephane, 2007; Schwartz et al., 1989; Schwartz et al., 1991; Vinogradov, 1998). For example, an often-cited study by Schwartz and colleagues (1989) observed reaction time using a simple manual response with participants with schizophrenia and affective disorders and found that while slowing of reaction time was related to psychotic symptoms, greater intra-individual variability of reaction time was observed independent of psychotic symptoms and specific to participants with schizophrenia (Schwartz et al.,1989). Of note, this conclusion stands in alignment with research finding that reaction time IIV is increased in participants with schizophrenia spectrum disorders compared to healthy controls, but not in those with major depression compared to healthy controls (Kaiser et al., 2008), and in contrast to research finding increased IIV in participants with bipolar disorder and major depressive disorder compared to healthy controls (Gallagher et al., 2015). Schwartz and colleagues (1991) then went on to explore the relationship between reaction time and negative symptoms among participants with schizophrenia and affective disorders using two reaction time tasks of lesser and greater complexity, and found that intra-individual variability of reaction time on both tasks was related to high negative symptom load among participants with schizophrenia. Individuals with schizophrenia with few negative symptoms and individuals with affective disorders evidenced comparable intra-individual variability (Schwartz et al., 1991), linking intra-individual variability in reaction time in schizophrenia to negative symptoms in particular. An association between reaction time variability and negative symptoms was later echoed by O'Gráda and colleagues (2009) who found that intra-individual variability on a reaction time task accounted for a small amount of variance in negative symptom scores. Vinogradov and colleagues (1998) explored the associations with intra-individual variability on a reaction time task among participants with schizophrenia and found that reaction time variability was related to severity of psychotic symptoms, disorganization, and tension/hostility symptoms. Pellizer & Stephane (2007) went on to challenge the idea that intra-individual variability is related to clinical symptoms by demonstrating that that intra-individual variability on a choice reaction time task was unrelated to negative, psychotic, or disorganized symptoms among participants with schizophrenia. It is therefore unclear as to the relationship between clinical symptoms and intra-individual variability among individuals with serious mental illness.

## Research Aims

To add to the literature concerning intra-individual variability and serious mental illness, we conducted a research project with several aims:

### Aim 1

To characterize intra-individual variability among participants with serious mental illness.

*1.1* We will explore whether there are significant relationships between intra-individual variability and demographic variables. We hypothesize a linear, positive relationship between age and intra-individual variability, indicating that older age is related to greater intra-individual variability among participants with serious mental illness, given research finding that older adults evidence increased intra-individual variability compared to younger adults (Hultsch et al., 2002).

*1.2* We will also explore whether there are relationships between intra-individual variability and clinical symptom variables. We hypothesize significant, positive relationships between intra-individual variability and positive and negative symptoms, indicating that greater symptom severity is related to greater intra-individual variability among participants with serious mental illness.

*1.3* We will explore whether there is a significant, inverse relationship between intra-individual variability and mean cognitive performance among participants with serious mental illness. We hypothesize a linear, negative relationship between mean cognitive performance and intra-individual variability among individuals with serious mental illness, indicating that lower mean cognitive performance is related to greater intra-individual variability, given evidence finding a relationship between similar variables in other clinical populations (e.g. Hill et al., 2013) and in participants with schizophrenia (Cole et al., 2011).

## Aim 2

To examine possible differences in levels of IIV across diagnostic and educational groups.

*2.1* Further, we will compare the degree of intra-individual variability among participants with a psychotic disorder versus participants with an affective disorder diagnosis. We hypothesize that individuals diagnosed with a psychotic disorder will evidence significantly greater intra-individual variability compared to individuals diagnosed with affective disorders.

*2.2* Thereafter, we will examine whether possible differences in intra-individual variability between participants with a psychotic disorder diagnosis and participants with an affective disorder diagnosis remain after controlling for the possible effects of negative and positive symptoms on intra-individual variability scores. We hypothesize that possible differences in intra-individual variability between groups will remain significant after controlling for positive and negative symptoms and their interaction, indicating that greater intra-individual variability is significantly related to a psychotic disorder diagnosis, irrespective of positive and negative symptoms.

*2.3* We further hypothesize no differences in intra-individual variability between participants with different levels of education, given preliminary evidence finding no relationship between education and intra-individual variability among individuals with schizophrenia (Cole et al., 2011).

Aim 3

To examine the functional significance of IIV among participants with serious mental illness.

*3.1* We will explore whether there are significant relationships between intra-individual variability and functional ability, including accuracy, speed and efficiency variables on a test of grocery shopping skills. We hypothesize significant, negative relationships between intra-individual variability and these variables.

*3.2* We further hypothesize differences in intra-individual variability between participants with different functional outcomes, including participants who were employed versus unemployed, and living independently versus non-independently. We hypothesize that unemployed participants will evidence greater intra-individual variability compared to employed participants, and non-independent participants will evidence greater intra-individual variability compared to independent participants.

*3.3* Lastly, we to aim to understand whether intra-individual variability has incremental validity above and beyond overall cognitive ability to predict employment status, living status, and grocery shopping skill, respectively. We hypothesize that intra-individual variability will have unique incremental validity above overall cognitive ability to predict outcomes related to a test of grocery shopping skills, employment and living status among individuals with serious mental illness.

CHAPTER 3

METHODOLOGY

## Design and Participants

This study was a secondary analysis of data (*N* = 217) from participants diagnosed with forms of serious mental illness, including schizophrenia (*n* = 89), schizoaffective disorder (*n* = 54), bipolar disorder (*n* = 33) and major depressive disorder (*n* = 26) and comorbid diagnoses (e.g., a diagnosis of schizophrenia/bipolar disorder due to diagnostic uncertainty) (*n* =15) from four prior studies. Participants were adults living in the community of a mid-size city in the midwestern region of the United States, who voluntarily enrolled in research studies recruiting individuals from an academic teaching hospital setting. We utilized this convenience sample of adults with serious mental illness, given that it represents a heterogeneous group of clinically stable outpatients without acute functional challenges or severe symptoms with the potential to invalidate neuropsychological performance, or limit functional outcomes by way of inhabiting artificially restrictive hospital context.

All four studies required participants to complete neuropsychological tasks during a single testing session. Participants in all four of these studies also provided their demographic information, and information about their functioning, including self-reported employment and living status. Three of the four studies included the Test of Grocery Shopping Skills (TOGSS). Study 1 examined relationships between measures of learning potential and their relationship with the TOGSS among people with serious mental illness (Rempfer et al., 2017). Study 2 examined relationships among functional capacity, cognitive ability, and the TOGSS among people with serious mental illness. (Rempfer & Fowler, 2018). Study 3 examined the relationships between stigma, insight and psychological recovery among individuals with serious mental illness (Fowler et al., 2015). Study 4 examined the efficacy of an intervention with the aim of increasing grocery shopping skill among individual with serious mental illness, utilizing the TOGSS (Brown et al., 2006; Rempfer et al., 2011). The data we utilized were baseline data of participants prior to the intervention. Prior studies have not utilized this larger dataset combining the participants of the four aforementioned studies. Although a prior study examined subgroups of performance ability on the TOGSS and its relationship with neuropsychological ability (Harris et al., 2020), none of the datasets have been used to explore intra-individual cognitive variability or its relationship with other variables of interest in this study. For the purposes of this study, participants diagnosed with schizophrenia and schizoaffective disorder were combined into a psychotic disorders group ($n$ = 143), and participants diagnosed with bipolar disorder or major depressive disorder were combined into an affective disorders group ($n$ = 59). Individuals diagnosed with comorbid diagnoses were included in the combined sample group ($n$ = 217).

