THE DEFINITIONS AND IMPLICATIONS OF COGNITIVE "NORMALITY" IN SCHIZOPHRENIA

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Abstract

Cognitive dysfunction is widely considered to be a core feature of schizophrenia, yet subpopulations that are cognitively "normal" have been repeatedly identified. There is no agreed upon definition of cognitive normality, with prevalence rates ranging from 0% to 55%, and the clinical and functional implications are unclear. Interpretation of cognitive normality is further complicated by the possibility that normal-range patients have declined relative to premorbid ability. The purpose of this dissertation was to provide a deeper understanding of cognitive normality and its clinical and functional implications. Study 1 assessed the prevalence and clinical and functional validity of two definitions of cognitive normality: a narrow (i.e., IQ) and a broad (i.e., MCCB) definition. Participants included 99 patients with schizophrenia or schizoaffective disorder and 80 healthy controls. Prevalence rates of cognitive normality ranged from 14% to 48%. Regardless of the criterion applied, cognitively normal patients were functionally disadvantaged relative to cognitively normal controls. They demonstrated no advantage in functionality or clinical symptom severity relative to cognitively impaired patients. Study 2 evaluated a cognitive decrement algorithm (Keefe, Eesley, & Poe, 2005) and its clinical and functional validity among 156 patients and 74 controls. Patients were classified as having average range cognition with a decrement (37.1%), average-range without a decrement (9.3%), and above-average range without a decrement (12.1%). The combination of above average-range cognition and lack of a cognitive decrement conferred a functional advantage among patients, but they remained functionally disadvantaged relative to controls. Study 3 assessed the utility of the functionally relevant Breakfast Task (Craik & Bialystok, 2006) in predicting disability relative to standard measures of cognition and

symptom severity among 30 patients and 37 controls. Breakfast Task performance increased the ability to predict disability beyond that provided by cognitive and symptom measures. Results suggest that the prevalence of cognitive normality (9.3% to 48%) is a byproduct of the definition used. There was insufficient evidence supporting the functional or clinical validity of any of the definitions of cognitive normality, suggesting that the role of cognition in functioning has been largely over-emphasized in the literature. Ecologically valid tools, however, may hold promise for disability assessment.

Dedication

To my parents, Mahmut and Irene, and my husband, Clay. Thank you for always believing in me.

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Introduction

Schizophrenia and Cognitive Functioning

Schizophrenia is considered the most severe mental disorder, striking in late adolescence or early adulthood, with only 13.5% of patients eventually meeting clinical and social recovery criteria (Jääskeläinen et al., 2013). Both the prevalence rate of 1% (which is consistent around the globe) and the burden of disease remain substantial, and according to the World Health Organization, it is among the top disabling conditions worldwide for young adults (Charlson et al., 2018; Murray & Lopez, 1997a, 1997b).

The concept and study of schizophrenia first emerged over a century ago, when Emil Kraepelin provided detailed accounts of what he formally termed *dementia praecox*; "psychic" symptoms (e.g., hallucinations) and "bodily" symptoms that were distinct from mood disorders (Kraepelin, 1896, 1919). The so-called "psychic" symptoms remain a core feature of schizophrenia today, a disorder which received its current name by Bleuler in 1950 (Bleuler, 1950) following his argument that the term "dementia" was inaccurate. Bleuler maintained that impaired thinking was the fundamental disturbance of schizophrenia. In fact, positive symptoms (i.e., hallucinations, delusions, and behavioral and speech abnormalities) were considered by Bleuler to be accessory symptoms, secondary to the more fundamental symptoms that were cognitive in nature. Nonetheless, for many years, there remained a consensus that cognitive functions were intact among patients with schizophrenia. When cognitive dysfunction was observed in a patient, it was typically attributed to effects of either medication or hospitalization (Torrey, Bowler, Taylor, & Gottesman, 1994).

It was not until the 1960s that cognitive dysfunction in schizophrenia gained wider attention. At that time, Watson's study assessing neuropsychological function in people with schizophrenia and people with "chronic brain syndrome" revealed that these two patient groups were neuropsychologically indistinguishable (Watson, Thomas, Anderson, & Felling, 1968). Over the next couple of decades, studies demonstrating cognitive dysfunction were replicated by several researchers, and it was firmly concluded in the 1980s that "approximately three-quarters of our rigorously defined schizophrenia subjects showed marked to severe cognitive impairment" (Taylor & Abrams, 1984).

Decades of research have since demonstrated that patients with schizophrenia exhibit impairment in various cognitive domains including sustained attention, verbal declarative memory, spatial working memory, executive functions, and general cognitive ability (Elvevag & Goldberg, 2000; Heinrichs & Zakzanis, 1998; Reichenberg & Harvey, 2007). Cognitive dysfunction is now widely considered to be a core feature of schizophrenia, meaning it is thought to reflect underlying processes that would be present in anyone with the disorder, as opposed to secondary consequences of symptoms or treatment (Kremen, Seidman, Faraone, Toomey, & Tsuang, 2000). Cognitive function is also regarded as a core feature because it is present prior to and at the onset of the illness (Kremen et al., 1998; Meier et al., 2014), it is found in non-psychotic biological relatives (Keefe et al., 1994; Toulopoulou et al., 2007), and it tends to be treatment-resistant compared to other illness characteristics (Keefe & Harvey, 2012). Cognitive impairment is rarely correlated with psychotic symptoms (for a review see Keefe & Harvey, 2012) and even when symptoms are relatively remitted, cognitive dysfunction persists (Gold & Harvey, 1993).

Importantly, a meta-analysis identified that the generalized cognitive impairment observed in schizophrenia has remained evident over nearly three decades of research, despite developments and changes in assessment tools and diagnostic criteria, and despite linguistic and cultural differences among the regions in which the studies have been conduced (Schaefer, Giangrande, Weinberger, & Dickinson, 2013). Cognitive deficits continue, therefore, to be considered the primary expression of schizophrenia (Heinrichs, 2005) with some researchers urging the field to shift diagnostic and treatment efforts on cognitive dysfunction, rather than continue the prevailing emphasis on psychotic symptoms (Kahn & Keefe, 2013).

Cognitive Normality in Schizophrenia

In 1997, Palmer et al. (Palmer, Heaton, Paulsen, Kuck, & Braff, 1997) posed a question that seemingly contradicted the extensive body of literature supporting impaired cognition as a core feature of schizophrenia. The question, posed in their article of the same name, was: "Is it possible to be schizophrenic yet neuropsychological normal?" (p. 437). They found that 11.1% of the patients with schizophrenia demonstrated no impairments on any measure within a comprehensive neuropsychological battery that assessed verbal ability, psychomotor skill, abstraction and cognitive flexibility, attention, learning and retention, motor skills, and sensory ability. This finding, according to the authors, confirmed the existence of patients with normal neuropsychological abilities. This claim that it was possible to be schizophrenic yet neuropsychologically normal was supported by several prior studies that reported a subset of schizophrenia patients were neuropsychologically unimpaired based on performance on the Luria-Nebraksa Neuropsychological Battery (Bryson, Silverstein, Nathan, & Stephen, 1993; Golden et

al., 1982; Silverstein, Mcdonald, & Meltzer, 1985; Silverstein & Zerwic, 1985), comprehensive neuropsychological batteries (Heinrichs & Awad, 1993), and executive function tasks (Goldstein, 1990). A substantial body of literature has since emerged reporting the existence of subgroups with preserved cognitive ability, yet with notable inconsistencies in the reported prevalence rates of normality.

To date, there have been different approaches used to define the construct of cognitive normality, applied individually or jointly, depending on the study. These approaches include relying on population norms, relying on control group performance as a comparison, directly indexing one's current performance against their premorbid or baseline cognitive functions, and using expert ratings of neuropsychological impairment. Within the literature, there are numerous different criteria used to classify normality, or impairment, based on an approach that relies on normative data from healthy control populations. For instance, the Global Deficit Score (GDS) approach for classifying neuropsychological impairment (Heaton et al., 1994) converts T-scores to deficit scores, with T-scores greater than 40 falling within normal limits and as such indicate no impairment. The magnitude of the deficit score increases as the T-score decreases (e.g., T-scores = 39 – 35 are assigned a deficit score of 1, whereas T-scores < 20 are assigned a deficit score of 4). Deficit scores across all administered tests are then averaged to generate a GDS. Applying this criterion, Reichenberg and colleagues classified 81.9% of patients with schizophrenia as impaired (and presumably 18.1% were normal) (Reichenberg et al., 2008) using a battery of neuropsychological tests assessing eight cognitive domains (i.e., general verbal ability, verbal declarative memory, visual declarative memory, abstraction-executive function, attention and processing speed,

simple motor skills, visual processing, and language ability).

Further, Leung et al. (2008) found in their study of older outpatients with schizophrenia that 18.5% of patients were classified as neuropsychologically normal according to GDS classification criteria. Chiang et al. (2016) also applied GDS criteria to a sample of patients of Han Chinese ethnicity with schizophrenia and reported that 41% of patients performed within the cognitively normal range. The GDS criteria have also been used to classify cognitive normality in schizophrenia in conjunction with an additional criterion that no more than 1 out of 6 cognitive dimensions are 1 SD below healthy controls' mean z-scores (González-Blanch et al., 2010). These criteria were applied to a sample of first-episode patients with schizophrenia who were administered a test battery consisting of measures of verbal learning and memory, verbal comprehension, speed of processing and executive functioning, visual memory, motor dexterity, and sustained attention/vigilance. Results of this study indicated that 23% of patients were identified as neuropsychologically within normal limits.

Another published classification system is based on the accepted definitions of clinically significant cognitive impairment (CSCI), used by Palmer et al. (1997) in their seminal study on cognitive normality in schizophrenia. Classification using the CSCI definitions considered impairment to be a performance of 1 SD or more below the general population mean based on corrected scores in at least two out of eight specific ability areas that were assessed (i.e., verbal ability, psychomotor skill, abstraction and cognitive flexibility, attention, learning, retention, motor skills, and sensory ability). This classification yielded 11% of patients who were classified as cognitively normal across all ability areas (Palmer et al., 1997). Similarly, Reichenberg et al., (2008) found that

16% of patients with schizophrenia were cognitively normal based on the CSCI criteria.

In addition to the GDS and CSCI classification systems, the Individual Rating Procedure (IRP) has been used to classify cognitive normality in patients with schizophrenia (Kremen et al., 2000). Using this method, Kremen et al. (2000) converted scores on neuropsychological tests assessing eight cognitive abilities (i.e., general verbal ability, general visual-spatial ability, verbal declarative memory, abstraction-executive function, executive-motor function, perceptual-motor speed, mental-control encoding, and sustained-attention vigilance) to z-scores. The mean of the z-scores of the individual measures comprising the ability area was calculated to represent performance in each ability area. A profile was considered abnormal if two or more ability areas were more than two SDs below the normative mean, or if one ability area was more than three SDs below the mean. Using the IRP, Kremen et al. (2000) found that 23% of patients with schizophrenia had a profile within normal limits (WNL). Applying the same IRP, Reichenberg et al. (2008) found that 45% of patients with schizophrenia were unimpaired (and 54% were impaired). When all three criteria (i.e., GDS, CSCI, IPR) were combined to create an omnibus impairment criteria, 15% of the patients with schizophrenia were classified as cognitively normal across all three criteria, and 53% were classified as impaired (Reichenberg et al., 2008).

Further, the Average Impairment Rating (AIR) criterion pertaining to the Halstead-Reitan Neuropsychological Battery (HRB) (Reitan & Wolfson, 1993) was used to classify performance on the major tests of the HRB (Allen, Goldstein, & Warnick, 2003). Results indicated that based on the AIR classification criteria, 19.5% of patients with schizophrenia were classified as neuropsychologically normal.

Other classification systems based on comprehensive neuropsychological batteries have been used to identify neuropsychologically normal patients with schizophrenia. For instance, Holthausen et al., (2002) classified cognitive impairment in schizophrenia as one z-score of 2 or more SDs below the normative mean within an assessed ability area (i.e., perceptual sensitivity, attention selectivity, perceptual and psychomotor speed, memory-verbal encoding, memory-verbal consolidation, memory-verbal retrieval, memory-visual, verbal fluency, and visuoconstruction). Using this criterion, the authors found that 19% of patients were cognitively unimpaired. As well, Heinrichs et al. (2015) defined cognitive normality as a MATRICS Consensus Cognitive Battery (MCCB) Composite T-score between 40 and 60. Using this MCCB-based definition of normality, 18% of patients were classified as cognitively normal.

The aforementioned studies largely defined cognitive normality based on a composite or summary score pertaining to a comprehensive neuropsychological battery assessing multiple cognitive domains. Ammari et al. (2010) assessed more specific ability measures as an indicator of cognitive normality, in particular verbal memory (CVLT-II), in addition to verbal (i.e., Vocabulary) and non-verbal (i.e., Matrix Reasoning) abilities on the WAIS-III (Wechsler, 1997a). Specifically, cognitive normality was defined as CVLT-II trials 1-5 T scores $\geq$ 43 and $\leq$ 60, and WAIS-III Scaled Scores $\geq$ 8 and $\leq$ 13. These criteria resulted in the identification of 15% of patients who were cognitively normal.

Among the studies that have examined cognitive normality, one which is frequently cited as reporting the highest prevalence of normality was conducted by Torrey, Bowler, Taylor, & Gottesman (1994). In their study of cognitive function among

identical twins with and without schizophrenia, they found that 13 out of 27 (48%) affected twins were classified as less impaired or completely unimpaired, whereas the remaining 14 affected twins were moderately or severely neuropsychologically impaired. Critically, with only three affected twins showing severe cognitive impairments, some sources (Harvey & Keefe, 2009) seem to interpret the results of this study to suggest that 11% of patients demonstrated cognitive impairment, and consequently 89% demonstrated cognitive normality. Therefore, even within one study (e.g., Torrey et al., 1994), the prevalence rates of cognitive normality may vary depending on the interpretation "normality" and/ or "impairment".

Perhaps the most definitively stated position on cognitive normality in schizophrenia comes from Wilk et al. (2005). The authors appear to respond to Palmer's seminal 1997 article ("Is it possible to be schizophrenic yet neuropsychological normal?"), by stating, "No, it is not possible to be schizophrenic and neuropsychologically normal" (p. 778) in their article of the same name. To assess whether normal-range performance does in fact preclude neuropsychological abnormality in patients with schizophrenia, the authors closely matched individual patients with schizophrenia and healthy controls in terms of age, education, and WAIS-III Full-Scale IQ (FSIQ) (Wechsler, 1997a). Results indicated that despite being closely matched on FSIQ, patients with schizophrenia demonstrated performance deficits in the processing speed and working memory indices on the WAIS-III, and in the general memory and immediate memory indices on the Wechsler Memory Scale (3rd ed.; Wechsler, 1997b). Therefore, despite normal range FSIQ scores, patients with schizophrenia still demonstrated neuropsychological abnormality upon closer inspection of domains such as

processing speed and memory. The authors therefore concluded that, "No, it is not possible to be schizophrenic yet neuropsychological normal" (p. 778).

Our understanding of cognitive normality in patients with schizophrenia considers that the issues are both complicated and nuanced, and that this area remains controversial, as cognitive dysfunction is widely considered to be a core feature of the illness. As well, the prevalence of cognitive normality varies widely, from 55% (Bryson et al., 1993) to 0% (Wilk et al., 2005), with the majority of prevalence rates falling within the 15% to 25% range. A critical issue in the field is that there is no agreed upon definition of cognitive normality, as has been demonstrated in the review of the aforementioned studies. As a result, there are various criteria in existing literature that have been used to classify patients as cognitively normal. This lack of consensus of cognitive normality definitions likely contributes to the inconsistencies in the prevalence of cognitive normality cited in the literature, and is therefore an obstacle to research efforts aiming to investigate the existence, nature and significance of this subgroup. Further, multiple definitions of cognitive normality are rarely applied within one research study, rendering the prevalence rates of cognitive normality more questionable given the likely participant heterogeneity between various research studies with their differing inclusion criteria (e.g., inpatients, outpatients, duration of illness, medication status, comorbidity). There is a need to critically examine the divergent definitions in order to resolve the methodological discrepancies that seem to be confounding the field, and to arrive at a more accurate estimate of the prevalence of cognitive normality.

Cognitive Decrement in Schizophrenia

Our understanding of cognitive normality and its implications is further

complicated by the possibility that patients who exhibit cognitive performance that overlaps with healthy control performance at the time of testing may have actually fallen below expectations based on premorbid *estimates* (i.e., premorbid abilities are assumed, rather than directly observed), reflecting a cognitive function decrement. Therefore, despite performing within the range of cognitive normality, these patients may be performing more poorly than would be expected if they had not developed schizophrenia. In addition to relying on population norms to define the construct of cognitive normality, a substantial body of literature has focused on directly indexing current performance against premorbid or baseline cognitive functions as an approach to assessing cognitive normality.

For instance, in their assessment of monozygotic twins discordant for schizophrenia, Goldberg et al. (1990) found that the majority of affected twins performed worse than their unaffected twins on a series of neuropsychological assessments, a pattern which remained even when affected twins' performance fell within normal limits. This was early evidence that patients who are cognitively normal may nonetheless have deficits compared to what their performance level would have been if they had not developed schizophrenia. The same pattern of findings pertaining to a potential cognitive decrement has been shown to apply to intellectually superior patients with schizophrenia as well, when intellectually superior patients were compared to IQ-matched healthy controls (Vaskinn et al., 2014).

As direct assessments of premorbid level of cognitive functioning are rarely available, different approaches are adopted to estimate if there has been a cognitive decline. For instance, objective records, such as school or employment records, or more

subjective indicators such as self-report data can be collected, but there are limitations inherent in these approaches, such as availability and accuracy (Gladsjo, Heaton, Palmer, Taylor, & Jeste, 1999). A preferred method for estimating premorbid cognitive functioning is the assessment of current abilities - for example oral reading - that are thought to be resistant to brain disorders (Nelson & O'Connell, 1978; Nelson, 1982). Indeed, tests of word reading have been shown to provide the most precise and reliable estimate of intellectual functioning, and their use in predicting premorbid IQ for a range of neurological conditions is well-supported (Bright, Jaldow, & Kopelman, 2002; Bright & van der Linde, 2018).

Performance on measures of oral reading has been used as an estimate of premorbid intellectual functioning to assess for cognitive function decline in patients with schizophrenia. Based on performance on an oral reading test, the Wide-Range Achievement Test – Revised Reading Subtest (WRAT-R; Jastak & Wilkinson, 1984), as an indicator of premorbid ability, patients with schizophrenia performing within normal limits on a comprehensive battery of neuropsychological tests (according to IRP criteria) demonstrated higher estimated premorbid ability compared to controls matched on overall neuropsychological test performance (Kremen et al., 2000). This finding suggests a decline from premorbid functioning among patients performing in the normal range. However, the reported prevalence of patients with schizophrenia that do not demonstrate a cognitive decline based on oral reading indicators of premorbid estimates varies in the literature, ranging from 4.7% to 29% (Keefe et al., 2005; Potter & Nestor, 2010; Woodward & Heckers, 2015).

In addition to performance on tasks of oral reading, parental education has also

been examined as an estimate of premorbid intellectual potential (Kareken, Gur, & Saykin, 1995). Parental education has been proposed to be especially useful in schizophrenia due to its heritability with genes and environment, the 48% to 60% heritability of IQ (Bouchard & McGue, 2003), and since parental education may be unaffected by the patient's level of motivation or disease onset that may impede their own educational achievement (Plomin, 1986; Resnick, 1992). Applying this premorbid estimate in the field of schizophrenia, Keefe et al. (2005) reported that only 3.8% of patients performed at or above cognitive levels predicted by maternal education. Keefe and colleagues also showed that when both reading scores and maternal education were combined to predict current cognitive performance, only 1.9% of patients performed at or above expectations. Critically, while Keefe and colleagues label this discrepancy between current cognitive performance and premorbid estimates as a "decrement", their data are not longitudinal in nature, and therefore the term decrement must be interpreted with caution, as a decrement has been assumed, rather than observed.

Work by Keefe and colleagues (2005) suggested that cognitive functioning is lower in all patients when compared with their genetic and environmental intellectual potential (e.g., parental education and reading scores). Their work has yet to be replicated, and it remains unknown if patients who are "truly" cognitively normal (i.e., performing in the "normal" range cognitively without having experienced a decline based on premorbid levels) differ functionally or clinically from patients who perform in the normal-range but have experienced a decline.

Cognitive Normality and Implications for Daily Functioning and Clinical Features

In addition to the long-standing consensus that cognitive impairment is a core

feature of schizophrenia, it is widely understood that patients with schizophrenia demonstrate impairments in multiple domains of everyday functioning, such as educational achievement, employment, independent living skills, ability to fulfill social roles, and the ability to seek needed healthcare services. These impairments are in turn related to increased rates of poverty, major medical morbidity, and social isolation among this population (Harvey, Velligan, & Bellack, 2007). Despite advancements in treating the positive symptoms of the disorder, with up to 40% of patients experiencing clinical remission (Hert et al., 2007), functional impairment tends to persist (Harvey et al., 2012). Therefore, there is a strong need for an increased understanding of the determinants of and treatment for functional impairments.

Cognitive impairment has long been regarded as a cause of impairment in functional capacity (i.e., daily living skills demonstrated by performance in ideal environments) and related outcomes, such as residential functioning, employment, quality of life, and medication adherence among patients with schizophrenia (Bowie, Reichenberg, Patterson, Heaton, & Harvey, 2006; Green, Kern, Braff, & Mintz, 2000; Keefe & Harvey, 2012; Kuo et al., 2018; Matza et al., 2006). A comprehensive meta-analysis, however, has shown that cognition accounts for only 6% of functionality variance, with the addition of social cognition accounting for up to about 16% (Fett et al., 2011). Further, cognitively normal patients fail to show any functional advantage in community adjustment relative to cognitively impaired patients (Alden, Cobia, Reilly, & Smith, 2015; Heinrichs et al., 2015; Heinrichs, Parlar, & Pinnock, 2017; Moore et al., 2015; Muharib et al., 2014). Leung et al. (2008a) did find, however, that cognitively normal patients (based on the GDS classification) had better functional capacity relative

to cognitively impaired patients. Critically though, these cognitively normal patients were still disadvantaged relative to controls in terms of functional capacity and independence in residential status. As well, while behavioural interventions demonstrate success at improving cognition, these interventions do not demonstrate a strong ability to generalize to daily life functioning (Kidd et al., 2014; Lin, Tsai, & Lane, 2014). Given the various definitions of cognitive normality used in the literature, it is unclear if different classifications of cognitive normality (e.g., more or less stringent classifications) may have different associations with functioning.

In addition to the association between cognition and functioning, many studies have investigated the association between cognition and symptom severity among patients with schizophrenia. The relation between symptom severity and cognitive functioning is less equivocal, with studies generally pointing towards a lack of association between the two (Ammari et al., 2010; Dibben, Rice, Laws, & McKenna, 2009; Nieuwenstein, Aleman, & De Haan, 2001). There are, however, reports that negative symptoms, but not positive symptoms, are associated with poorer cognitive function among patients (Addington, Addington, & Maticka-Tyndale, 1991; de Gracia Dominguez, Viechtbauer, Simons, van Os, & Krabbendam, 2009; Harvey, Koren, Reichenberg, & Bowie, 2006). The extent to which different classifications of cognitive normality are related to symptom severity remains relatively understudied.

Novel Approaches to Assessing Cognitive Function Underlying Daily Functioning and Disability

Despite the common conception that cognition is considered a primary predictor of functioning, the meta-analytic finding that cognition (and social cognition) accounts

for only 6-16% of the variance in functional outcome (Fett et al., 2011) cannot be ignored. This finding suggests that either cognition does not play a substantial role in daily functioning and disability among schizophrenia, or that perhaps cognitive measures that incorporate more functionally relevant stimuli may have better utility than traditional neuropsychological assessments in accounting for variance in daily functioning. The latter interpretation is supported by Harvey et al. (2007), who posited that performance-based measures of functional skills could provide a more valid estimate of functional impairment as compared to traditional neuropsychological assessment measures. Further, measures of executive function, a cognitive domain that supports the ability to carry out many instrumental activities of daily living, have been criticized for their poor generalizability to real-world behavior. For instance, poor performance on the widely used Wisconsin Card Sorting Task (Grant & Berg, 1948) is not necessarily related to poor executive behavior in everyday life, while good performance on this task can still be accompanied by dysexecutive problems in everyday life, a pattern that has been repeatedly demonstrated among patients with frontal lesions (Tanguay, Davidson, Guerrero Nuñez, & Ferland, 2014).

An alternative approach to the use of standard cognitive measures in the prediction of real world functioning is to employ more real-world tasks that rely on multiple executive functions. These tasks are considered to be more ecologically valid in their relevance to carrying out a task in the real world. For instance, the Canadian Objective Assessment of Life Skills (COALS; (McDermid Vaz et al., 2012) is a performance-based measure designed to assess routine procedural knowledge and executive operations involved in functional outcome domains such as health and hygiene,

time management, transportation, crisis management, and domestic activates. Critically, performance on the COALS provided predictive validity of community independence above and beyond that provided by symptoms and intellectual ability among patients with schizophrenia (McDermid Vaz et al., 2012). However, scores on the University of California San Diego Performance Skills Assessment (UPSA), another measure of functional capacity, failed to significantly enhance the validity achieved with standard cognitive measures in predicting community functioning (Heinrichs, Ammari, Miles, & McDermid Vaz, 2010). These findings are in contrast with those pertaining to the COALS (McDermid Vaz et al., 2012). Therefore, the incremental validity of functional competence measures in predicting community functioning relative to standard cognitive measures is equivocal, and may relate at least partially to the specific measure utilized.

A challenge inherent in the design and ecological validity of real-world tasks is the consideration of which day-to-day tasks draw heavily on cognitive domains such as executive functioning. Cooking has long been regarded as a solid example of a task that is highly reliant on frontal lobe/executive functions. This was first demonstrated by Wilder Penfield (Penfield & Evans, 1935) in a study documenting the effects following a frontal lobe resection he performed on his sister. Penfield and Evans (1935) made the following observation regarding Penfield's sister:

> One day about fifteen months after operation she had planned to get a simple supper for one guest and four members of her own family. She had looked forward to it with pleasure and had the whole day for preparation. This was a thing she could have done with ease ten years before. When the appointed hour arrived she was in the kitchen, the food was all there, one or two things were on

> the stove, but the salad was not ready, the meat had not been started and she was distressed and confused by her long continued effort alone. It seemed evident that she would never be able to get everything ready at once. (p. 131)

The etiology (frontal lobe resection) underlying the executive dysfunction in Penfield's case study differs from the current study among patients with schizophrenia, yet the principle that cooking relies on executive functions remains the same.

Craik and Bialystok (2006) developed The Breakfast Task, a computer game that provides a naturalistic measure of different aspects of executive functioning for cognitive rehabilitation purposes. This computerized game simulates cooking breakfast while setting a table, achieving a balance of the advantages of experimental control inherent to traditional tasks of executive function, with the varying demands of real-world situations that draw largely on executive functions. To date, performance on this computerized task has been studied in patients with acquired brain injury (ABI) (Tanguay et al., 2014), and older adults (Craik & Bialystok, 2006; Rose et al., 2015). Relative to controls, patients with ABI perform worse on all measures of the Breakfast Task as compared to controls (Tanguay et al., 2014). Evidence suggests that the Breakfast Task provides measures of global and local planning abilities that are related to task switching, working memory, and prospective memory (Craik & Bialystok, 2006; Rose et al., 2015). Therefore, there is preliminary support for the use of the Breakfast Task in assessing real-world planning and monitoring, and also for its ability to distinguish healthy controls from those with an ABI. This task has yet to be used among patients with schizophrenia and its utility in this population in terms of accounting for variance in community independence remains unclear. Given the well-supported findings that real-world and cognitive (including

executive) functions are impaired in patients with schizophrenia, the Breakfast Task may strike a balance between the two areas of functioning in such a way that offers a strong predictive validity of disability in this population.

Current Program of Research

The current program of research consists of three studies that aimed to further our understanding of cognitive normality in schizophrenia by: i) examining the prevalence and clinical and functional validity of broad and narrow definitions of cognitive normality, ii) evaluating a cognitive decrement algorithm (Keefe et al., 2005) and its clinical and functional validity, and iii) examining the utility of a real-world functional task in predicting disability.

With the existing literature, we are only able to compare prevalence rates across different studies with heterogeneous participant samples recruited using different inclusion and exclusion criteria. These heterogeneous participant groups may have inherent confounding variables that impact the prevalence rates of cognitive normality. The purpose of Study 1 was to assess and report the prevalence of different definitions of cognitive normality criteria (i.e., "Narrow" and "Broad") among the same study sample. Specifically, the criteria for the Narrow classification of normality consisted of an IQ summary index (e.g., Ammari et al., 2010; Kremen, Seidman, Faraone, & Tsuang, 2001), and the criteria for the Broad classification consisted of the MATRICS Consensus Cognitive Battery (MCCB: Nuechterlein et al., 2008) composite scores, for a more broad-based measure. This approach to cognitive normality classification therefore relied on population norms. To understand the clinical and functional implications of the different definitions of cognitive normality, patients who met criteria for different definitions of

cognitive normality were compared to cognitively normal healthy controls as well as cognitively impaired patients on measures of community independence and symptom severity.