## Measures

*Neuropsychological measures*

Wisconsin Card Sorting Test (WCST)

The 64-card version of the WCST was used to assess participant problem-solving and abstract reasoning (Kongs et al., 2000; Nyhus & Barceló, 2009) The WCST has been found to demonstrate acceptable reliability for use with individuals with forms of serious mental illness (Chiu & Lee, 2021), and acceptable validity for use with clinical populations (Chiu et al., 2018). The WCST task consists of four key cards and 128 response cards. Each card has one or more geometric symbols on it that vary according to color, form or number. To begin, four key cards are displayed in front of the participant. Participants are then asked to match 128 individual response cards with one of the four key cards according to an unstated sorting rule. Participants use trial-and-error to discover the sorting rule following feedback from the administrator of the task, who conveyed to the participants whether the sort was correct or incorrect. After ten correct sorts, the sorting rule changes without warning, and participants have to adapt their sorting to be line with to the new rule. The WCST requires intact set-shifting ability, or a complex executive ability to flexibly move attentional focus in response to changing schedules of reinforcement (Monchi et al., 2001). The variable of interest used was total correct sorts.

California Verbal Learning Test/Rey Auditory Verbal Learning Test (CVLT/RAVLT)

The Rey Auditory Verbal Learning Test (RAVLT; Rey, 1964) was administered in Study 4 and the California Verbal Learning Test-II (CVLT-II; Delis et al., 2000) were administered in studies 1 and 2 and 3 in order to assess auditory verbal memory. The CVLT-II has been found to demonstrate good reliability (Delis et al., 2000; Woods et al., 2006) and ecological validity for everyday functioning problems among individuals with serious mental illness (Heinrichs et al., 2008). The RAVLT has also been found to demonstrate good reliability (Ryan et al., 1986; Crawford et al., 1989) and moderate validity in use with clinical and healthy participants (Crossen & Wiens, 1994; Macartney-Filgate & Vriezen, 1988). For both CVLT-II and the RAVLT, participants are first asked to listen to, remember and recall an orally presented list of words. The list is read to participants five times, and after each reading, the participant is asked to recall the list of words in any order. Participants are then asked to listen to, remember and recall a separate, list of interference words. After the interference list reading and associated recall task, participants are then asked to recall as many words as they can from the first list, in any order. The outcome variable of interest we used for this study is the total number of words correctly recalled following the interference list and its recall, or Trial 1.

The CVLT-II and the RAVLT share significant overlap conceptually, empirically and in common use to assess for auditory verbal learning and memory. Conceptually, both measures assess auditory verbal memory by asking participants to remember and recall an orally presented list of words in any order following five learning trials and associated recall tasks, and an interference list and associated recall task. The RAVLT is a non-proprietary measure available in the public domain that has been used in lieu of the CVLT-II to assess for auditory verbal learning and memory in prior research as part of a larger cognitive battery (Filser et al., 2018). Prior research has also demonstrated significant similarity of these two measures in healthy (Crossen & Wiens, 1994) and clinical samples with cognitive impairment (Beier et al., 2019). Specifically, Crossen and Weins (1994) found that heathy controls performed similarly on the two assessments, with slight differences in raw score values. Further, Beier and colleagues (2019) found that scores on the RAVLT showed good agreement with scores on the CVLT-II in use with participants with cognitive impairment. Although the CVLT-II list consists of 16 semantically-related words and the RAVLT list consists of 15 non-related words, there is evidence to suggest that participants with cognitive impairment may use semantic clustering strategies less often than healthy controls on the CVLT (Crosson et al., 1988; Levin & Goldstein, 1986). For these reasons, we *Z*-transformed all scores for these measures to create a single verbal memory variable.

D2 Test of Attention (d2)

A paper-and-pencil version of the d2 was used to assess processing speed and selective attention (Brickenkamp & Zillmer, 1998). The d2 has been found to demonstrate good reliability in use with healthy participants (Brickenkamp & Zillmer, 1998) and participants with serious mental illness (Lee et al., 2017). Further, the d2 has been found to demonstrate good validity in use with various populations (Bates & Lemay, 2004; Zillmer, 1999).The d2 consists of 14 rows, each with 47 randomly mixed target and nontarget characters. Participants are asked to cancel out target characters that are similar but distinct from nontarget characters. Participants are allotted 20 seconds per row to accomplish this task, with no pause allotted between rows. The variable of interest in this study was concentration performance, which indexes both processing speed and visual scanning accuracy. Concentration performance was derived from the total number of correctly crossed out characters minus the total number incorrectly cancelled out characters.

Letter-Number Sequencing/Digit Span Backwards (LNS/DSB)

The Digit Span Backwards task (DSB; Wechsler, 1997) was administered in Study 4, and the Letter-Number Sequencing task (LNS; Wechsler, 1997) was administered in Studies 1, 2 and 3 in order to assess auditory working memory of participants. The DBS is a widely used measure included in the Wechsler Adult Intelligence Scale and has been found to be a reliable and valid assessment of working and short-term memory (Woods et al., 2010). The Letter-Number Sequencing task is similarly commonly used, included in the Wechsler Adult Intelligence Scale, and found to be a reliable and valid measure of working memory (Wechsler, 2008). The DSB requires the participant to attend to an orally presented sequence of numbers and then repeat them back in reverse serial order. The LNS requires the participant to listen to an orally presented sequence of alternating letters and numbers and repeat them back by initially sorting the numbers in ascending order, and then sorting the letters in alphabetical order. The variable of interest was the total span score for both the LNS and the DBS.

The LNS and DSB share significant conceptual and empirical similarities. The Digit Span Backwards and the Letter-Number Sequencing task are considered measures of working memory tapping the central executive component of working memory, including both short-term storage and manipulation of information. Participant scores on these assessments have been found to load onto a single latent factor representing auditory working memory ability in a confirmatory factor analysis of working memory tasks (Egeland, 2015). Further, performance on the Digit Span Backwards has been found to be moderately largely correlated with performance on the Letter-Number Span ($r = 0.46$, $p < 0.001$) and to be a significant predictor of performance on the Letter-Number Span (Crowe et al., 2000). For these reasons, we *Z*-transformed all scores for these measures to create a single auditory working memory variable.

Trail Making Test (TMT)

The Trail Making Test was used to assess mental flexibility and processing speed of participants (Reitan & Wolfson, 1992). The Trail Making Test is one of the most widely used assessments of cognitive processing, and has been found to evidence good reliability (Bornstein et al., 1987; des Rosiers & Kavanaugh, 1987; Dikmen et al., 1999; Matarazzon et al., 1974;) and validity (des Rosiers & Kavanaugh, 1987) in use with clinical participants. The Trail Making Test A (TMTA) and the Trail Making Test B (TMTB) are timed tasks. Both tasks require the participant to draw a line between 24 circles randomly arranged on a page. The TMTA is made up of circles containing consecutive numbers and the TMTB is made up of circles containing consecutive numbers and letters. The TMTA requires participants to draw a line connecting circles in ascending order. The TMTB requires participants to draw a line connecting circles, alternating between ascending numbers and letters in alphabetical order. Both the TMTA and TMTB are scored by the time it takes to complete the task. For these measures, longer completion time indicates a greater level of impairment. The variable of interest was the adjusted duration of test score, with longer completion times reflecting greater impairment. This outcome controls for psychomotor effects by subtracting the timed score of TMTA from the timed score of TMTB (Chaytor et al., 2006).