The purpose of Study 2 was to expand on work done by Keefe et al. (2005) by evaluating the reproducibility of their results pertaining to their cognitive function decrement algorithm. In their approach, Keefe et al. (2005) directly indexed participants' current performance against their premorbid or baseline cognitive functions, specifically using parental education and reading scores as estimates. Following an evaluation of Keefe's cognitive decrement algorithm, Study 2 also examined the clinical and functional implications of being a "truly" cognitively normal patient. That is, analyses focused on the subset of patients who met criteria for cognitive normality based on a composite z-score, and who have not experienced a cognitive decrement based on genetic and environmental expectations (parental education and reading scores). This study aimed to further our knowledge of cognitive normality by determining the proportion of patients who, despite meeting cognitive normality criteria, have actually experienced a decline in their cognitive function.

In addition to assessing the clinical and functional implications of different definitions of cognitive normality and cognitive function decrement, the current investigations included an assessment of the incremental validity of a naturalistic measure of varied aspects of executive functioning in predicting disability relative to standard measures of cognition and symptom severity (Study 3). The naturalistic measure used in Study 3 was The Breakfast Task, a computerized task that may hold more functional relevance as compared to standard measures of cognition.

Study 1

As discussed, the purpose of Study 1 was to assess and report the prevalence of and functional and clinical implications of different definitions of cognitive normality (i.e., "Narrow" and "Broad") among patients with schizophrenia.

Hypotheses

It was predicted that prevalence rates of cognitive normality among both patients and controls would vary based on the two different definitions of normality. These definitions included: i) Narrow-Normal Range (NaNR); and ii) Broad-Normal Range (BrNR). It was also expected that prevalence rates would vary as a result of the stringency of the definition, with the following prevalence rates: NaNR > BrNR. As well, regardless of the definition of cognitive normality (NaNR and BrNR), it was hypothesized that patients who are cognitively normal would exhibit a functional, but not clinical advantage (i.e., reduced symptom severity) relative to patients who performed below the range of cognitive normality.

Methods

Participants

Participants included 99 patients (76 males, 23 females) who met diagnostic criteria for schizophrenia (n = 77) or schizoaffective disorder (n = 22) and 80 non-psychiatric controls (54 males, 26 females). Diagnosis was confirmed by the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (First, Spitzer, Gibbon, & Williams, 1996). Patients were included if they met the following criteria: 1) age 18-65 years; 2) no history of developmental disability or serious neurological or endocrine disorder; 3) no concurrent DSM-IV diagnoses of substance

abuse or dependence; and 4) willingness and ability to sign informed consent. Patients were recruited from outpatient settings in south central Ontario, and controls were recruited by posting for paid research participation in community newspapers and online advertisements. Controls were excluded for medical, neurological, and psychiatric illness, and for developmental disability based on responses provided on a screening questionnaire. Control participants were group matched to patients on age, gender, language background and parental socioeconomic background

Measures

Current clinical symptom severity was evaluated with the Positive and Negative Syndrome Scale (PANSS; Opler et al., 1999). Neurocognitive assessment in both patients and non-psychiatric controls included the MATRICS Consensus Cognitive Battery (MCCB; Nuechterlein et al., 2008), which is comprised of measures of working memory, attention, verbal memory, visual learning, processing speed, reasoning and problem-solving, and social cognition. The MCCB yields a composite score representing an overall measure of cognitive performance. The Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) Vocabulary and Matrix Reasoning subtests were administered to obtain an estimate of general intellectual ability (i.e., WASI Two-Subtest IQ).

Community independence was measured with the overall Global rating from the Multidimensional Scale of Independent Functioning (MSIF; Jaeger, Berns, Multidimensional, & Functioning, 2003) in both patients and healthy controls. The MSIF comprises a structured interview and self-report measure. The Global Rating reflects the level of functioning across residential, work, and educational settings while considering

role position, level of performance, and degree of assistance required. Scores range from one to seven, with higher scores indicating poorer function. That is, a score of one indicates essentially normal functioning with little-to-no support, whereas a rating of seven indicates total disability. The interclass correlation coefficients for the overall global rating has been shown to be 0.90, and there is moderate internal consistency among the subcomponents of the MSIF (Jaeger et al., 2003).

Analyses

Group assignment procedure

Group assignment to the Narrow Normal-Range (NaNR) group was based on the following criteria: WASI Two-Subtest IQ score equal to or between 90 and 109, to reflect Average range performance according to Wechsler qualitative descriptors. Based on this narrow measure of cognition, cognitively below-normal range was defined as a WASI Two-Subtest IQ score less than 90. This classification yielded 47 NaNR patients (48%), 18 above NaNR patients (18%), and 34 patients falling below the NaNR (34%) when applying these criteria to the entire sample of patients (n = 99). This classification yielded 28 NaNR controls (35%), 41 above NaNR controls (51%), and 11 below NaNR Controls (14%) when applying these criteria to the entire sample of controls (n = 80).

Group assignment to the Broad Normal-Range (BrNR) group was based on the following criteria: MCCB composite *T* score equal to or between 40 and 60, consistent with previous studies employing this criterion with the MCCB (Heinrichs et al., 2015; Muharib et al., 2014). If participants met criteria for both NaNR and BrNR, they were classified as BrNR for the purpose of statistical analysis to ensure that no participants were included in both cognitive subtype groups for group comparisons. Based on this

broad measure, cognitively below-normal range was defined as an MCCB composite *T* score ranging from 20 to 39. This classification yielded 13 BrNR patients (14%), 0 above BrNR patients (0%), and 82 patients falling below the BrNR (86%) when applying these criteria to the entire sample of patients (n = 95). The classification yielded 52 BrNR controls (65%), one above BrNR control (1%), and 26 below BrNR Controls (33%) when applying these criteria to the entire sample of controls (n = 79).

Given the low prevalence (14%) of BrNR patients, and to ensure demographic similarity with comparison subgroups, these patients' age range and sex proportion were used as criteria in assigning controls to a normal range (NR) ability group, patients to the NaNR ability group, and patients to the below-normal range group for statistical analyses. Hence, inclusion criteria for the normal range control group were: 1) age 20 – 46, 2) sex ratio 65-85% male; and 3) MCCB composite T score between 40 and 60 or IQ between 90 – 109. There were only three controls within the NaNR group who met age-range criteria, as the majority of controls also met criteria for the BrNR group. Therefore, NaNR and BrNR controls were combined to form one normal-range control group, rather than separating controls into their NaNR and BrNR groups for analyses. A total of n = 25 controls met these criteria and were assigned to a normal-range group. For patients, inclusion criteria for the NaNR group included: 1) age 20 – 46; 2) sex ratio 65-85% males; and 3) WASI Two-Subtest IQ score equal to or between 90 and 109. These requirements were met by n = 25 patients, who were therefore assigned to the NaNR category. The cognitively below-normal range (BNR) patient group was defined as an MCCB composite score less than or equal to 39 and an IQ score less than or equal to 89.

Applying the age, sex, IQ, and MCCB criterion to the pool of patients yielded n = 13 patients falling into the BNR group (see Table 1).

See Appendix A for additional analyses pertaining to group assignment to the BrNR group based on MCCB composite *T* scores equal to or between 43 and 57, with those *T* score parameters set in order to achieve psychometric equivalence with the WASI IQ score criterion for average-range performance (based on Wechsler Classification).

Results

Demographic characteristics of the NaNR, BrNR patient groups, the BNR patients, and the NR comparison controls are presented in Table 1. Patient and control subgroups did not differ significantly in terms of age, sex distribution, or proportion for whom English was their first language. Groups did differ in terms of years of education; the NR controls reported significantly higher levels of education compared to the three patient groups ($ps < .05$), however patient groups did not differ from one another in terms of years of education.

Table 1

Descriptive and Criterion Data for Below Normal-Range (BNR) Patients, Narrow Normal-Range (NaNR) Patients, Broad Normal-Range (BrNR) Patients, and Normal Range (NR) Controls

Variables	BNR Patients (n = 13)	NaNR Patients (n = 25)	BrNR Patients (n = 13)	NR Controls (n = 25)	Statistic
Age, yrs *(M, SD)*	35.31 (6.46)	34.96 (6.54)	30.31 (7.29)	30.32 (8.49)	F(3,72) = 2.66
Sex (males %)	85	76	77	68	FET = 1.26
Years Education *(M, SD)*	11.69 (1.25)	13.08 (2.64)	13.92 (1.98)	16.44 (2.29)	F(3,72) = 15.94 **
First Language English (%)	83	84	69	58	FET = 4.66
MCCB Composite *T* *(M, SD)*	20.62 (8.64)	30.04 (7.17)	48.08 (5.01)	46.28 (6.81)	F(3,71) = 57.0 **
WASI 2-Subtest IQ *(M, SD)*	78.22 (7.42)	99.44 (5.28)	114.00 (11.39)	106.64 (18.05)	F(3,72) = 21.94 **

Note: FET = Fisher's Exact Test; *M* = mean; MCCB = MATRICS Consensus Cognitive Battery; SD = standard deviation; WASI = Wechsler Abbreviated Intelligence Scale.
** $p < .001$

Functional implications of NaNR and BrNR subtypes

Assumptions for ANOVA were assessed. Based on the interquartile range and boxplot, there were no outliers among MSIF scores. Results of the Shapiro-Wilk test (p = .01) indicated that the distribution of the residuals of MSIF scores was not normal, and residuals remained non-normally distributed following log transformation. Therefore, the

non-parametric Kruskal-Wallis test was performed to compare the effect of group (i.e., BNR patients, NaNR patients, BrNR patients, and NR Controls) on community outcome (i.e., MSIF global scores), with post-hoc Mann-Whitney tests conducted with Bonferroni correction.

MSIF scores were significantly affected by participant group ($H(3) = 36.80$, $p < .001$). Mann-Whitney tests were used to follow up on this finding based on the following comparisons: i) BNR patients vs. NaNR patients; ii) BNR patients vs. BrNR patients; iii) NaNR patients vs. NR controls; and iv) BrNR patients vs. NR controls, with only these select Mann-Whitney tests chosen to reduce the Type I error rate while addressing the primary study aims, and a Bonferroni correction applied with effects reported at a .0125 (.05/4) level of significance. Effect size values were calculated as follows: $r = Z/\sqrt{n}$, with r values above 0.1 representing a small effect size, values above 0.3 representing a medium effect size, and values above 0.5 representing a large effect size.

Results indicated that MSIF scores did not differ between the BNR patient group and both the NaNR patient group ($U = 128.5$, $p > .05$, $r = -.097$), and the BrNR patient group ($U = 72.0$, $p > .05$, $r = -.067$). When comparing the patients with the controls, results indicated that MSIF global scores were significantly higher among the NaNR patient group as compared to the NR control group ($U = 49.5$, $p < .01$, $r = -.75$), and MSIF scores were also significantly higher among the BrNR patient group as compared to the NR control group ($U = 23.0$, $p < .01$, $r = -.72$) (Table 2).

Table 2

Community Independence and Clinical Data for Below Normal-Range (BNR) Patients, Narrow Normal-Range (NaNR) Patients, Broad Normal-Range (BrNR) Patients, and Normal-Range (NR) Controls

Variable	1. BNR Patients (n = 13)	2. NaNR Patients (n = 25)	3. BrNR Patients (n = 13)	4. NR Controls (n = 25)	Statistic	Post-hoc
MSIF Global Scores, *(M, SD)*	4.17 (1.40)	3.88 (1.04)	4.00 (1.16)	1.80 (.86)	H(3) = 36.80 **	2, 3 > 4 1 = 2 = 3
PANSS Positive *T (M, SD)*	47.46 (9.12)	46.36 (8.22)	44.31 (7.81)	n/a	λ = .92	n/a
PANSS Negative *T (M, SD)*	44.31 (10.16)	40.04 (6.96)	38.77 (8.68)	n/a	λ = .92	n/a

Note: MSIF = Multidimensional Scale of Independent Functioning; PANSS = Positive and Negative Syndrome Scale.
** $p < .001$

Clinical implications of NaNR and BrNR subtypes

Assumptions for MANOVA were assessed. All observations were statistically independent, and data were randomly sampled from the population. Based on Mahalanobis distance ($df = 2$, cut off = 13.82), there were no multivariate outliers among the residuals (all values were less than 8.718). Multivariate normality was assessed in R Studio using Mardia's multivariate test of normality. Based on the residuals of PANSS Positive and Negative *T* scores, the Skewness (Mardia's = 6.01, $p = .20$) and Kurtosis (Mardia's = -.81, $p = .42$) indicated multivariate normality. Box's test of equality of covariance matrices was not violated (M = 12.43, F(6, 16693.13) = 1.93, $p = .072$).

The MANOVA, with patient group (i.e., BNR, NaNR, and BrNR) set as the independent variable, and the PANSS Positive and Negative *T* scores set as dependent variables, did not show a significant difference between patient groups in terms of symptom severity ($\lambda = .92$, $F(4, 94) = .994$, $\eta_P^2 = .041$, $p = .415$). Therefore, BNR, NaNR and BrNR patient groups did not differ in terms of their positive and negative symptom severity (Table 2).

Summary

Study 1 assessed the prevalence and clinical and functional validity of two definitions of cognitive normality: i) a narrow definition (i.e., WASI Two-Subtest IQ score equal to or between 90 and 109) and ii) a broad definition (i.e., MCCB composite *T* score between 40 and 60). Participants included 99 patients with schizophrenia or schizoaffective disorder and 80 healthy controls. Prevalence rates of cognitive normality ranged from 14% (MCCB broad normal-range) to 48% (IQ narrow normal-range). Regardless of the cognitive normality criteria applied, cognitively normal patients were functionally disadvantaged, based on MSIF scores, relative to cognitively normal controls. They demonstrated no advantage in functionality or clinical symptom severity, based on PANSS symptom scores, relative to cognitively impaired patients. A full discussion pertaining to the findings and implications of Study 1 is presented in the Discussion section, beginning on page 62.

Study 2

As previously described, the purpose of Study 2 was to evaluate Keefe et al.'s (2005) cognitive function decrement algorithm and to examine the clinical and functional implications of being a "truly" cognitively normal patient.

Hypotheses

It was predicted that findings by Keefe et al. (2005) pertaining to their definition of a cognitive function decrement would be replicable in our sample. If "truly" normal patients emerged who have not experienced a cognitive function decrement, it was hypothesized that they would have a functional advantage relative to patients who have experienced a cognitive function decrement, but that patients in the two groups would not differ in terms of symptom severity. It was also expected that prevalence rates emerging in Studies 1 and 2 would vary as a result of the stringency of the definition, with the following prevalence rates: NaNR > BrNR > Non-Decrement Subtype.

Methods

Participants

Participants in Study 2 included 156 patients (99 males, 57 females) who met diagnostic criteria for schizophrenia (n = 95) and schizoaffective disorder (n = 61) and 74 controls (56 males, 18 females). Medical chart review indicated that 152 patients were receiving antipsychotic medication at the time of data collection, with 129 patients treated with second-generation drugs. Diagnosis was confirmed by the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (First et al., 1996). The same inclusion criteria for patients and controls were applied to Study 1 and Study 2. Patients were recruited from outpatient settings in south central Ontario, and controls were recruited by postings for paid research participation in community newspapers.

Measures

Current clinical state and severity were evaluated with the Positive and Negative Syndrome Scale (PANSS; Opler et al., 1999). Community independence was measured

with the overall global rating from the Multidimensional Scale of Independent Functioning (MSIF; Jaeger, Berns, Multidimensional, & Functioning, 2003) in both patients and healthy controls. As mentioned, the MSIF global rating reflects the level of functioning across residential, work, and educational settings while considering role position, level of performance, and degree of assistance required. Scores range from one to seven, with higher scores indicating greater dependency.

Premorbid ability was estimated with the Wide Range Achievement Test Reading subtest, 3rd Edition (WRAT-3; Snelbaker, Wilkinson, Robertson, & Glutting, 2001). Participants provided data pertaining to the highest grade of education achieved by either parent.

Keefe et al.'s (2005) composite z-scores were based on a cognitive battery assessing domains of verbal memory, working memory, motor function, processing speed, attention, and reasoning and problem solving abilities (Keefe et al., 2004). To replicate Keefe's calculation of the composite *z*-score as closely as possible, measures from our cognitive test battery that assessed analogous domains were used. Specifically, calculation of the composite *z* -score in the current study was based on the following cognitive measures: i) California Verbal Learning Test Trials 1-5 Total raw score (measure of verbal memory) (CVLT-II: Delis, Kramer, Kaplan, & Ober, 2000); ii) Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III: Wechsler, 1997) Letter-Number Sequencing raw score (measure of working memory); iii) WAIS-III Symbol Search raw score (measure of processing speed); iv) Conners' Continuous Performance Test Omission errors raw (measure of attention) (CPT-II: Conners, 2000); and v) WAIS-III Matrix Reasoning raw score (measure of reasoning and problem solving). The

cognitive battery administered as part of the current study did not include a measure of motor function, unlike Keefe et al.'s (2005) study.

Statistical Analyses

Calculation of the composite *z*-score included the following steps: i) *z*-score calculation for each of the five raw test scores, based on the healthy control mean and standard deviation; ii) calculation of the mean of the five *z*-scores; iii) *z*-score of the mean of the *z*-scores was calculated to represent the composite *z*-score.

Following methods by Keefe et al., (2005), three linear regression analyses were performed on the control population to determine the predicted cognitive composite *z*-score based on the i) highest educational grade achieved by either parent; ii) WRAT-3 Reading scores; and iii) highest parental education and WRAT-3 Reading scores. Cognitive function decrement was defined as a composite *z*-score falling below the regression line. In line with methods by Keefe et al., (2005), a one-tailed 95% confidence interval was calculated for the regression line for each of the three models. A one-tailed confidence interval was used because their hypothesis regarded only the accuracy of estimates for the lower side of the regression line, that is for patients who performed worse than expected (i.e., cognitive decrement subgroup). The proportion of patients meeting this definition of cognitive decrement, and the proportion of patients meeting a definition of no cognitive decrement (i.e., performing at or above the regression line) were calculated for each of the three regression models. The participants who performed worse than expected were classified as having experienced a cognitive decrement, whereas those who performed at or above expectations were classified as belonging to the non-decrement group. The proportion of patients and controls whose cognitive

composite scores fell within the range of the 95% one-tailed confidence interval on the lower side of the regression line was reported, and these participants were not included in subsequent analyses comparing decrement vs. non-decrement subtypes.

To assesses the prevalence and functional implications of cognitively normal patients who have not experienced a cognitive function decrement, patients and controls were further classified based on their composite *z*-scores and were included in further analyses if their performance fell within the average-range (AR). According to *z*-scores and their performance relative to the regression line, patients were classified as: i) AR (i.e., *z*-scores between -0.67 and +0.67) non-decrement; or ii) AR decrement (i.e., *z*-scores between -0.67 and +0.67, but with their composite *z*-score falling below predicted values). The same classification criteria were applied to controls to generate i) AR non-decrement controls and ii) AR decrement controls. The *z*-score normality criterion of less than 0.67 and greater than -0.67 was selected to reflect average-range performance according to the Wechsler qualitative descriptors and the corresponding scaled scores of 8 to 12.

Functional and Clinical Implications of the Non-Decrement Subtype

To assess functional and clinical implications of having experienced a cognitive decrement, analysis included a univariate ANOVA to compare the effect of cognitive decrement group on community outcome, with post-hoc multiple comparisons conducted to explore any main effects. For symptom severity, a one-way MANOVA was conducted among the schizophrenia group, setting Cognitive Decrement as a fixed factor (i.e., Yes or No), and PANSS positive and negative symptoms as dependent variables.

These analyses were conducted again among patients and controls who have and have not experienced a cognitive decrement, and who also performed within the average-range based on their composite *z*-scores.

Results

Predicted Composite *z*-score

The means and standard deviations among the healthy control group, whose data were used to calculate the composite *z*-score used in the prediction models, were as follows: i) CVLT Trials 1-5 Total raw (M = 50.88, SD = 11.23); ii) WAIS-III Letter-Number Sequencing raw (M = 11.18, SD = 3.03); iii) WAIS-III Symbol Search raw (M = 29.59, SD = 10.04); iv) CPT-II Omission errors raw (M = 3.31, SD = 7.31); and v) WAIS-III Matrix Reasoning raw (M = 17.45, SD = 4.87).

WRAT-3 Reading Score as a Predictor

Assumptions of multiple regression were assessed for the model with WRAT-3 Reading scores set as a predictor of composite z-scores (among healthy controls). Residual values were normally distributed, errors were independent based on a Durbin-Watson test (p = .584), component plus residual plots confirmed that the linearity assumption was met, and there was no evidence of heteroscedasticity based on the non-constant variance score test (p = .80). No outliers were identified in the data.

WRAT-3 Reading scores explained 11.5% of the variance in cognitive composite scores (R^2 = .115, $F(1,72) = 9.36$, $p < .01$). WRAT-3 Reading was a significant predictor of composite *z*-scores (β = .339, $t = 3.06$, $p < .01$).

Predicted composite *z*-score values among the patient and healthy control groups were obtained using the Predict method for linear model fits in R Studio based on the

linear model obtained from the healthy control data. The regression equation was as follows:

$$Y_i = b_0 + b_1 X_{i1}$$

$$composite\ score_i = -1.913 + .0507\ (WRAT\text{-}3)$$

When WRAT-3 Reading scores were used in the regression equation, 69.2% (n = 108) of patients had cognitive composite scores falling below the regression line, and 19.2% (n = 30) performed above expected levels. Eighteen patients (11.5%) had cognitive composite scores that fell within the range of the 95% one-tailed confidence interval. Among controls, 39.2% (n = 29) had cognitive composite scores falling below the regression line, and 54.1% (n = 40) had scores falling above the regression line (see Figure 1). A total of 5 controls (6.8%) performed within the range of the 95% one-tailed confidence interval and they were therefore not included in either the decrement or no-decrement group.

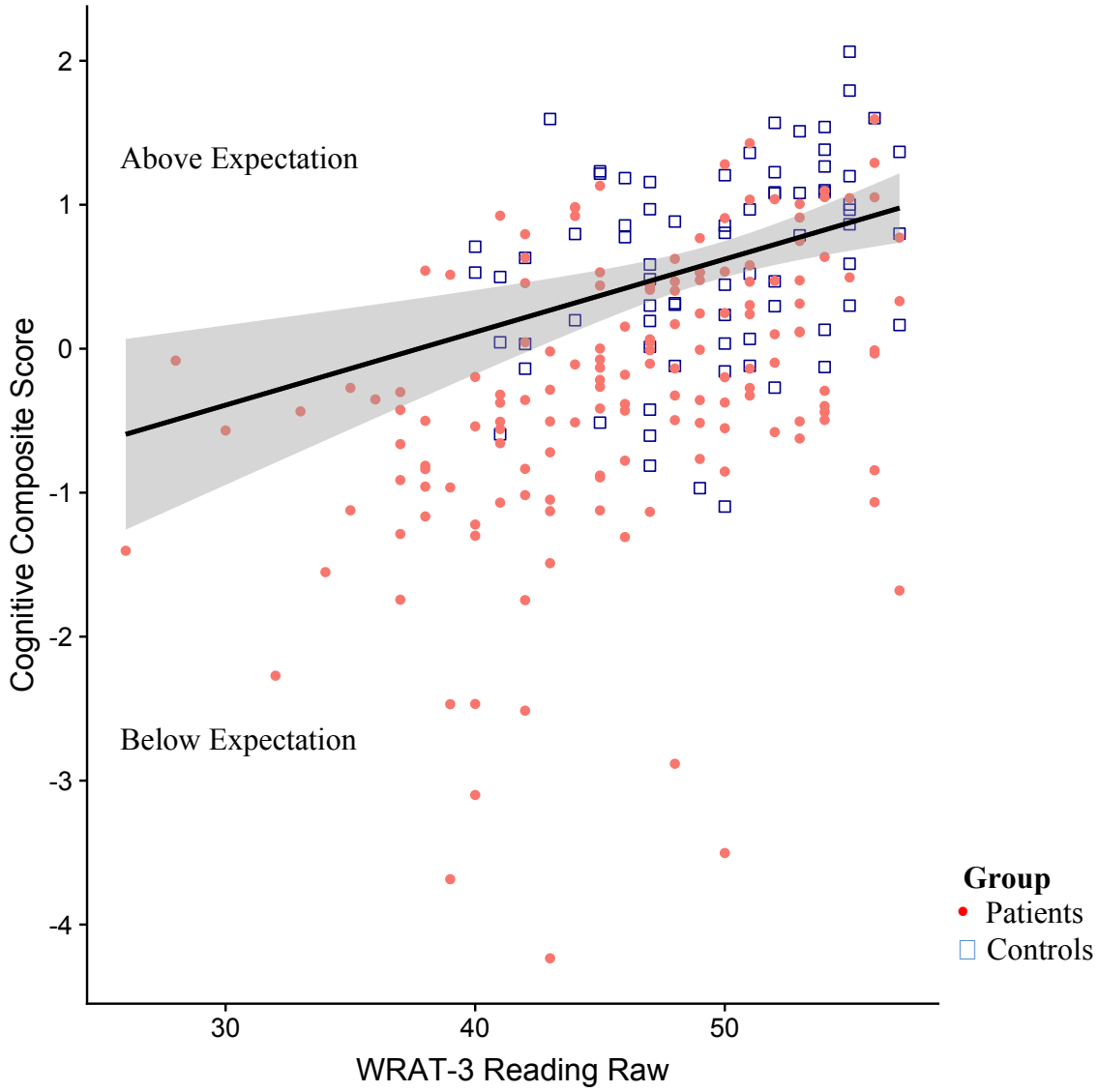

Figure 1. Cognitive Composite Score Predicted by WRAT-3 Reading Scores. The curved lined represents the 90% confidence interval of the regression line, with participants falling within the lower bounds excluded from analysis. Participants falling above the regression line performed above the expectations based on their WRAT-3 Reading scores, and those falling below the regression line performed below expectations.

Parental Education as a Predictor

Assumptions of linear regression were assessed for this model that included parental education as a predictor of composite *z*-scores (among healthy controls). Residual values were normally distributed, errors were independent based on a Durbin-

Watson test (p = .89), component plus residual plots confirmed that the linearity assumption was met, and there was no evidence of heteroscedasticity based on the non-constant variance score test (p = .91). No outliers were identified in the data. Years of parental education explained 5.9% of the variance of cognitive composite scores (R^2 = .059, F(1,62) = 3.82, p = .055). Parental education was a marginally significant predictor of composite z-scores (β = .243, t = 1.96, p = .055).

The highest number of years of education achieved by patients' parents were applied to the regression equation obtained from the healthy control population to determine whether patients performed above or below the expected cognitive composite score. The regression equation was as follows:

$$Y_i = b_0 + b_1 X_{i1}$$

$$composite\ score_i = -.0833 + .05333\ (Parental\ Education)$$

When years of parental education were used in the regression equation, 70.9% (n = 100) of patients had cognitive composite scores falling below the regression line and 16.3% (n = 23) performed above expected levels. Eighteen patients (12.8%) had composite cognitive scores falling within the 95% one-tailed confidence interval below the regression line. Among controls, 36.5% (n = 23) had composite scores falling below the regression line, and 54.0% (n = 34) performed above the expected value (see Figure 2). Six controls (9.5%) had composite z-scores falling within the 95% one-tailed confidence interval below the regression line.