*Functional Measures*

The Test of Grocery Shopping Skills (TOGSS)

A subset of participants from Studies 1, 2 and 4 completed the Test of Grocery Shopping Skills. The TOGSS is a naturalistic, ecologically valid and reliable performance measure (Faith & Rempfer, 2018; Hamera & Brown, 2000) administered to participants in a real-world grocery shopping setting (Brown et al., 2009; Hamera & Brown, 2000). The TOGSS requires participants to shop for 10 specific food items using a list provided to them. The list includes the instruction to locate and select a specific food item (e.g., yogurt), of a specific size, at the lowest price available in the store. Prior to beginning the task, participants are informed that an examiner will accompany them throughout the store in order to observe and time their performance. Participants are further informed that they are required to shop as quickly and as accurately as possible. The variables of interest were three outcome scores, including accuracy, time and redundant stops. Accuracy scores range from 0 to 30. For each item, participants are able to earn between zero and three points depending on whether they selected the correct item (1 point), at the specified size (1 point), at the lowest price (1 point). Time is a measure of the total minutes and seconds used by participants to complete the task. Redundant stops are a measure of the number of aisles the participant enters to look for an item, minus the minimum number of stops necessary to complete the task. Fewer redundant stops therefore indicate greater shopping efficiency. In line with recommendations of Brown and colleagues (2009), the task was standardized by using a midsized grocery store outside of the participants' immediate community. All participants completed the task during midday and on weekdays.

Living Status and Employment Status

All participants self-reported their residential setting. Participants indicated one of the following options to describe their level of residential independence: independent living; lives with relatives (largely independent); supervised care housing (with live in staff); lives with relatives (heavily dependent for personal care); long-term care facility; emergency shelter; other; don't know. For the purposes of this proposed study, participants were classified as living in an independent setting if they indicated that they lived independently or lived with relatives but were largely independent. Participants were classified as living in a non-independent setting if they indicated living in a long-term care facility, emergency shelter, or with relatives with the designation of being heavily dependent for personal care. Participants also self-reported their employment status by indicating whether they were employed or unemployed.

*Clinical symptoms*

Positive and negative symptoms were collected for participants using the Brief Psychiatric Rating Scale-Expanded (BPRS-E) version (Lukoff et al., 1986) or the Scale for Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984). Study 1 utilized the SANS and SAPS and Studies 2, 3 and 4 utilized the BPRS-E. Scores on the SANS and SAPS were summed to create overall negative and positive symptom scores. The SANS is a 25-item scale that measures negative symptoms using a 6-point scale. Scores on the SANS were summed to produce totals that represent five negative symptom subdomains, including alogia, avolition/apathy, affective blunting, anhedonia/asociality, and attention. The SAPS is a 34-item scale that measures positive symptoms using a 6-point scale. Scores on the SAPS were summed to produce totals that represent four positive symptom subdomains, being delusions, hallucinations, bizarre behavior, and positive formal thought disorder. The BPRS-E is a 24-item scale that measures symptom domains applicable to multiple diagnostic groups.

A subset of scores on the BPRS-E were summated to produce totals for negative and positive symptoms based on a previously established factor structure (Ventura, et al., 2000) and a review of studies comparing the intercorrelation of items on symptom scales, including the BPRS, SANS and SAPS (Lyne et al., 2012). Lyne and colleagues (2012) reviewed the existing literature and concluded that a BPRS subscale composed of blunted affect, emotional withdrawal and motor retardation items, and the SANS tend to correlate between $r$=(.70) and $r$=(.95) in the literature. However, they also noted that the SANS contains additional information compared to the BPRS-18 negative symptom subscale. For this reason, we referenced an established factor structure by Ventura and colleagues (2000) which used the expanded BPRS-24 item version of the scale rather than the 18-item version of the scale. They found a loading of self-neglect on the negative symptom factor in addition to the items on the BPRS-18 negative symptom subscale. Negative symptoms were therefore indexed by four items on the BPRS-E, including blunted affect, emotional withdrawal, motor retardation, and self-neglect in this study. The review by Lyne and colleagues (2012) further noted evidence of a high correlation between the BPRS-18 Positive Symptom (BPRS-PS) subscale composed of hallucinatory behavior, unusual thought content, suspiciousness, and conceptual disorganization items and the SAPS in the literature. We referenced Ventura and colleagues (2000), which found a loading of bizarre behavior on the positive symptom factor in addition to the items on the BPRS-PS, using the BPRS-24. Positive symptoms were therefore indexed by five items on the BPRS-E, including bizarre behavior, conceptual disorganization, hallucinationatory behavior, suspiciousness, and unusual thought content.

## Data Analysis

We utilized an across-domain derivation of intra-individual variability composed of five neurocognitive domains. This conceptualization goes beyond the strict definition of executive functioning to encompass a more inclusive construct of fluid cognition. Compared to a strict definition of executive functioning, fluid cognition includes other cognitive functions like working memory and processing speed, which are proposed to be cognitive processes that function co-operatively with executive functions in order to carry out goal-directed behavior (Alvarez & Emory, 2006). All neuropsychological tasks were completed by participants during a single testing session. In order to calculate a measure of dispersion, or IIV across neurocognitive domains, we used scores from the WCST, the TMT, LNS/DBS, d2 and RVLT/CVLT. Raw neuropsychological scores were converted to *Z*-scores. Thereafter, all *Z*-scores were averaged in order to calculate each participant's individual, overall test battery mean (OTBM) as an index of overall cognitive ability. To calculate intra-individual variability, five *Z*-transformed subtest scores were entered into Holtzer's equation (Figure 1) (Holtzer et al., 2008), consistent with methods used in prior research estimating intra-individual variability among individuals with schizophrenia (e.g., Ahn et al., 2019; Cole et al., 2011). Larger values represented greater intra-individual neurocognitive performance variability and smaller values indicated lesser intra-individual neurocognitive performance variability.

In order to compare intra-individual variability between participants with a psychotic disorder versus participants with an affective disorder diagnosis, participants were divided based on diagnosis, placing individuals diagnosed with schizophrenia or schizoaffective disorder into a psychotic disorders group and participants with bipolar disorder and major depressive disorder into and affective disorders group. Thereafter, a multivariate analysis of variance (MANOVA) was used to compare age, OTBM, IIV, positive symptoms and negative symptoms variables between these two groups. An analysis of covariance (ANCOVA) was used to adjust IIV scores and observe possible differences between groups, controlling for positive and negative symptom scores and their interaction.

In order to accomplish the second aim to examine the relationship between IIV and mean cognitive performance, Pearson's correlations were used to examine the relationship between IIV and the overall test battery mean (OTBM) variables. A scatterplot was created to visually represent the relationship between the overall test battery mean and IIV.

In order to accomplish the third aim to examine the functional significance of IIV among participants with serious mental illness, analysis of variance (ANOVA) tests were used to compare the IIV variable between employed and unemployed participants, and between participants who live independently and participants who did not live independently. Pearson's correlations were used to examine the relationship between the IIV variable and continuous outcome variables on the TOGSS (i.e., accuracy, time, redundant stops). Hierarchical logistic regressions were used to examine whether the IIV variable has incremental predictive ability above and beyond the OTBM to predict employment status and living status. Three hierarchical linear regressions were used to understand whether the IIV variable has incremental predictive ability above the OTBM to predict accuracy, time and redundant stops indexing dimensions of grocery shopping skill.

An apriori power analysis was conducted using G*Power (Erdfelder et al., 1996) to determine the minimum sample sizes required to test study hypotheses. First, minimum sample sizes were determined for two- and three-variable linear regression equations. The recommended effect sizes used for these assessments were: small ($f^2 = .02$), medium ($f^2 = .15$) and large ($f^2 = .35$) (Cohen, 1977). Results indicated that the required sample size to achieve 80% power for detecting a medium effect, at a significance criterion of $\alpha = .05$ was $N = 77$ for a three-variable regression equation (Aim 2.2). Results further indicated that the required sample size to achieve 80% power for detecting a medium effect, at a significance criterion of $\alpha = .05$ was $N = 68$ for a two-variable regression equation (Aim 3.3).

Next, the sample size required for a multivariate analysis of variance was determined using two groups and six response variables. Results indicated that the required sample size to achieve 80% power for detecting a medium effect, at a significance criterion of $\alpha = .05$ was $N = 98$. Then, sample sizes required for ANOVA and ANCOVA equations were determined. The recommended effect sizes used for these assessments were: small ($f = .10$), medium ($f = .25$) and large ($f = .40$) (Cohen, 1988). Results indicated that for an analysis of covariance using two groups, one covariate, and one degree of freedom, the required sample size to achieve 80% power for detecting a medium effect, at a significance criterion of $\alpha = .05$ was $N = 128$. Results further indicated that for three separate analyses of variance using four groups (educational groups), two groups (employed versus unemployed), and two groups (independent versus non-independent), the required sample sizes to achieve 80% power for detecting a medium effect, at a significance criterion of $\alpha = .016$ was $N = 232$, $N = 172$, and $N = 172$ respectively.

We used the rule of a minimum of 10 events per predictive variable (EPV) to ensure an adequate sample size for the hierarchical logistic regression equations. The number of EPV is the number of events divided by the number of predictor variables in the prediction model (Peduzzi et al., 1996). The smaller of the two groups representing one of the binary outcomes is typically used as the number of events, given the smaller of the two groups will have a smaller EPV using the suggested formula. For the logistic regression examining predictors of living status outcomes (*n* = 177 independent living status; *n* = 25 non-independent living status) predicted by two variables, including the overall test battery mean and the IIV variable, the EPV was therefore (25/2) = 12.5 for the sample. For the logistic regression examining predictors of employment status outcomes (*n* = 31 employed; *n* = 184 unemployed) predicted by two variables, including the overall test battery mean and the IIV variable, the EPV was (31/2) = 15.5 for the sample.

# CHAPTER 4

# RESULTS

The Structured Clinical Interview for DSM-IV (SCID-IV) was used to confirm participant diagnoses (First et al., 2002). SCID-IV interviewers were completed by clinical psychology doctoral students who were trained and supervised by a licensed clinical psychologist. The combined sample consisted of individuals diagnosed with schizophrenia ($n$ = 89; 41.0%), schizoaffective disorder ($n$ = 54; 24.9%), bipolar disorder ($n$ = 33; 15.2%) and major depressive disorder ($n$ = 26; 12.0%). The remainder of the sample were individuals with comorbid diagnoses of SMI disorders ($n$ = 15; 6.9%). Descriptive statistics of participant characteristics by diagnostic group and in the combined sample are demonstrated in Table 1.

A Mann-Whitney *U* test showed no significant difference between the psychotic disorders group and the affective disorders group on the basis of education ($U$ = 3877, $p$ = 0.39); however, there were significant differences between groups on the basis of marital status ($U$ = 3877, $p$ = 0.006) and race/ethnicity ($U$ = 3103.5, $p$ = 0.001). A chi-square test of independence demonstrated the percentage of participants who were male differed between the psychotic disorders and affective disorders groups $\chi^2$ (1, $N$ = 201) = 9.69, p = .002. Chi-square tests of independence further demonstrated the percentage of participants who lived independently did not differ between psychotic disorders and affective disorders groups $\chi^2$ (1, $N$ = 188) = 1.35, $p$ = .25), and the percentage of participants who were employed did not differ between psychotic disorders and affective disorders groups $\chi^2$ (1, $N$ = 201) = 0.62, $p$ = .43).

A MANOVA was used to examine differences between psychotic disorders and affective disorders groups on the following continuous variables: age, OTBM, IIV, positive symptoms, and negative symptoms. Results demonstrated a significant multivariate effect (Pillai's trace =.09, $F(5, 192) = 3.98$, $p = .002$, partial $\eta 2 = .09$) and a significant main effect for positive symptoms, $F(1, 196) = 17.51$, $p < .001$, partial $\eta 2 = .08$) indicating greater positive symptoms among participants in the psychotic disorders group. There were no significant main effects for age, OTBM, IIV (Aim 2.1) and negative symptoms. Individuals diagnosed with a psychotic disorder did not evidence significantly greater intra-individual variability compared to individuals diagnosed with affective disorders. An ANCOVA was used to examine differences in IIV between psychotic disorders and affective disorders groups while controlling for positive and negative symptoms and their interaction. Results demonstrated no significant differences in IIV between psychotic disorders and affective disorders groups when controlling for positive and negative symptoms and their interaction (Aim 2.2) ($F(1, 196) = 0.17$, $p = .68$).

ANOVA tests examined differences in intra-individual variability between education groups, living status groups, and employment status groups. Using a Bonferroni adjusted alpha of 0.016 to control for the probability of committing a type I error, results demonstrated no significant differences in IIV between education groups (Aim 2.3) ($F$[3, 211]) = 1.76, $p = .16$), between participants living independently and participants living non-independently ($F$[1, 200] = 2.28, $p = .13$), and between employed participants and unemployed participants (Aim 3.2) ($F$[1, 213] =.52, $p = .47$). There were no differences in intra-individual variability between participants with differing levels of education, nor between participants who were employed versus unemployed.

Pearson's correlations coefficients were used to examine the relationship of IIV to demographic, cognitive and clinical variables in the combined sample, as well as in psychotic disorders and affective disorders groups, respectively. Pearson's correlations coefficients were also used to examine the relationship of IIV to TOGSS accuracy, speed and efficiency variables. Results demonstrated no significant relationships between IIV and age (Aim 1.1), positive symptoms, negative symptoms (Aim 1.2) and the OTBM (Aim 1.3), in the combined sample, as well as in the psychotic disorders and affective disorders groups respectively (Table 2). Results demonstrated no significant associations between IIV and TOGSS variables (Aim 3.1). A visual representation of the relationship between IIV and the OTBM in the combined sample is depicted in Figure 2. Intra-individual variability was not significantly related to age, clinical symptoms, overall cognitive ability, nor accuracy, speed, or efficiency of performance on a test of grocery shopping skills.