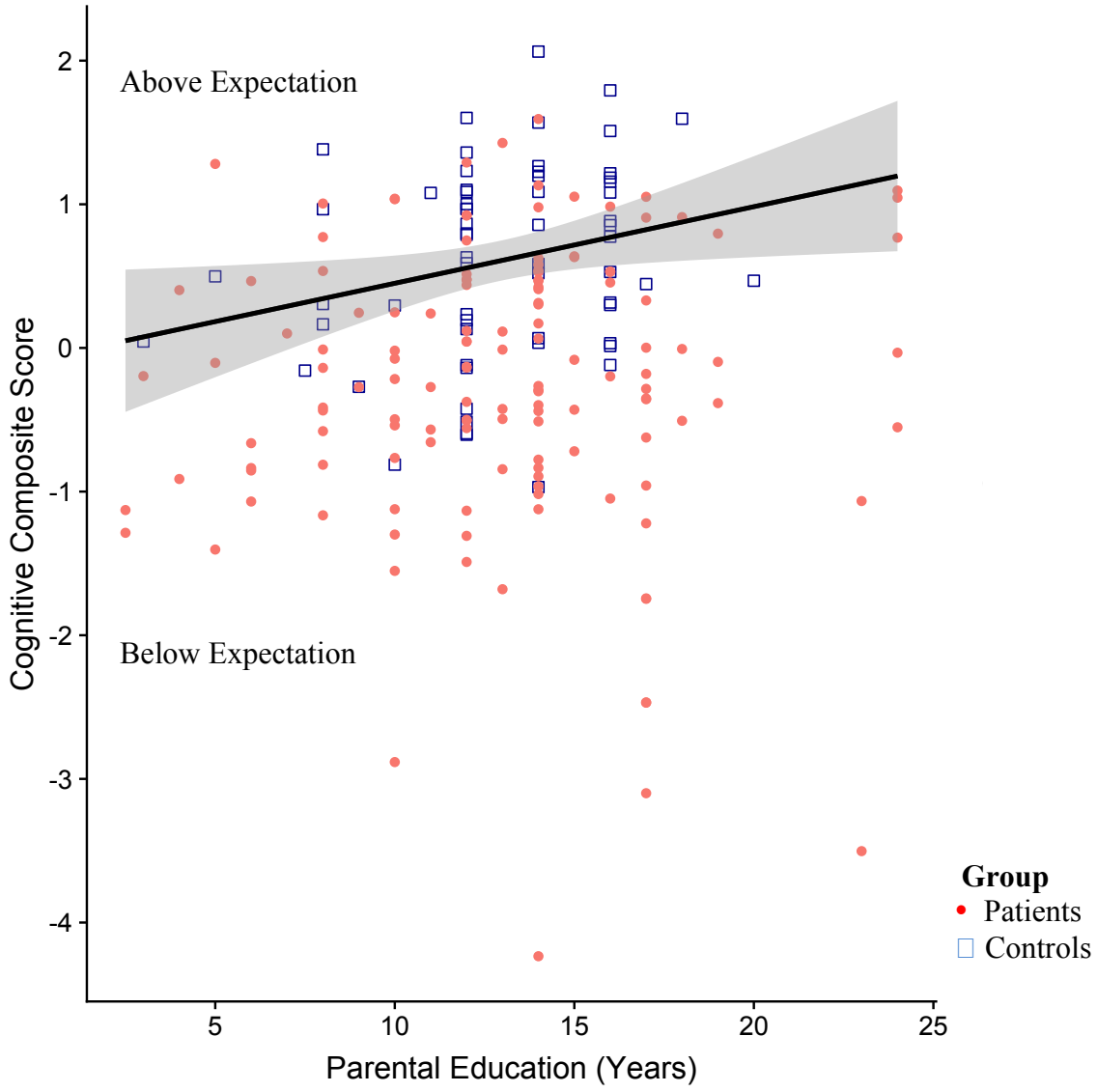

Figure 2. Cognitive Composite Score Predicted by Parental Education (Highest Level Achieved by Either Parent). The curved lined represents the 90% confidence interval of the regression line, with participants falling within the lower bounds excluded from analysis. Participants falling above the regression line performed above the expectations based on their parents' highest level of education, and those falling below the regression line performed below expectations.

WRAT-3 Reading Scores and Parental Education as Predictors

Assumptions of multiple linear regression among healthy controls with both WRAT-3 Reading and parental education set as predictors demonstrated that residual values were normally distributed (based on the Normal Q-Q plot), errors were

independent based on a Durbin-Watson test (p = .812), component plus residual plots confirmed that the linearity assumption was met, and there was no evidence of heteroscedasticity based on the non-constant variance score test (p = .75). No outliers were identified in the data.

When both WRAT-3 Reading score and parental education were used in the regression equation to predict the cognitive composite score, the two predictors explained 18.3% of the variance (R^2 = .183, F(2,60) = 6.72, p < .01). Parental education significantly predicted composite z-scores (β = .233, t = 2.0, p = .05), as did WRAT-3 Reading scores (β = .352, t = 3.02, p < .01).

Patient WRAT-3 Reading scores and parental education were applied to the regression equation obtained from the healthy control population to determine whether patients performed above or below the expected cognitive composite score. The regression equation was as follows:

$$Y_i = b_0 + b_1X_{i1} + b_2X_{i2}$$

$$composite\ score_i = -2.700 + .05343\ (WRAT\text{-}3) + .05128\ (Parental\ Education)$$

Based on the linear model with both parental education and reading scores set as predictors, 62.1% (n = 87) of patients failed to perform at the expected level on the cognitive composite score, and 21.4% (n = 30) performed above the expected level. A total of 23 patients (16%) performed within the range of the 95% one-tailed confidence interval and they were therefore not included in either the decrement or no-decrement group. Among controls, 41.3% (n = 26) failed to perform at the expected level, and 58.7% (n = 37) performed above the expected level.

Patient classification based on the combination of WRAT-3 Reading and parental

education as predictors will be used for subsequent analysis of functional and clinical validity of the non-decrement patient subtype, as this regression model is both the most comprehensive (as it includes two predictors), and it also has the smallest Akaike Information Criterion (AIC) value (WRAT-3 Reading as a predictor AIC = 149.65; parental education as a predictor AIC = 130.99; WRAT-3 Reading and parental education as predictors AIC = 124.09).

Comparison with Keefe et al., (2005): Proportion of Cognitive Decrement

A Fisher's Exact test was conducted to compare the frequency of patients who have/ have not experienced a cognitive function decrement between the current study and Keefe et al., (2005), according to the regression model with both WRAT-3 Reading scores and parental education set as predictors. Results indicated that there was a significant association between the research study and whether or not patients were classified as having experienced a cognitive decrement $p < .001$ (see Table 3). Calculation of the odds ratio demonstrated that if a participant was in the Keefe et al., (2005) study, they were 18 times more likely to have experienced a cognitive function decrement than if they had participated in the current study.

Table 3

Contingency Table Showing the Proportion of Participants that were Classified as Having Experienced a Cognitive Function Decrement in the Current Research Study and Keefe et al. (2005).

		Research Study		
		Keefe et al. (2005)	Current Study	Total
Cognitive Decrement?	Yes	105	87	214
	No	2	30	32
	Total	107	117	246

Functional and Clinical Validity of the Non-Decrement Subtype

Given the low prevalence (n = 30) of the non-decrement patient group, and to ensure demographic similarity with comparison subgroups, these patients' age range and sex proportion were used as criteria in assigning controls to the non-decrement group, controls to the decrement group, and patients to the decrement group for statistical analyses. Table 4 shows the descriptive statistics for all four study groups, after classification based on age and sex matching. Patients and control subgroups did not differ significantly with respect to age, sex distribution, years of parental education, or proportion who learned English as their first language. Patients in the cognitive decrement subgroup had significantly lower WRAT-3 Reading scores as compared to healthy controls in the non-decrement subgroup ($t(118) = -3.08$, $p < .01$). High school completion rates were equivalent in non-decrement patients and decrement patients. However, high school completion rates were lower among patients with a decrement compared to controls with a decrement (FET $p < .05$) and controls without a decrement (FET $p < .05$). High school completion rates were also lower among patients without a decrement compared to controls with a decrement (FET $p < .05$) or without a decrement (FET $p < .01$). As well, patients with a cognitive decrement had significantly lower composite *z*-scores compared to patients without a cognitive decrement ($t(115) = -11.24$, $p < .01$), and controls without a cognitive decrement ($t(118) = -14.26$, $p < .01$). Further, patients without a cognitive decrement had significantly higher composite *z*-scores than controls who have experienced a decrement ($t(48) = 6.16$, $p < .01$). Lastly, controls without a cognitive decrement had significantly higher composite *z*-scores compared to controls with a cognitive decrement ($t(51) = -8.98$, $p < .01$).

Table 4

Demographic and Clinical Variables for Patients and Controls Classified as Decrement or No Decrement According to Parental Education and WRAT-3 Reading as Predictors of Cognitive Performance

	SCZ with Decrement (n = 87)	SCZ without Decrement (n = 30)	Controls with Decrement (n = 20)	Controls without Decrement (n = 33)	Test Statistic
Age, yrs *(M, SD)*	41.74 (9.17)	37.87 (10.32)	42.95 (11.56)	37.73 (12.32)	F (3, 166) = 2.130
Sex (males %)	68.9%	46.7%	80.0%	72.7%	FET = 7.31
WRAT-3 Reading Score Raw *(M, SD)*	46.49 (5.82)	46.40 (6.89)	48.75 (3.29)	50.00 (4.81)	F (3, 166) = 3.815 *
Parental Education *(M, SD)*	13.30 (4.17)	11.8 (4.03)	13.18 (3.03)	12.58 (3.20)	F (3, 165) = 1.238
High School Completion (%)	67.8%	73.3%	100%	96.7%	FET = 20.812**
First Language English (%)	85.0%	73.3%	75.0%	72.7%	$\chi 2$ (3) = 3.51
Composite z-score (M, SD)	-0.67 (0.88)	0.74 (0.46)	-.06 (0.45)	1.01 (0.41)	F (3, 166) = 60.64**

Note: FET = Fisher's Exact Test; M = mean; SCZ = schizophrenia; SD = standard deviation; WRAT-3 = Wide Range Achievement Test – 3rd Ed.
** $p < .001$ * $p < .05$

To assess whether MSIF global scores differed significantly between groups, assumptions for a one-way ANOVA were tested, setting MSIF scores as the dependent

variable, and group (i.e., i) schizophrenia with decrement; ii) schizophrenia without decrement; iii) HC with decrement; iv) HC without decrement) as the independent variable. Bartlett's test indicated that the variances in the four groups did not differ significantly (p = .11). There was no indication of outliers in the MSIF data. Visual inspection of Q-Q plot indicated that residuals of MSIF scores showed mild deviation from normality, yet there was not strong evidence that transformation was required because the hypothesis that $\lambda = 1$ was not rejected (p = .88) (based on the PowerTransform function carried out in R Studio, which generates a maximum-likelihood estimation of the power λ most likely to normalize the variable). Taken together, the data appeared to fit the ANOVA model.

The univariate F ratio showed a significant group difference for the MSIF scores. Additional testing of group means was carried out using Tukey HSD testing, adjusted for multiple comparisons. Results indicated that MSIF scores were significantly higher among patients who have experienced a cognitive decrement as compared to patients who have not experienced a cognitive decrement, as well as both control groups. Patients who have not experienced a cognitive decrement, however, had significantly higher MSIF scores than both control groups, suggesting that they remained at a functional disadvantage relative to controls, despite their functional advantage relative to patients who have experienced a decrement. The two control groups did not differ in terms of their MSIF scores (see Table 5).

To assess the effect of cognitive decrement on symptom severity (i.e., PANSS Positive and Negative symptom T scores) among the patients with schizophrenia, assumptions for MANOVA were first assessed. All observations were independently

distributed and symptom severity scores were continuous. Based on Mahalanobis distance (*df* = 1, cut off = 10.828), there were no multivariate outliers among the residuals (all values were less than or equal to 10.8). An assessment of multivariate normality was conducted in R Studio using Mardia's multivariate test of normality. Based on the residuals of the PANSS positive and negative *T* scores, the skewness (Mardia's = 5.48, $p = .24$) and kurtosis (Mardia's = -.09, $p = .93$) estimates indicated that the distribution of residuals was multivariate normal. Visual inspection of a chi-square Q-Q plot suggested a mild deviation from normality. Box's test of equality of covariance matrices was not violated (M = .373, F(3, 48899.60) = .121, $p = .95$).

The MANOVA, with patient group (i.e., patient group with decrement, patient group without decrement) set as the independent variable, and the PANSS Positive and Negative *T* scores set as dependent variables, showed a significant difference between patient groups in terms of symptom severity ($\lambda = .94$, F (2, 114) = 3.92, $\eta_P^2 = .064$, $p = .023$). Follow-up one-way ANOVAs indicated that groups did not differ significantly in terms of PANSS positive symptoms severity (p = .09), but the patients with a cognitive decrement reported significantly greater PANSS negative symptom severity relative to the group who had not experienced a cognitive decrement (F(1,115) = 6.24, $\eta_P^2 = .052$, $p = .014$) (Table 5).

Table 5

Community Independence and Clinical Variables among the Subgroups with and without Cognitive Decrements

Variable	1. SCZ with Decrement (n = 87)	2. SCZ without Decrement (n = 30)	3. Controls with Decrement (n = 20)	4. Controls without Decrement (n = 33)	Statistic	Post hoc
MSIF Global Scores, *(M, SD)*	4.68 (0.99)	3.93 (1.14)	2.10 (1.37)	1.58 (1.03)	$F(3,166) = 81.67^{**}$	1>2,3,4 2>3,4 3=4
PANSS Positive *T (M, SD)*	50.55 (8.74)	47.37 (9.00)	n/a	n/a	Wilk's $\lambda = .94^{*}$	1=2
PANSS Negative *T (M, SD)*	46.89 (9.55)	41.93 (8.76)	n/a	n/a	Wilk's $\lambda = .94^{*}$	1>2

Note: MSIF = Multidimensional Scale of Independent Functioning; PANSS = Positive and Negative Syndrome Scale; SCZ = schizophrenia.
** $p < .001$

Functional and Clinical Validity of the "Truly Normal" Average-Range Non-Decrement Subtype

Clinical and demographic characteristics of the average-range (AR) patient and control subgroups are presented in Table 6. Groups did not differ with respect to age. AR decrement patients had a significantly higher proportion of males compared to the AR non-decrement patients (FET $p < .05$), but the AR decrement patients did not differ from the AR decrement and non-decrement control groups in terms of sex distribution. The non-decrement AR patients had a significantly higher proportion of females compared to the non-decrement AR controls (FET $p < .05$), and compared to the controls who experienced a cognitive decrement in terms of sex distribution. (FET $p < .05$)

To assess whether MSIF global scores differed significantly between groups, assumptions for a one-way ANOVA were tested, setting MSIF scores as the dependent variable, and group (i.e., i) AR schizophrenia with decrement; ii) AR schizophrenia without decrement/ "truly normal"; iii) AR control with decrement; iv) AR control without decrement) as the independent variable. Bartlett's test indicated that the variances in the four groups differed significantly ($p = .03$). There was no indication of outliers in the MSIF data. Visual inspection of Q-Q plot indicated that residuals of MSIF scores show some deviation from normality. Due to violations of homogeneity of variances, and deviation of residuals from normality, data were analyzed using a non-parametric Kruskal-Wallis test to compare the effect of group (i.e., AR patients with decrement, AR patients without decrement, AR controls with decrement, and AR controls without decrement) on community outcome (i.e., MSIF global scores), with post-hoc Mann-Whitney tests conducted with Bonferroni correction.

MSIF scores were significantly affected by participant group ($H(3) = 30.26$, $p < .001$). Mann-Whitney tests were used to follow up on this finding based on the following comparisons: i) AR decrement patients vs. AR non-decrement patients (i.e., "truly normal"); and ii) AR non-decrement patients (i.e., "truly normal") vs. AR non-decrement controls, with only these select Mann-Whitney tests chosen to reduce the Type I error rate while addressing the primary study aims, and a Bonferroni correction applied with effects reported at a .025 level of significance (.05/2).

Results indicated that MSIF scores did not differ between the AR decrement patient group and the AR non-decrement patient group ($U = 305.50$, $p > .05$, $r = -.07$). However, AR non-decrement patients reported significantly higher MSIF scores as

compared to the AR non-decrement controls ($U = 11.50$, $p = .012$, $r = -.57$), suggesting poorer community independence among "truly normal" patients compared to "truly normal" control participants (Table 6).