A hierarchical logistic regression ($N$ = 202) was conducted to evaluate the prediction of living status above and beyond the OTBM. For the first block analysis, the predictor variable OTBM was analyzed. The results of the first block hierarchical logistic regression analysis revealed the model was not significant, $\chi^2(1) = 2.81$, $p = .09$. For the second block analysis, the IIV predictor was added to the analysis. The results of the second block hierarchical logistic regression analysis revealed the model including both OTBM and IIV were not significant predictors of living status, $\chi^2(2) = 4.95$, $p = .08$ (Aim 3.3). Individual variability did not have incremental validity above overall cognitive ability to predict living status among individuals with serious mental illness.

A hierarchical logistic regression ($N$ = 215) was conducted to evaluate the prediction of employment status above and beyond the OTBM. For the first block analysis, the predictor variable OTBM was analyzed. The results of the first block hierarchical logistic regression analysis revealed the model to not be significant, $\chi^2(1) = .58$, $p = .45$. For the second block analysis, the IIV predictor was added to the analysis. The results of the second block hierarchical logistic regression analysis revealed the model including both OTBM and IIV to not be significant predictors of employment status, $\chi^2(2) = 1.08$, $p = .58$ (Aim 3.3). Individual variability did not have incremental validity above overall cognitive ability to predict employment status among individuals with serious mental illness.

A hierarchical linear regression ($N = 153$) was conducted to evaluate the incremental validity of IIV to predict the TOGSS accuracy score above and beyond the OTBM. For the first block analysis, the predictor variable OTBM was analyzed. The results of the first block hierarchical linear regression analysis indicated that the model was a significant predictor of TOGSS accuracy scores. It was found that OTBM explained a significant amount of variance in TOGSS accuracy scores ($F[1, 151] = 19.40$, $p < .001$, $R^2 = .11$). The $R^2$ value of this regression model suggested that the OTBM accounted for 11.4% of the variation in TOGSS accuracy scores, which means that 89.6% of the variation in accuracy scores could not be explained by OTBM alone. For the second block analysis, the IIV predictor was added to the analysis. The results of the second block hierarchical linear regression analysis revealed the model including both OTBM and IIV to be statistically significant. It was found the OTBM and IIV variables together explained a significant amount of variance in TOGSS accuracy scores ($F[2, 150] = 9.79$, $p < .001$, $R^2 = .12$). While OTBM contributed significantly to the model (B = 2.70, $p < .001$), IIV did not (B = -.40, $p = .61$) (Aim 3.3). Individual variability did not have incremental validity above overall cognitive ability to predict accuracy on a test of grocery shopping skill among individuals with serious mental illness. Tables 3–6 depict descriptive statistics, a correlation matrix, model coefficients, and $R^2\Delta$ values for the analysis.

A hierarchical linear regression ($N$ = 151) was conducted to evaluate the incremental validity of IIV to predict the TOGSS time score above and beyond the OTBM. For the first block analysis, the predictor variable OTBM was analyzed. The results of the first block hierarchical linear regression analysis revealed a model to be significant ($F$[1, 149]=4.46, $p$ = .04, $R^2$ = .03). It was found that OTBM explained a significant amount of variance in the TOGSS time scores (B = -3.47, $p$ = .04). The $R^2$ value associated with this regression model suggested that the OTBM accounted for 2.9% of the variation in TOGSS accuracy scores, which means that 97.1% of the variation in time scores could not be explained by OTBM alone. For the second block analysis, the IIV predictor was added to the analysis. The results of the second block hierarchical linear regression analysis indicated that the model including both OTBM and IIV to be not significant ($p$ = .11). It was found the OTBM and IIV variables together did not explain a significant amount of variance in TOGSS time scores ($F$[2, 148] = 2.23, $p$ = .11, $R^2$ = .03 (Aim 3.3). Individual variability did not have incremental validity above overall cognitive ability to predict speed on a test of grocery shopping skills among individuals with serious mental illness. Tables 7–10 depict descriptive statistics, a correlation matrix, model coefficients, and $R^2\Delta$ values for the analysis.

A hierarchical linear regression ($N$ = 152) was conducted to evaluate the incremental validity of IIV to predict the TOGSS redundant stops score above and beyond the OTBM. For the first block analysis, the predictor variable OTBM was analyzed. The results of the first block hierarchical linear regression analysis revealed a model to be significant ($F$[1, 150] = 10.44, $p$ = .002, $R^2$ = .07). It was found that OTBM explained a significant amount of variance in the TOGSS redundant stops scores (B = 3.54, $p$ = .002). The $R^2$ value associated with this regression model suggested that the OTBM accounted for 6.5% of the variation in TOGSS redundant stops scores. For the second block analysis, the IIV predictor was added to the analysis. The results of the second block hierarchical linear regression analysis revealed the model to be statistically significant. It was found the OTBM and IIV variables together explained a significant amount of variance in TOGSS redundant stops scores ($F$[2, 149] = 3.58, $p$ =.01, $R^2$ = .002). While OTBM contributed significantly to the model (B = -1.81 $p$ = .002), IIV did not (B = -.05, $p$ = .94) (Aim 3.3). Individual variability did not have incremental validity above overall cognitive ability to predict efficiency on a test of grocery shopping skills among individuals with serious mental illness. Tables 11–14 depict descriptive statistics, a correlation matrix, model coefficients, and $R^2\Delta$ values for the analysis.

# CHAPTER 5

# DISCUSSION

Our study had several aims. One aim was to characterize across-domain intra-individual variability among participants with serious mental illness by examining its relationship to demographic, clinical and cognitive variables. We found that age was not linearly related to intra-individual performance variability among our sample of participants with forms of serious mental illness. Further, clinical symptoms and an index of overall cognition were not significantly related to intra-individual variability among participants. We additionally aimed to examine levels of IIV across diagnostic and educational groups. The psychotic disorders group and the affective disorders group evidenced similar levels of intra-individual variability, irrespective of positive and negative symptoms. Further, intra-individual variability did not vary across education groups. Lastly, we aimed to examine the functional significance of IIV among participants with serious mental illness, including its incremental validity to predict living and employment status, and performance on a naturalistic test of grocery shopping skill above and beyond an index of overall cognitive ability. Intra-individual variability was not related to these functional outcomes nor incrementally predictive of them above and beyond overall cognitive ability. Results showing the overall test battery mean was a significant predictor of outcomes on the test of grocery shopping skill aligns with research finding performance on the TOGSS is related to performance on several cognitive tasks, including tasks measuring verbal memory, sustained attention, and executive functioning (Rempfer et al., 2003).

Our analyses add to a small body of evidence concerning intra-individual performance variability among individuals with forms of serious mental illness. Although intra-individual performance variability has been found to increase with age generally (Hultsch et al., 2002; MacDonald et al., 2006; Williams et al., 2005), and among individuals with schizophrenia specifically (Cole et al., 2011) we failed to find evidence of a relationship between age and intra-individual variability among our sample of participants diagnosed with serious mental illness. This finding also stands contrary to expectations based on the neural noise hypothesis (Li et al., 2001; Li et al., 2002; MacDonald et al., 2006; MacDonald et al., 2012; Salthouse & Lichty, 1985) positing that with greater age comes increased neural noise, and interference with efficient transmission of information in the central nervous system, causing increased intra-individual performance variability. It may be that our findings suggest evidence against the neural noise hypothesis. Alternatively, it may be that there is a non-linear increase in intra-individual variability as a function of age. For example, while De Felice and colleagues (2018) did not find significant differences in intra-individual variability between age cohorts, they found a non-linear trend of increased intra-individual variability among healthy participants 75 years and older compared to younger cohorts. It may be that our analysis did not account for the possibility of a non-linear increase in dispersion with age. Moreover, it is possible that our sample did not adequately represent older individuals with serious mental illness, given relatively fewer participants above the age of 55 in our sample compared to younger and middle-aged participants.

Additionally, we failed to find a relationship between positive and negative symptom variables, and intra-individual variability, contrary to our hypothesis. There exists mixed evidence as to the potential contributions of these symptoms to intra-individual variability among individuals with serious mental illness. Our finding aligns with research showing that intra-individual variability is independent of psychotic symptoms (Schwartz et al.,1989;

Pellizer & Stephane, 2007) and negative symptoms (Pellizer & Stephane, 2007) and in contrast with research finding that intra-individual variability is associated with these clinical features (Schwartz et al., 1991; Vinogradov et al., 1998). There may be multiple reasons for these mixed findings. One reason may pertain to the fact that rating of symptom presence and severity is a process which involves subjectivity. Studies that utilize multiple raters and examine inter-rater agreement regarding clinical symptoms can assist with overcoming the potential for imprecision during the rating process. Further, evidence suggests that individuals with serious mental illness are a heterogeneous group of individuals. Studies detailing clinical presentations beyond broad symptom categories are warranted to understand whether specific symptoms, such as disorganization, may affect intra-individual performance variability.

Further contrary to our expectations, we failed to find a negative association between intra-individual variability and overall cognitive performance among participants with serious mental illness. Some research suggests that intra-individual variability is related to intelligence or overall cognitive performance (Hultsch & MacDonald, 2004; Schinka et al., 1994) while others find only modest relationships between these constructs (Ram et al., 2005). Others suggest that even marked intra-individual variability in neuropsychological test performance is common among healthy adults and should not necessarily be interpreted as an indication of decrement in central nervous system integrity (Binder et al., 2009; Gontkovsky et al., 2021). Theoretical interpretation of the relationship between overall cognitive ability and intra-individual variability requires further clarification. However, a lack of a negative association between overall cognitive performance and intra-individual variability in our sample was contrary to the results of Cole and colleagues (2011), who found a small, negative association between general cognitive ability and intra-individual variability among individuals with schizophrenia. It may be that our overall test battery mean was insufficient to capture overall cognitive ability comparable to their index of general cognition. It is unclear how Cole and colleagues indexed general cognition; future research may be served by greater explanation and consistency pertaining to how constructs like overall cognitive ability and intra-individual variability are measured across studies. Alternatively, there may be no significant, negative relationship between overall cognitive ability and intra-individual variability among individuals with serious mental illness.

The psychotic disorders group and the affective disorders group evidenced similar levels of intra-individual variability, irrespective of positive and negative symptoms, contrary to our expectations. Our finding of similar levels of intra-individual variability in these groups provides evidence against the suggestion that increased intra-individual performance variability may be specific to individuals with psychotic disorders (Schwartz et al., 1989). Further, it may provide indirect evidence supporting the idea that intra-individual variability may be a core feature of forms of serious mental illness like bipolar disorder or major depressive disorder (Gallagher et al., 2015). Our finding that intra-individual performance variability was not significantly different between groups with different levels of educational attainment supports preliminary evidence that education is not significantly related to intra-individual performance variability among individuals with a schizophrenia diagnosis (Cole et al., 2011).

Our study further adds to a small body of literature focused on the functional significance of intra-individual variability among individuals with schizophrenia. While preliminary studies have suggested associations between intra-individual performance variability and work performance among individuals with schizophrenia (Rentrop, 2010; Wexler & Nicholas, 2004), we failed to find differences in intra-individual performance variability among employed versus unemployed individuals with serious mental illness. Further, we found no differences in intra-individual among individuals living independently versus non-independently. Moreover, intra-individual performance variability was not incrementally predictive of employment status, living status, nor accuracy, speed or efficiency on a naturalistic test of grocery shopping skills. It may be that this parameter may be unrelated to functional and real-world outcomes among individuals with serious mental illness broadly. Alternatively, crude measures of functioning represented by binary outcomes (e.g. employed versus unemployed) in our study may lack sensitivity or specificity to adequately capture more nuanced differences in functioning among participants. It may also be that across-trial intra-individual performance variability is related to functioning while across-domain intra-individual performance variability is not. Additional research is necessary to understand under what conditions intra-individual variability may have functional significance among individuals with serious mental illness diagnoses.

In addition to the potential limitations previously addressed, our study had several other limitations which warrant consideration. We combined distinct datasets collected at different timepoints in order to ensure sufficient variability in participant characteristics relevant to our aims and analyses; separate recruitment and research procedures may have systematically affected participants recruited to individual studies and the quality of variables of interest. For example, our methods of combining clinical symptoms and neuropsychological performance scores across datasets (e.g. standardizing and collapsing CVLT and RAVLT raw scores to create a single auditory verbal memory variable) may have led to imprecise measurement of participant abilities, despite similar methods and theoretical consistency across these separable tasks. Another limitation of our study was our approach to indexing overall cognitive ability and intra-individual performance variability. While there is no standard number of neuropsychological indices recommended to compute the across-domain intra-individual variability score, and some studies have indexed dispersion using as few as five neuropsychological domains (Sheppard et al., 2018), others have used greater than ten neuropsychological domains (Morgan et al., 2012; Thaler et al., 2015). Our intra-individual performance variability and overall cognitive ability indices created using performance across five neuropsychological domains may have been insufficient to comprehensively represent these constructs, and therefore insensitive to potential relationships with other variables of interest.

The study also had some strengths. First, our sample was large and relatively representative of adult individuals with serious mental illness living in a metropolitan community setting. Further, while other studies of intra-individual variability among individuals with serious mental illness have consisted of majority White participants, or neglected to provide a full account of participant characteristics, our study includes participants with diverse racial and ethnic backgrounds and offers a richer depiction of life contexts (e.g. living status, employment status, level of education) potentially relevant to cognition and functioning. Neglect for diversity in sampling or to provide more detailed information about participants may result from the perception that intra-individual variability reflects central nervous system integrity, independent of contextual factors. However, interactions between the individual and their environmental context play a crucial role in determining nervous system health (Rogers et al., 2019).

It bears noting that the results of this study may only be generalizable to a subgroup of community-dwelling adults diagnosed with forms of serious mental illness living in a metropolitan area of the United States. Although this sample of participants was large and evidenced life circumstances consistent with the overall population in the United States (e.g. a high rate of unemployment) (National Alliance on Mental Illness, 2014), participants were not randomly selected for the study. Our results may therefore be applicable to adults diagnosed with forms of serious mental illness with the ability and support necessary to partake in a community-based research study. Accordingly, our results may not be as applicable to individuals diagnosed with serious mental illness who experience greater functional or cognitive challenges, and less support or community involvement compared to our sample. Future research may seek to examine intra-individual performance variability among individuals with specific characteristics (e.g. older individuals above the age of 60) or life contexts (e.g. individuals living non-independently) to better understand whether this construct has relevance for a more homogenous subgroup of individuals diagnosed with serious mental illness.