To assess the effect of cognitive decrement on symptom severity among patients performing within the average range, assumptions for MANOVA were first assessed. All observations were independently distributed and symptom severity scores were continuous. Based on Mahalanobis distance ($df = 1$, cut off = 10.828), there were no multivariate outliers among the residuals (all values were less than or equal to 10.2). An assessment of multivariate normality was conducted in R Studio using Mardia's multivariate test of normality. Based on the residuals of the PANSS positive and negative T scores, the skewness (Mardia's = 1.84, $p = .76$) and kurtosis (Mardia's = .18, $p = .85$) estimates indicated that the distribution of residuals was multivariate normal. Visual inspection of a chi-square Q-Q plot suggested a mild deviation from normality. Box's test of equality of covariance matrices was not violated (M = 3.04, F(3, 6546.59) = .950, $p = .42$).

A MANOVA was performed with patient group (i.e., AR patient group with decrement, AR patient group without decrement) set as the independent variable, and the PANSS Positive and Negative *T* scores set as dependent variables. Results indicated that AR patients who have experienced a cognitive decrement do not differ from AR patients without a cognitive decrement (i.e., "truly normal") with respect to their self-reported severity of positive or negative symptoms (F(1, 62) = .809, $\eta_P^2 = .025$, $p = .45$) (see Table 6).

Table 6

Demographic, Community Independence, Clinical Variables among the Average-Range Subgroups with and without Cognitive Decrements

Variable	1. SCZ AR with Decrement (n = 52)	2. SCZ AR without Decrement (n = 13)	3. Controls AR with Decrement (n = 18)	4. Controls AR without Decrement (n = 6)	Statistic	Post hoc
Age *(M, SD)*	40.85 (9.82)	40.15 (11.34)	43.78 (11.65)	46.50 (11.57)	$F_{(3,85)}$ = .855	n/a
Sex (males %)	69.2%	30.7%	77.7%	100%	FET = 10.72**	
MSIF Global Scores, *(M, SD)*	4.42 (1.00)	4.23 (.73)	2.11 (1.45)	2.17 (1.60)	H(3) = 30.26**	1=2 2>4
PANSS Positive *T (M, SD)*	48.79 (8.01)	50.15 (8.06)	n/a	n/a	Wilk's λ = .975 (p = .45)	n/a
PANSS Negative *T (M, SD)*	45.90 (8.79)	43.08 (5.79)	n/a	n/a	Wilk's λ = .975 (p = .45)	n/a

Note: FET = Fisher's Exact Test; MSIF = Multidimensional Scale of Independent Functioning;
PANSS = Positive and Negative Syndrome Scale.
** $p < .001$ * $p < .05$

Post-Hoc Analysis of Functional and Clinical Implications of Above Average-Range, Non-Decrement Patients

Given that non-decrement patients reported less dependency on the MSIF and less severe negative symptoms on the PANSS compared to decrement patients when the entire sample was combined (first analysis), but not when only AR patients were assessed (second analysis), post-hoc analyses were conducted to determine if perhaps the above-

AR patients who were not included in the second analysis were driving the finding in the first analysis. A total of 12.1% of patients were classified as above average-range (i.e., composite z-score > .67) without having experienced a decrement. Above-AR patients without a cognitive decrement (MSIF Mean = 3.71, SD = 1.36) showed a functional advantage relative to AR patients with a cognitive decrement (MSIF Mean = 4.42, SD = 1.0) (U = 300.5, r = -.25, p = .041). AR patients with and without a cognitive decrement, and above-AR patients without cognitive decrement, however, all remained functionally disadvantaged compared to cognitively NR and above-NR controls (ps < .05).

Further, above-AR patients without a cognitive decrement showed a clinical advantage relative to AR patients with a decrement. Specifically, above-AR non-decrement patients reported a reduced severity of negative symptoms on the PANSS (Mean = 41.2, SD = 10.59 relative to AR patients with a decrement (Mean = 45.9, SD = 8.79) (U = 306.5, r = -.22, p = .059). Notably, however, this finding was only approaching significance.

Prevalence of Normal/ Non-Decrement Patients in Studies 1 and 2

Based on findings from Studies 1 and 2, the prevalence of cognitive normality/ lack of cognitive decrement varies depending on the criteria applied. Specifically, prevalence rates vary from 9.3% to 48%, depending on the classification used (See Figure 3).

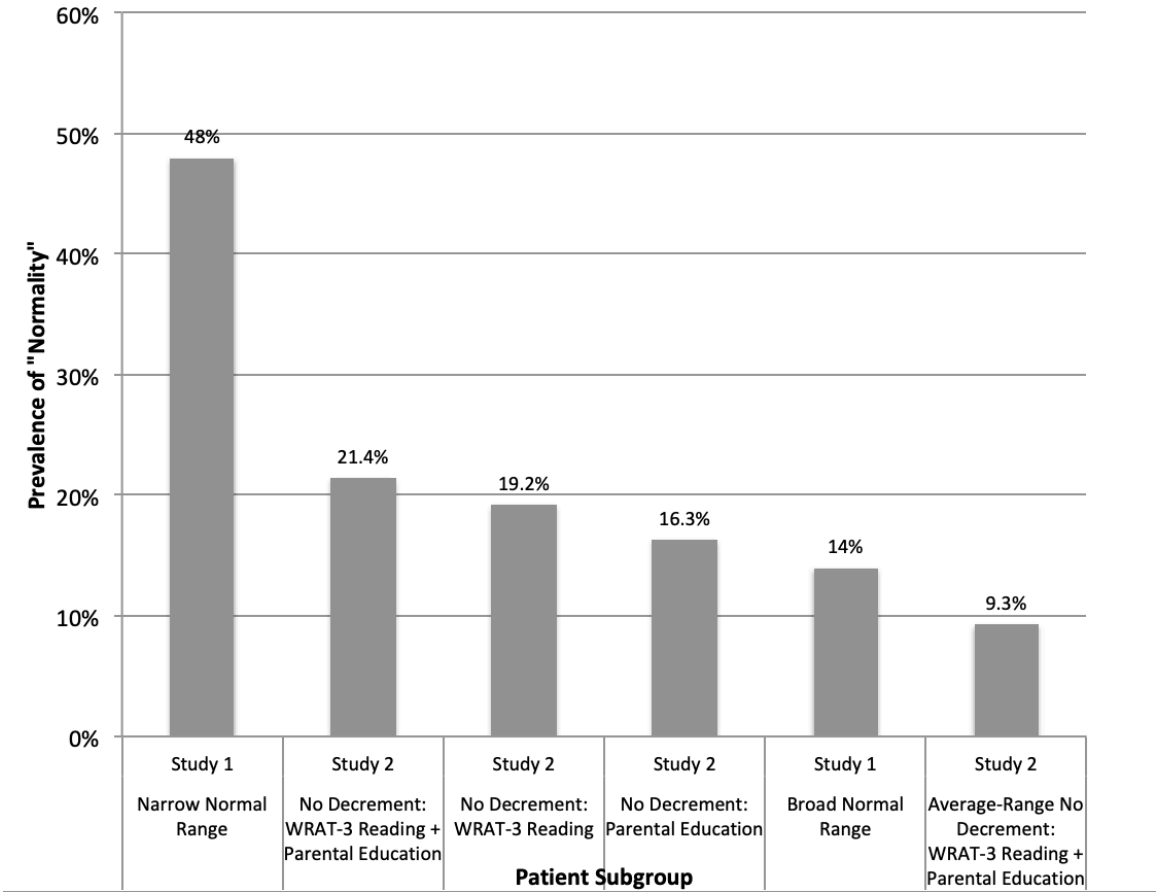

Figure 3. Prevalence of patients meeting criteria for cognitive normality according to two distinct classification methods (Study 1) and prevalence of patients who did not experience a cognitive decrement based on predictive models (Study 2).
Note: WRAT-3 = Wide Range Achievement Test – 3rd Ed.

Summary

Study 2 evaluated a cognitive decrement algorithm (Keefe et al., 2005) and its clinical and functional validity among 156 patients and 74 controls. Following methods by Keefe et al., (2005), a cognitive decrement was defined as current cognitive performance falling below expected levels based on estimates of premorbid intellectual ability (e.g., parental education and reading scores). Patients were classified as having average-range cognition with a decrement (37.1%), average-range cognition without a decrement (9.3%), and above-average range cognition without a decrement (12.1%),

confirming the existence of "truly" cognitively normal (or above-average range) patients who show no evidence of a decline relative to premorbid estimates. However, these patients were relatively rare (prevalence of 9-12%), and less common than some previous estimates. Average-range patients without a decrement did not show a functional (i.e., MSIF scores) or clinical (i.e., PANSS scores) advantage relative to average-range patients demonstrating a decrement. The combination of both *above*-average range cognition and lack of a cognitive decrement, however, conferred a functional advantage among patients (with a finding pertaining to reduced negative symptom severity among this above-average group approaching significance). However, these high-functioning patients remained functionally disadvantaged relative to controls. A discussion pertaining to the findings and implications of Study 1 is presented in the Discussion section, beginning on page 62.

Study 3

As previously discussed, the purpose of this study was to assess the incremental validity of the Breakfast Task in predicting disability relative to standard measures of cognition and symptom severity.

Hypotheses

It was predicted that patients with schizophrenia would perform more poorly than healthy controls on The Breakfast Task. Among the patient group, it was expected that the Breakfast Task would have greater predictive validity of disability relative to standard measures of cognition and symptom severity.

Methods

Participants

Participants in Study 3 included 30 patients (19 males and 11 females) with a diagnosis of schizophrenia (n = 21) or schizoaffective disorder (n = 9) and 37 non-psychiatric controls (20 males and 17 females). Thirty patients were receiving antipsychotic medication at the time of data collection, with 25 patients treated with second-generation drugs. Controls were excluded based on a history of a neurological disorder, major medical condition, psychiatric illness, or developmental disability. Inclusion and exclusion criteria were assessed using a screening questionnaire. Patients were recruited through outpatient settings in southern Ontario, and controls were recruited by postings and advertisements online and within the community.

Measures

The Vocabulary and Matrix Reasoning subtests of the Wechsler Abbreviated Scale of Intelligence, Second Edition were administered to obtain a measure of general intellectual ability (WASI-II; Wechsler, 2011).

Psychiatric symptomatology was assessed using the 24-item Brief Psychotic Rating Scale (BPRS: Overall & Gorham, 1962). BPRS Positive symptom (bizarre behaviour, unusal thought content, disorientation, hallucinations, and suspiciouness) and Negative symptom (blunted affect, motor retardation, emotional withdrawal, self-neglect) subscales were used in statistical analyses.

The World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0: Üstün, 2010) was administered to assess disability. The WHODAS 2.0 is a 36-item self-report instrument that measures functioning in six domains of life: cognition,

mobility, self-care, getting along, life activities, and participation. Summary scores on the WHODAS 2.0 range from 0 to 100, with higher scores representing greater levels of self-reported disability across the six domains. The WHODAS 2.0 Without Work Summary score was used for analysis.

The Breakfast Task

The Breakfast Task (Craik & Bialystok, 2006) is a computerized working memory and executive test that simulates cooking breakfast. A distractor task (i.e., setting a table) is included in order to increase demands on prospective memory and planning. Participants were instructed that their primary goal was to cook five foods (i.e., eggs, sausage, toast, coffee, and pancakes) for the correct specified duration (i.e., avoid over- or under-cooking the food) and to have each of the foods prepared at the same time. Participants were informed that their secondary goal was to complete as much of the table setting as possible. Each of the five foods were shown on the screen with their respective required cook time (i.e., 2.5 minutes, 4.5 minutes, 1 minute, 2 minutes, and 3 minutes), along with a thermometer indicating the cooking progress for each food, and a "start" and "stop" button. Participants used a mouse to click on the start and stop buttons to initiate and end the cooking of each food. In order to have all foods finished cooking at the same time, participants were required to calculate when to start each food, as there was no signal as to when each food item should start its cooking process. The computer program recorded the time that the "start" and "stop" buttons were pressed in order to monitor and calculate the extent of over- or under-cooking. Regarding the table setting task, participants were required to place forks, knives, spoons, and plates arranged at the bottom of the screen in their correct positions for four place settings. Items were placed

around the table by first using the mouse to click on an item with the cursor, and then clicking on its destination on the table. Participants were instructed that once they finished setting the last place at the table, all the settings would drop to the bottom of the screen, and they would be required to set the table again.

The Breakfast Task consists of three conditions with varying complexity: i) one-screen (performed first); ii) two-screen (performed second); and iii) six-screen condition (performed last). The one-screen condition consisted of all of the foods and the table present on the same screen (Figure 4). In the two-screen condition, the table was shown on one screen, whereas the five foods, their cook times and thermometer indicators were all shown together on a second screen. Unlike the one-screen condition, the two-screen condition required switching between two screens. The six-screen condition consisted of one screen showing the table, and five screens each showing a separate food with its respective cook time and thermometer indicator. Relative to the one- and two-screen conditions, the six-screen condition required the most screen switching and is considered the most complex. The one-screen and two-screen conditions were used as practice trials, and the results of the six-screen condition were the focus of the present study and subsequent analyses.

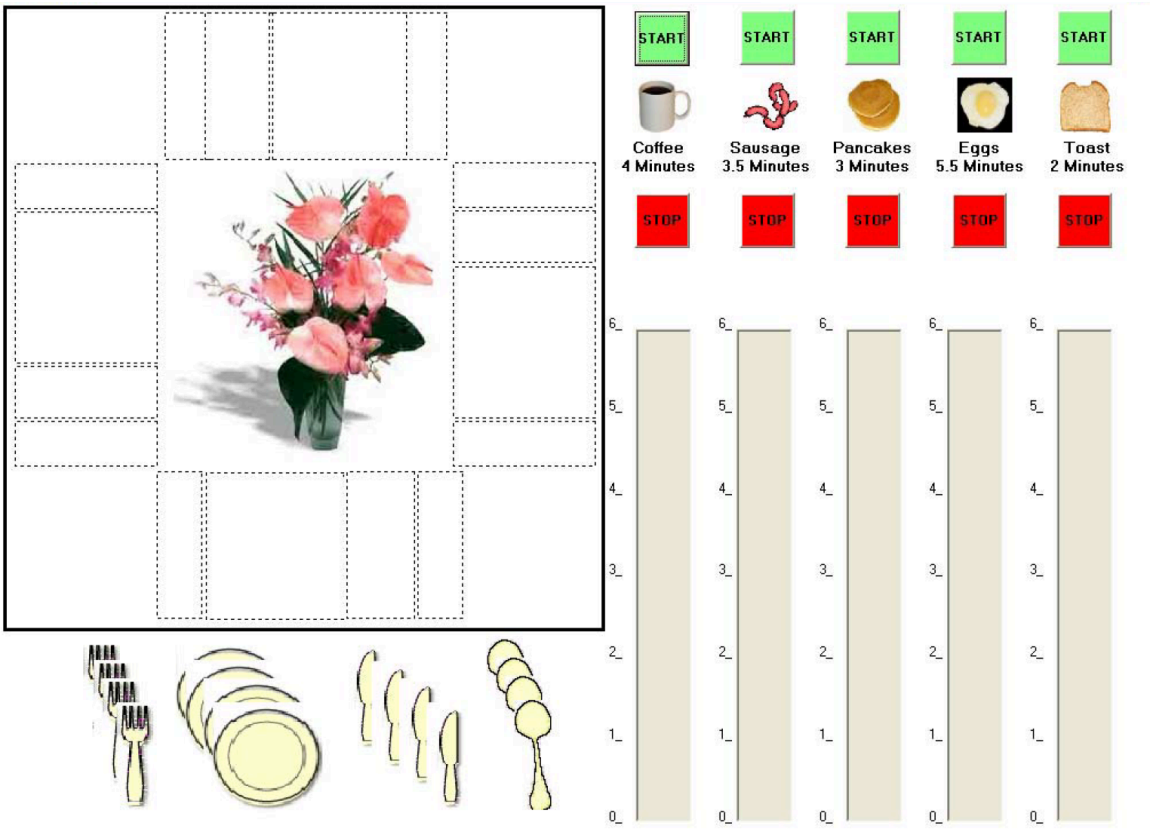

Figure 4. Sample Screen from the One-Screen Condition of the Breakfast Task. This shows the five foods to be cooked, the table to be set, and the cooking indicators for each of the five foods. (Reproduced with permission from the Breakfast Task Manual (Craik & Bialystok, 2004)).