Future research may also seek to explore how variables like fatigue, practice effects, or effort may affect intra-individual variability among individuals with forms of serious mental illness in the absence of clear relationships between clinical symptoms, overall cognitive ability, and intra-individual performance variability. Hill and colleagues (2013) proposed that one possible cause of increased intra-individual performance variability is inconsistent effort during testing by examinees with traumatic brain injury. Given that insufficient or inconsistent mental effort is considered a core feature of schizophrenia, future inquiries probing the relationship between intra-individual performance variability and effort allocation may reveal yet unexplored contributions to this observed phenomena among individuals with forms of serious mental illness. Another area of exploration with potential significance to the study of intra-individual variability among individuals with serious mental illness lies at the intersection of cognition and the environment. Previous research has suggested that an engaged lifestyle, including social, physical and/or cognitive activities, may decrease cognitive dispersion and promote greater well-being among older individuals experiencing cognitive decline (Halliday et al., 2018). Given that some individuals with serious mental illness are at risk for disengaged lifestyle due to circumstances like physical health challenges, poverty and lack of interpersonal support, a subset of individuals may be uniquely or especially vulnerable to increased intra-individual performance variability. Greater exploration of the role of lifestyle on cognitive dispersion, and the potential for lifestyle interventions to reduce IIV and increase functioning (e.g., Bielak et al., 2019; Brydges et al., 2021; Garrett et al., 2012; Smart et al., 2016) among individuals with serious mental illness may provide a more robust empirical basis for the need for environmental enrichment to support cognition and functioning in this population.

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TABLES

Table 1 *Descriptive Statistics of Participant Characteristics*

| Participant Characteristic | Psychotic Disorders Diagnosis (*n*=143) | Affective Disorders Diagnosis (*n*=59) | Combined Sample (*n*=217) |
|---|---|---|---|
| N (% male) | 143 (55.2) | 59 (30.5) | 217 (47.4) |
| Age | | | |
| Mean (SD) | 42.5 (9.5) | 44.8 (9.8) | 42.8 (9.8) |
| Minimum | 20 | 18 | 18 |
| Maximum | 63 | 61 | 63 |
| Diagnosis, n (%) | | | |
| Schizophrenia | 89 (62.2) | 0 (0) | 89 (41.0) |
| Schizoaffective disorder | 54 (37.8) | 0 (0) | 54 (24.9) |
| Bipolar Disorder | 0 (0) | 33 (55.9) | 33 (15.2) |
| Major Depressive Disorder | 0 (0) | 26 (44.1) | 26 (12.0) |
| Comorbid | 0 (0) | 0 (0) | 15 (6.9) |
| Race/Ethnicity, n (%) | | | |
| American Indian or Alaskan Native | 3 (2.1) | 3 (5.1) | 7 (3.2) |
| Asian or Pacific Islander | 1 (0.7) | 0 (0.0) | 1 (0.5) |
| African American/Black | 75 (52.4) | 11 (18.6) | 88 (40.6) |
| Caucasian/White | 50 (35.0) | 41 (69.5) | 100 (46.1) |
| Hispanic | 4 (2.8) | 1 (1.7) | 6 (2.8) |
| Multi-racial | 6 (4.2) | 1 (1.7) | 8 (3.7) |
| Other | 3 (2.1) | 2 (3.4) | 5 (2.3) |
| Marital Status, n (%) | | | |
| Never Married | 84 (58.7) | 24 (40.7) | 117 (53.9) |
| Divorced/Annulled | 35 (24.5) | 17 (28.8) | 56 (25.8) |
| Separated | 7 (4.9) | 5 (8.5) | 13 (6.0) |
| Married | 10 (7.0) | 9 (15.3) | 19 (8.8) |
| Widowed | 5 (3.5) | 2 (3.4) | 7 (3.2) |
| Common Law/Living Together | 1 (0.7) | 2 (3.4) | 3 (1.4) |
| Living Status, n (%) | | | |
| Independent | 116 (86.6) | 50 (92.6) | 177 (81.6) |
| Non-independent | 18 (13.4) | 4 (7.4) | 25 (11.5) |
| Employment Status, n (%) | | | |

| | | | |
|---|---|---|---|
| Employed | 23 (16.1) | 7 (11.9) | 31 (14.3) |
| Unemployed | 119 (83.8) | 52 (88.1) | 184 (84.4) |
| Education, n (%) | | | |
| Up to some high school | 36 (25.4) | 10 (16.9) | 46 (21.2) |
| High school graduate | 48 (33.8) | 18 (30.5) | 70 (32.3) |
| Some college/Post high school training | 45 (31.7) | 28 (47.5) | 82 (37.8) |
| College graduate/ Post graduate degree | 13 (9.2) | 3 (5.1) | 17 (7.8) |
| Positive Symptoms | | | |
| BPRS Positive Symptoms | 9.06 (4.7) | 5.55 (2.5) | 7.4 (4.2) |
| SAPS Positive Symptoms | 32.5 (16.9) | -- | 32.5 (16.9) |
| Negative Symptoms | | | |
| BPRS Negative Symptoms | 6.95 (2.7) | 7.08 (2.8) | 7.0 (2.7) |
| SANS Negative Symptoms | 30.7 (16.4) | -- | 30.7 (16.4) |

Table 2

*Pearson's correlations relating IIV to demographic, cognitive and clinical variables in the whole sample, and in separate diagnostic groups*

| | Psychotic Disorder Diagnosis | Affective Disorders Diagnosis | Combined Sample |
|---|---|---|---|
| Age | .02 | .15 | .08 |
| Overall Test Battery Mean (OTBM) | -.03 | .17 | .05 |
| Positive Symptoms | -.12 | -.10 | -.127 |
| Negative Symptoms | -.02 | -.001 | .003 |
| TOGSS Accuracy | .02 | -.05 | -.006 |
| TOGSS Time | .008 | -.17 | -.03 |
| TOGSS Redundant Stops | .06 | .05 | .06 |

Table 3

*Descriptive statistics for the hierarchical linear regression predicting the TOGSS accuracy score*

| Variable | *N* | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|---|
| Y[a] | 153 | 24.44 | 3.67 | 12 | 30 |
| X1[b] | 153 | .01 | .46 | -1.24 | 1.81 |
| X2[c] | 153 | .87 | .36 | .26 | 3.11 |

[a]Y=Test of Grocery Shopping Skills accuracy score; [b]X1=Overall Test Battery Mean (OTBM) score; [c]X2=Intra-individual Variability (IIV) score

Table 4

*Correlation matrix for the hierarchical linear regression predicting the TOGSS accuracy score*

| | Y | X1 | X2 |
|---|---|---|---|
| Y[a] | 1 | – | – |
| X1[b] | .34 | 1 | – |
| X2[c] | -.01 | .10 | 1 |

[a]Y=Test of Grocery Shopping Skills accuracy score; [b]X1=Overall Test Battery Mean (OTBM) score; [c]X2=Intra-individual Variability (IIV) score

Table 5

*Model coefficients for the hierarchical linear regression predicting the TOGSS accuracy score*

| Coefficient | Estimate | SE | p-value |
|---|---|---|---|
| Intercept | 24.76 | .74 | <.001 |
| *b1* | 2.70 | .61 | <.001 |
| *b2* | -.40 | .78 | .61 |