The primary scores obtained from the Breakfast Task were as follows: i) Discrepancy Score (actual time – ideal time); ii) Range Score (time last food stopped – time first food stopped); iii) Deviation Score (deviation from ideal start times); and iv) Times Checked Score (number of times progress of food checked). In addition to the four primary scores, the Number of Table Settings was recorded. Each of the four table settings included a plate, fork, spoon, and a knife. Therefore, sixteen table settings were required to set the entire table; however, since participants were instructed to continue to re-set the table as the task progressed, participants' Number of Table Settings could be greater than sixteen.

The Discrepancy Score reflects prospective memory, with a low score suggesting one was able to disengage from the table-setting task to tend to the food. The Range Score is indicative of planning ability and working memory, with a lower range score reflecting a greater ability to account for the varying cooking times for each food. Craik and Bialystok (2006) suggest that the Range Score is most reflective of the ability to prepare a good meal in real life (i.e., ensuring all foods are ready at the same time). The Deviation Score is indicative of planning ability, with lower scores reflecting a better ability at ensuring foods finished cooking simultaneously. The final primary score, the Times Checked score, is reflective of monitoring and prospective memory. The Number of Table Settings (distractor task) score is associated with executive functions, but not prospective memory (Rose et al., 2015).

Statistical Analyses

To assess group differences in demographic, psychological, intellectual functioning, and disability variables, data were first tested for normality ($p > .05$, Shapiro-Wilk test) and group comparisons were calculated using independent samples t-tests or Mann-Whitney U test, depending on distribution of data. Group differences in sex were assessed with a Chi-Square test, and differences in high school completion were assessed with a Fisher's Exact Test.

Due to non-normality ($p < .05$, Shapiro-Wilk test) of the four primary Breakfast Task Six-Screen Condition scores, they were log transformed in order to perform independent samples t-tests. The log transformation, however, did not result in a normal distribution among all of the scores. The scores on these measure were therefore analyzed using non-parametric Mann-Whitney U tests, setting Group (i.e., Patient, Healthy

Control) as the independent variable, and scores on the Breakfast Task (i) Discrepancy Score; ii) Range Score; iii) Deviation Score; and iv) Times Checked Score) as the dependent variables. The Number of Table Settings variable was normally distributed ($p > .05$, Shapiro-Wilk test) and an independent samples t-test was therefore conducted to assess for group differences.

Among the patient group, associations between scores on the Breakfast Task and clinical (i.e., BPRS Positive and Negative Symptoms) and intellectual functioning (i.e., WASI-II 2 subtest IQ) variables were calculated using Spearman's rho (two-tailed).

A hierarchical regression was carried out among patients with schizophrenia with predictors entered in the following order: i) BPRS Positive and Negative scores; ii) WASI-II 2-subtest IQ-scores; and iii) Breakfast Task Six-Screen condition primary scores that differ significantly between patient and control groups, with the WHODAS 2.0 Summary (Without Work) Scores set as the dependent variable.

Results

Demographic characteristics of the patient group and comparison controls are presented in Table 7. The groups did not differ significantly in age, sex distribution, frequency of English as the first language, rates of employment, or high school completion. In terms of intellectual functioning, groups did not differ in their WASI-II 2-subtest IQ scores ($p = .089$). Groups differed in terms of their self-reported levels of disability on the WHODAS 2.0 Summary Without Work Scores ($U = 186.5$, $p < .01$, $r = -.55$; large effect size).

Table 7

Demographic and Clinical Characteristics of Patients and Controls

	Schizophrenia (n = 30) Mean (SD)	Controls (n = 37) Mean (SD)
Demographic Variables		
Age, years (Mean, SD)	46.0 (9.5)	45.6 (9.0)
High school completion, n (%)	24 (80%)	34 (92%)
Sex (males), n (%)	19 (63%)	20 (54%)
First language English, n (%)	28 (93%)	29 (78%)
Employment, n (%)	12 (40%)	18 (49%)
Clinical Characteristics		
BPRS Positive Symptoms	11.7 (2.5)	N/A
BPRS Negative Symptoms	9.5 (1.5)	N/A
Intellectual Functioning		
WASI-II 2-Subtest IQ	97.2 (16.5)	104.0 (15.2)
Disability Scores		
WHODAS 2.0	**28.6 (13.1)	**11.5 (12.4)

Note. BPRS: Brief Psychiatric Rating Scale; WASI-II Two-Subtest: Wechsler Abbreviated Scale of Intelligence, Matrix Reasoning and Vocabulary; WHODAS 2.0: WHO Disability Assessment Schedule 2.0. ** $p < .01$ * $p < .05$

Group Differences on The Breakfast Task

On the Breakfast Task, patients performed significantly worse than controls on the Range Score (i.e., their ability to ensure all five foods were completed at the same time) (U = 243, p = .001, r = -.43; medium effect size). As well, patients completed significantly fewer table settings relative to controls (t(65) = -6.5, p = .001, d = 1.5; large effect size). Groups did not differ in terms of their performance on the remaining Breakfast Task Scores (i.e., Discrepancy, Deviations, and Checked Scores) (see Table 8).

Table 8

Breakfast Task Performance

Breakfast Task Scores (Six-Screen Condition) (Mean, SD)	Patients (n = 30)	Controls (n = 37)	p	Effect Size (r)
Range	35.0 (47.0)	26.4 (54.9)	.001	.42
Discrepancy	29.0 (43.6)	16.3 (15.2)	.830	.04
Deviation	24.6 (24.9)	35.6 (68.9)	.685	.05
Times Checked	21.4 (5.3)	21.6 (6.2)	.909	.01
Number of Table Settings	18.7 (9.5)	32.8 (8.4)	.001	*1.5

Note: *Cohen's d

Association Between Scores on the Breakfast Task, Intellectual Functioning, Symptom Severity, and Disability

Intellectual functioning and disability correlates emerged in relation to Breakfast Task Six-Screen Condition performance scores among the group with schizophrenia (see Table 9). Better performance based on the Range, Deviation, and Number of Table

Settings Scores scores was associated with higher levels of intellectual functioning (r_s = -.53, p = .006; r_s = -.51, p = .005, and r_s = .55, p = .002, respectively). Better performance based on the Range and Deviation scores was related to lower levels of self-reported disability (r_s = .40, p = .038; r_s = .49, p = .006, respectively). No significant correlations emerged between Range and Deviation scores and positive or negative symptom severity. As well, no significant correlations emerged between the Breakfast Task Discrepancy and Times Checked scores, and symptom, intellectual functioning, or disability variables. Exploratory analysis revealed that intellectual functioning did not correlate with WHODAS 2.0 disability scores (r_s = -.06, p = .76) or BPRS positive (r_s = -.27, p = .16) or negative (r_s = -.24, p = .20) symptoms.

Table 9

Correlates of Breakfast Task Scores Among the Patient Group

	BPRS Positive Symptoms	BPRS Negative Symptoms	WASI-II IQ	WHODAS 2.0 Summary Without Work
Breakfast Task				
Range	+.06	+.10	**-.53	*+.40
Discrepancy	+.39	+.46	-.31	-.08
Deviation	+.16	+.05	**-.51	**+.49
Times Checked	-.13	-.10	-.16	+.04
Number of Table Settings	-.08	-.18	**.55	-.27

Note: BPRS: Brief Psychiatric Rating Scale; WASI-II Two-Subtest: Wechsler Abbreviated Scale of Intelligence, Matrix Reasoning and Vocabulary; WHODAS 2.0: WHO Disability Assessment Schedule 2.0.
All correlation values are Spearman's correlation coefficients.
* $p < .05$ ** $p < .01$

Incremental Validity of the Breakfast Task

Assumptions for regression were assessed. Based on Mahalanobis distance (*df* = 4, cut off = 18.47), no multivariate outliers were identified amongst the residuals. Overall, only one case had extreme influence (Cook's distance value = 1.060), and extreme leverage (hat value = .735), with a Leverage cut-off value of .60 (((k+1)/n) x3) (Stevens, 2002). The hierarchical regression analysis was conducted twice, first with the outlier case included, and then with the outlier case excluded.

Assumptions for multiple regression were assessed for the model that included the outlier case. There was no multicollinearity (VIF range from 1.0 – 1.4), there was independence of errors (Durbin-Watson = 1.570), the residuals were normally distributed, and there was no evidence of heteroscedasticity. Incremental validity of the Breakfast Task Six-Screen Condition Range score, relative to symptom and intellectual functioning data was evaluated using hierarchical regression. First, the WHODAS 2.0 Summary Without Work score was regressed on a block of symptom variables consisting of the BPRS Positive and Negative Symptoms. This yielded a non-significant F Ratio (F(2,22) = .66, ns) and accounted for 5.7% of the variance in WHODAS 2.0 scores. Next, the WASI-II 2-subtest IQ estimate was entered into the model. The addition of IQ into the model failed to add significantly to the validity (F_{change} (1,21) = .018, ns). Finally, the Breakfast Task Range scores were entered into the model, which resulted in a significant increase in validity (F_{change} (1,20) = 4.75, p = .04). The complete model accounted for 23.9% of the variance in WHODAS 2.0 Summary Without Work scores (see Table 10).

Table 10

Disability Scores Regressed Hierarchically on Symptoms, Intellectual Functioning, and Breakfast Task Performance Among Patients with Schizophrenia

Predictor Variables	Step 1 Beta	Step 2 Beta	Step 3 Beta
BPRS Positive Symptoms	.186	.175	.215
BPRS Negative Symptoms	-.137	-.144	-.092
WASI-II Two-Subtest IQ	--	-.031	.234
Breakfast Task Range Scores	--	--	.492
R^2	.057	.058	.239
R^2 Change	.057	.001	.181

Note. BPRS: Brief Psychotic Rating Scale; WASI-II: Wechsler Abbreviated Scale of Intelligence. * $p < .05$

Assumptions for multiple regression were assessed for the model that excluded the outlier case. There was no multicollinearity (VIF range from 1.0 – 1.5), there was independence of errors (Durbin-Watson = 2.3), the residuals were normally distributed, and there was no evidence of heteroscedasticity.

When the WHODAS 2.0 Summary Without Work score was regressed on a block of symptom variables consisting of the BPRS Positive and Negative Symptoms, this yielded a non-significant F Ratio ($F(2,21) = .66$, ns) and accounted for 6.0% of the variance in WHODAS 2.0 scores. Next, the WASI-II 2-subtest IQ estimate was entered into the model. The addition of IQ into the model failed to add significantly to the validity ($F_{change}(1,20) = .072$, ns). Finally, the Breakfast Task Range scores were entered into the model, which resulted in a marginally significant increase in validity (F_{change}

(1,19) = 4.21, p = .054). The complete model accounted for 23.3% of the variance in WHODAS 2.0 Summary Without Work scores.

Summary

Study 3 assessed the utility of the functionally relevant Breakfast Task (Craik & Bialystok, 2006) in predicting disability relative to standard measures of cognition (i.e., WASI-II) and symptom severity (i.e., BPRS) among 30 patients and 37 controls. Results showed that on the Breakfast Task, patients were impaired relative to controls in their ability to ensure all of the foods finish cooking at the same time (Range Score, reflecting reflects planning ability and working memory), and they set fewer places at the table compared to controls. Further, performance on the Breakfast Task increased the ability to predict disability (i.e., WHODAS scores) beyond that provided by standard cognitive (i.e., WASI-II) and symptom (i.e., BPRS) measures. A full examination of the findings and implications of Study 3 appears in the following Discussion section.

Discussion

The concept of cognitive normality in patients with schizophrenia is a controversial one. It has long been understood that cognitive impairment is a core feature of the disorder; yet, subsets of patients, whose performance on standardized cognitive tasks overlaps with that of community controls, are repeatedly identified in the literature. The prevalence of cognitive normality, with reported rates ranging from 0% (Wilk et al., 2005) to 55% (Bryson et al., 1993), is unclear, as are the clinical and functional implications of this subgroup. The aim of the present investigation was to estimate the prevalence of cognitive normality corresponding to narrow, broad, and non-decrement definitions, to examine the clinical and functional validity of each definition, and to

examine the utility of a naturalistic task of executive functioning (the Breakfast Task) in predicting disability. Overall, the results suggest that the prevalence of cognitive normality is a byproduct of the definition used. They point towards some functional validity of classifying above-average range, non-decrement patients as cognitively normal, and they also suggest that the Breakfast Task may be a promising tool to improve our understanding and assessment of disability.

Approaches to Defining Cognitive Normality

Three different definitions of cognitive normality were applied to two samples of patients with schizophrenia and controls: i) a narrow (IQ) definition (Study 1); ii) a broad (MCCB) definition (Study 1); and iii) a non-decrement, average-range definition (Study 2). Critically, the same inclusion and exclusion criteria were applied to participants in Studies 1 and 2. The review of prevalence rates reported in the existing literature may be confounded by the heterogeneity that is likely inherent in the various research studies. Applying definitions of cognitive normality to study samples that are relatively homogenous was an attempt to reduce the impact that heterogeneity of study samples may have on our ability to compare prevalence rates. Findings from the current study indicated that the reported prevalence of cognitive normality among patients ranges from 9.3% (non-decrement, average range), to 14% (broad definition), to 48% (narrow definition). Therefore, even when the study samples are relatively homogenous, as in the current study, the wide range of prevalence rates still emerges. This finding suggests that the wide range of prevalence rates of cognitive normality reported in the literature (i.e., 55% (Bryson et al., 1993) to 0% (Wilk et al., 2005)), is likely a byproduct of the definition of normality.