Note: $F(2, 150) = 9.79$, $p < .001$, $R^2 = .12$

Table 6

*Summary of $R^2\Delta$ for the hierarchical linear regression predicting the TOGSS accuracy score*

| Set | Predictors | $R^2\Delta$ | *p*-value |
|---|---|---|---|
| 1 | X1[a] | .11 | <.001 |
| 2 | X2[b] | .002 | .61 |

[a] X1=Overall Test Battery Mean (OTBM) score; [b] X2=Intra-individual Variability (IIV) score

Table 7

*Descriptive statistics for the hierarchical linear regression predicting the TOGSS time score*

| Variable | *N* | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|---|
| Y[a] | 151 | 23.43 | 9.48 | 1.00 | 57.49 |
| X1[b] | 151 | .01 | .47 | -1.24 | 1.81 |
| X2[c] | 151 | .87 | .36 | .26 | 3.11 |

[a]Y=Test of Grocery Shopping Skills time score; [b]X1=Overall Test Battery Mean (OTBM) score; [c]X2=Intra-Individual Variability (IIV) score

Table 8

*Correlation matrix for the hierarchical linear regression predicting the TOGSS time score*

| | Y | X1 | X2 |
|---|---|---|---|
| Y[a] | 1 | – | – |
| X1[b] | -.17 | 1 | – |
| X2[c] | -.03 | .10 | 1 |

[a]Y=Test of Grocery Shopping Skills time score; [b]X1=Overall Test Battery Mean (OTBM) score; [c]X2=Intra-individual Variability (IIV) score

Table 9

*Model coefficients for the hierarchical linear regression predicting the TOGSS time score*

| Coefficient | Estimate | SE | *p*-value |
|---|---|---|---|
| Intercept | 23.75 | 2.01 | <.001 |
| *b1* | -3.47 | 1.66 | .04 |
| *b2* | -.33 | 2.12 | .88 |

Note: $F(2, 148)=2.23$, $p=.11$, $R^2= .03$

Table 10

*Summary of $R^2\Delta$ for the hierarchical linear regression predicting the TOGSS time score*

| Set | Predictors | $R^2\Delta$ | *p*-value |
|---|---|---|---|
| 1 | X1[a] | .03 | .04 |
| 2 | X2[b] | .00 | .88 |

[a] X1=Overall Test Battery Mean (OTBM) score; [b] X2=Intra-Individual Variability (IIV) score

Table 11

*Descriptive statistics for the hierarchical linear regression predicting the TOGSS redundant stops score*

| Variable | *N* | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|---|
| Y[a] | 152 | 3.51 | 3.31 | -2 | 15 |
| X1[b] | 152 | .01 | .47 | -1.24 | 1.81 |
| X2[c] | 152 | .87 | .36 | .26 | 3.11 |

[a]Y=Test of Grocery Shopping Skills redundant stops score; [b]X1=Overall Test Battery Mean (OTBM) score; [c]X2=Intra-Individual Variability (IIV) score

Table 12

*Correlation matrix for the hierarchical linear regression predicting the TOGSS redundant stops score*

| | Y | X1 | X2 |
|---|---|---|---|
| Y[a] | 1 | – | – |
| X1[b] | -.26 | 1 | – |
| X2[c] | -.03 | .10 | 1 |

[a]Y=Test of Grocery Shopping Skills redundant stops score; [b]X1=Overall Test Battery Mean (OTBM) score; [c]X2=Intra-Individual Variability (IIV) score

Table 13

*Model coefficients for the hierarchical linear regression predicting the TOGSS redundant stops score*

| Coefficient | Estimate | SE | *p*-value |
|---|---|---|---|
| Intercept | 3.58 | .69 | <.001 |
| *b1* | -1.81 | .57 | .002 |
| *b2* | -.05 | .73 | .94 |

Note: $F(2, 149)=5.19$, p=.007, $R^2= .002$

Table 14

*Summary of $R^2\Delta$ for the hierarchical linear regression predicting the TOGSS redundant stops score*

| Set | Predictors | $R^2\Delta$ | *p*-value |
|---|---|---|---|
| 1 | X1[a] | .07 | .002 |
| 2 | X2[b] | .00 | .94 |

[a] X1=Overall Test Battery Mean (OTBM) score; [b] X2=Intra-Individual Variability (IIV) score

ILLUSTRATIONS

Figure 1

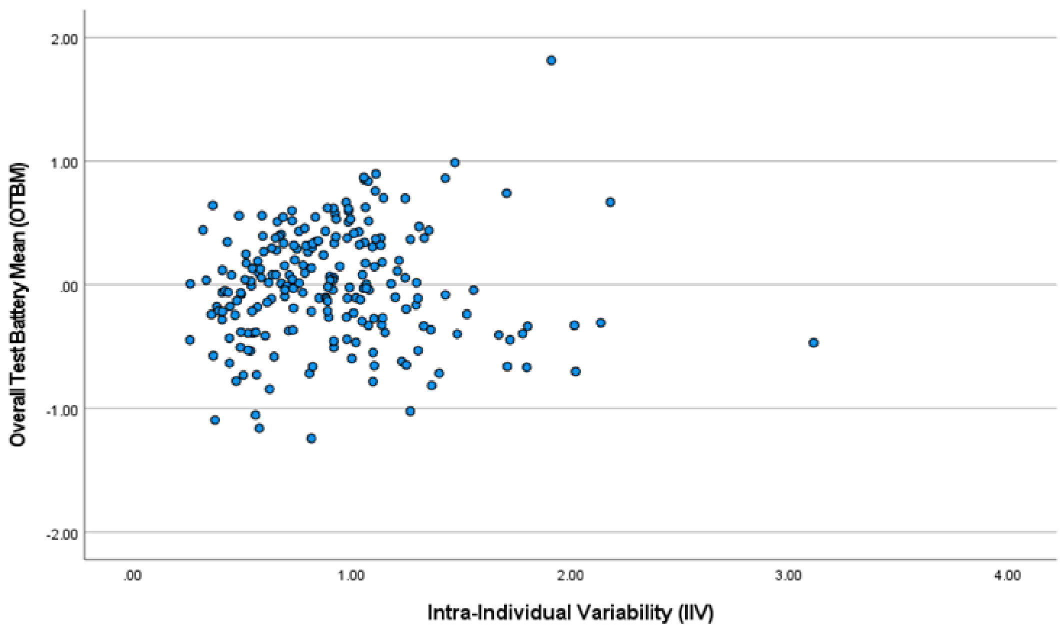
*Holtzer's equation*

$$\text{IIV} = \sqrt{\sum_{k=1}^{K} \frac{(Z_{ik} - A_i)^2}{(K-1)}}$$

$$A_i = \sum_{k=1}^{K} \frac{Z_{ik}}{K}$$

Figure 2

*Scatterplot relating IIV and the OTBM in the combined sample*



# VITA

Emily A. Blanco was born on September 29, 1992 in Morristown, New Jersey. She attended elementary schools in Morris and Sussex County School Districts and graduated from High Point High school in June 2011. The following August she entered Boston College and in May 2015 received the degree of Bachelor of Arts in Psychology and Political Science. She entered the University of Missouri-Kansas City in August 2019 and received a Master of Arts Degree in Clinical Psychology in May 2022.