The conceptualization of cognitive normality differs between the three definitions used in the current studies. The commonality between the broad and narrow range definitions used in Study 1 is that they rely on population norms as an indication of whether or not patients perform within expected limits. The narrow (IQ) definition, while a commonly used measure of defining normality (Kremen et al., 2001), has been criticized for not capturing the true breadth of cognitive impairment expressed in schizophrenia (Gray, McMahon, & Gold, 2013; Vaskinn et al., 2014; Wilk et al., 2005). As predicted, the narrow definition of cognitive normality captured the largest proportion of patients, with 48% meeting the IQ criterion for normality. While these patients were seemingly intellectually preserved, this definition has not captured cognitive weaknesses that may have emerged on more broad-based and inclusive measures. That is, fewer patients emerged as cognitively normal when the broader MCCB criterion was applied – 14%. Previous research using the MCCB to classify normality in schizophrenia found no subtest profile differences between cognitively normal patients and controls (Muharib et al., 2014), suggesting that our broad-based definition is more stringent than the narrow definition and does not fail to capture any cognitive weaknesses that may have emerged on individual subtests. Therefore, when relying on population norms, the findings of the current study suggest that a greater level of stringency in the definition of normality is related to a reduced estimate of normality.

The definition of cognitive normality used in Study 2 differed from those used in Study 1, as it directly indexed current cognitive performance against premorbid estimates based on reading scores and parental education. Notably, all three regression equations predicting current cognitive composite scores based on reading scores and parental

education were statistically significant (or approaching significance); however, these models accounted for only 5.9% to 18.3% of the variance in cognitive composite scores. Parental education and reading scores explained only 5.9% and 11.5% of the variance, respectively, indicating that approximately 85 – 90% of the variance remained unexplained. When these two predictors were combined in a regression equation, they accounted for 18.3% of the variance in cognitive composite scores, indicating that nearly 80% of the variance continued to remain unexplained. This suggests that despite the popular use of parental education and oral reading as predictors of premorbid intellectual functioning, there remains a substantial amount of unexplained variance when they are used to predict current intellectual functioning. Results pertaining to this approach to defining a cognitive function decrement should therefore be interpreted with this limitation in mind. Keefe et al. (2005) did not report R^2 values associated with their regression equations, and therefore a comparison between their findings and the current results cannot be performed.

In Study 2, patients were classified as "truly" cognitively normal if they i) performed within the average-range based on a composite cognitive score, and ii) reached the expected level of cognitive functioning based on premorbid estimates. In study 2, 9.3% of patients met these criteria. Consistent with findings by Keefe et al. (2005) and with conclusions drawn in a review of the literature by Harvey and Keefe (2009), when cognitive functioning is compared against the expected level of cognitive function, this leads to the greatest reduction in estimates of normality. Therefore, the current findings from Studies 1 and 2 are consistent with the study hypotheses pertaining to the prevalence rates of normality, with the lowest proportion of cognitive normality (9.3%)

emerging when performance was directly indexed against presumed premorbid functions. In conclusion, the level of stringency of the definition of cognitive normality, and reliance on population norms versus premorbid functions, leads to differences in estimates of normality.

Functional and Clinical Validity of Cognitive Normality

To determine whether the broad or narrow definitions of cognitive normality used in Study 1 provided greater functional or clinical validity, normal-range patients based on both classifications were compared to below-normal range patients, and controls. Regardless of the criterion applied (i.e., broad or narrow), cognitively normal patients remained functionally disadvantaged relative to cognitively normal controls. As well, however defined, cognitively normal patients demonstrated no advantage in functionality or clinical symptom severity relative to cognitively impaired patients. Overall, results suggested that the varying definitions of cognitive normality/impairment that rely on population norms do not have implications for the severity of psychotic psychopathology or community independence in treated outpatients.

Given that cognitive impairment is commonly regarded as the determinant of poor functional outcome in schizophrenia (Bowie et al., 2006; Green et al., 2000; Keefe & Harvey, 2012; Kuo et al., 2018; Matza et al., 2006), it would have been reasonable to predict that those who are cognitively normal would have a functional advantage relative to those who are putatively cognitively impaired. However, according to meta-analytic findings by Fett et al. (2011), cognition accounts for only 6% of the variance in community functioning (with a correlation of .25); therefore the role of cognition in functional outcome may be over-emphasized. The lack of clinical advantage conferred by

either definition of cognitive normality is in line with previous studies that reported a lack of association between cognition and symptoms (Ammari et al., 2010; Dibben et al., 2009; Nieuwenstein et al., 2001). The large body of evidence that suggests that cognition may be one of the best predictors of daily functioning cannot be dismissed; yet, the current findings suggest that normal cognition is not sufficient to achieve a level of community independence that is equivalent to that of healthy controls, consistent with previous studies where cognitively normal or above-normal patients remained functionally disabled relative to controls (Heinrichs et al., 2008; Leung et al., 2008a). Investigators may wish to focus future studies on factors that account for unexplained variance in community functioning (e.g., socio-environmental supports, brain network connectivity) (Raphael, 2006; Wojtalik, Smith, Keshavan, & Eack, 2017).

Study 2 found that there is, in fact, of a proportion of patients with schizophrenia who perform in the cognitively normal range and who have not experienced a cognitive decrement, confirming the existence of "truly" normal patients. Among the patients with schizophrenia, 9.3% met these criteria, whereas 37.1% of patients performed in the average range, but have experienced a decrement based on presumed premorbid estimates (i.e., not "truly" normal patients). Results indicated that community independence did not differ between the AR decrement patient group and the AR non-decrement patient group. However, the combination of both *above*-AR cognition and lack of a cognitive decrement, a subset of patients making up 12.1% of the patient sample, conferred a functional advantage relative to AR patients with a cognitive decrement. This is consistent with Heinrichs et al.'s (2008) finding that verbally superior patients showed an advantage in terms of community independence relative to patients scoring below the

superior range. With respect to the functional advantage obtained by the above-AR non-decrement patients, it is critical to note that these patients, as well as the AR non-decrement patients continue to report significantly higher MSIF scores as compared to the AR non-decrement controls. These results indicate poorer community independence among "truly" normal or above normal patients compared to "truly" normal controls, again consistent with findings by Heinrichs et al. (2008). This study therefore demonstrated that despite a functional advantage that is conferred by being both cognitively above average and without having a history of a decrement, these patients ultimately remained functionally impaired relative to community controls. This finding is consistent with results from Study 1, and previous studies (Heinrichs et al., 2008; Leung et al., 2008a), where regardless of the classification of cognitive normality, patients remained functionally disadvantaged relative to controls. This finding again highlights that future research may wish to identify factors, apart from cognition, that may be contributing to functional disability in schizophrenia.

With respect to the clinical validity of the decrement classification, results indicated that patients with a cognitive decrement reported greater negative symptom severity relative to patients who have not experienced a cognitive decrement, yet the two groups did not differ in terms of positive symptoms. Previous studies have reported an association between cognition and negative symptoms, but not positive symptoms (Addington, Addington, & Maticka-Tyndale, 1991; de Gracia Dominguez, Viechtbauer, Simons, van Os, & Krabbendam, 2009; Harvey, Koren, Reichenberg, & Bowie, 2006). Using a similar approach to classifying patients as cognitively normal or impaired, Ammari et al. (2010) reported that, much like the current findings, cognitively normal

patients reported a reduced severity of negative symptoms as compared to impaired patients. Given the cross-sectional nature of the current studies, it is not possible to determine the directionality of this relationship between lack of a cognitive decrement and negative symptom severity. However, it is noteworthy that the two definitions of cognitive normality (broad and narrow) in Study 1 were unrelated to symptom severity, whereas the notion of a cognitive decrement/ lack of decrement in Study 2 was related to symptoms. According to a review of the nature of negative and cognitive symptoms by Harvey et al. (2006), these two symptoms may be conceptually independent with separate yet related etiologies, which yields a correlation between them. For instance, pathological changes in separate brain regions due to related underlying white matter pathology may bring about cognitive and negative symptoms. Therefore, the etiology underlying negative symptom expression could be related to the etiology underlying a cognitive function decrement. That is, rather than one symptom causing the other, they may both occur as a result of an association between their respective etiologies. This hypothesis has yet to be tested, but future studies may wish to examine the mechanisms underlying a cognitive decrement, and protective factors that may be at play in those patients who have not experienced a cognitive decrement.

In addition to the functional implications of the above-AR non-decrement group of patients, it is important to also consider that this study has provided evidence that such a subgroup of patients does in fact exist. The existence of this subgroup is inconsistent with findings by Vaskinn et al. (2014), who reported that intellectually superior patients with schizophrenia were impaired on specific cognitive functions relative to healthy controls with similar superior intellectual abilities, suggesting they have experienced a

cognitive decrement. The current finding of an above-average group of patients without a cognitive decrement is, however, in line with other previous studies (Heinrichs et al., 2008; MacCabe et al., 2012). The inconsistent findings between Vaskinn et al. (2014), who reported that superior patients have experienced a decrement, and Heinrichs et al. (2008) and MacCabe et al. (2012), who reported that it is possible to be intellectually superior without having had a decrement, have been attributed to small sample sizes and lack of statistical power in the latter studies (Vaskinn et al., 2014). A challenge inherent in this research is obtaining adequate sample sizes, given the low prevalence in the population of the patient group of interest (i.e., intellectually superior patients with schizophrenia). To elucidate the discrepancies in the literature surrounding the existence of this subgroup of patients, investigators may wish to recruit larger sample sizes to optimize statistical power. As well, the studies to date have been cross-sectional, and as such, conclusions regarding cognitive decrement have been based on estimates, rather than documentation of cognitive decline based on objective cognitive test scores.

Evaluation of Keefe et al.'s (2005) Cognitive Function Decrement Algorithm

Regarding the prevalence rates that emerged from Study 2, when WRAT-3 Reading scores were used as an estimate of premorbid intellectual ability, 69.2% of patients with schizophrenia experienced a cognitive decrement according to their current cognitive performance, and 19.2% of patients performed at or above expected levels, and have therefore not experienced a cognitive decrement. Similar prevalence rates emerged when parental education was used as an estimate of premorbid ability, with 70.9% of patients meeting criteria for a cognitive decrement, and 16.3% of patients performing above expected levels. In the most comprehensive model, with both WRAT-3 Reading

scores and parental education set as predictors of current cognitive performance, 62.1% of patients experienced a cognitive decrement, whereas 21.4% have not.

The preceding proportions differed significantly from those reported by Keefe et al. (2005), who had used the same method to assess for a cognitive decrement. Calculation of the odds ratio demonstrated that if a participant was in the Keefe et al. (2005) study, the odds of them being classified as having experienced a cognitive function decrement was 18 times higher than if they had participated in the current study. To understand the differences between the study findings, it is critical to consider that while the methods were similar, they were not identical. Specifically, Keefe's (2005) cognitive battery was more comprehensive, including multiple measures from each cognitive domain. As well, Keefe et al. (2005) included measures of motor speed; the current study did not. Therefore, Keefe's estimates of current cognitive functioning may be more precise than the estimates generated in the current study. An additional factor that differed between the two studies was inclusion criteria. Keefe et al.'s (2005) study included participants from both outpatient and inpatient clinics, whereas the current study recruited solely from outpatient clinics. This may be an important distinction between the two studies, as there is evidence supporting the association between hospitalization and cognitive decline, in a variety of hospital settings (Mathews, Arnold, & Epperson, 2014). Further, hospitalized patients with schizophrenia performed worse than outpatients on tasks of processing speed and flexibility (Laere, Tee, & Tang, 2018). It may be, therefore, that the inclusion of inpatients in Keefe et al.'s (2005) study resulted in lower overall cognitive performance, compared to the current study that included only outpatients. This could at least partially account for the greater number of patients meeting criteria for a

cognitive decrement in Keefe et al. (2005). Nonetheless, the current findings contradicted the conclusion drawn by Keefe et al. (2005) that cognitive normality in patients with schizophrenia largely represents a decline from premorbid estimates, and that nearly all patients with the disorder have sustained a cognitive decrement.

An important finding pertaining to the cognitive decrement algorithm is the proportion of community controls that meets criteria for a decrement. The proportion of controls demonstrating a presumed cognitive decrement in the current study ranged from 36.5% to 41.3%, depending on the predictors applied to the model. In Keefe et al.'s (2005) study, 30% to 48% of controls met criteria for a cognitive decrement, depending on the predictors applied. Given the nature of regression analyses, approximately half of the sample used to define the regression line will fall below the line, and half will fall above the line. However, this substantial proportion of controls who have experienced a decrement raises issues surrounding the validity of the cognitive decrement algorithm. According to typical estimates of impairment based on one standard deviation below the normal mean, 15% of the general population would be considered impaired, yet the current study and Keefe et al.'s (2005) study have identified a much larger proportion of controls who have had a decrement. Keefe et al. (2005) argued that among healthy controls, falling below the regression line is not necessarily indicative of being "cognitively unhealthy", but rather simply indicates that controls are performing lower than would be expected according to different estimates (e.g., reading scores and parental education). Critically, an inspection of Figures 1 and 2 in Study 2 reveals that controls that show a "decrement" do so to a lesser degree relative to patients, with many control data points appearing to fall within one standard deviation below expectations. Patients'

data points, on the other hand, tend to fall much more than one standard deviation below the regression line. This begs the question: should all scores below the regression line be considered a decrement, or should more stringent criteria be applied? According to Keefe et al. (2005), the answer would likely be that any points below the regression line indicate a cognitive decrement for patients, but not necessarily for controls.

Another critical limitation of the cognitive decrement algorithm is the use of the word "decrement". Neither Keefe et al.'s (2005) study, nor the current study, included longitudinal analyses that allowed for a direct observation of a cognitive decrement. Rather, what the studies more accurately demonstrated is a *discrepancy* between participants' current cognitive performance and an estimate of premorbid performance based on commonly used (yet not unflawed) predictors of intellectual functioning. The term "decrement" has been used in the current investigations for consistency with Keefe et al.'s (2005) approach. It is critical though that this term be used and interpreted with the aforementioned limitations in mind.

The Breakfast Task

The aim pertaining to Study 3 was to assess the utility of a naturalistic measure of executive functioning in predicting disability above and beyond clinical symptoms and cognition. As Studies 1 and 2 demonstrated, apart from patients who are both above-AR and have not experienced a cognitive decrement, cognitive normality did not confer a clinical or functional advantage relative to cognitively impaired patients. One hypothesis, therefore, is that performance on classic standardized cognitive tasks may not be generalizable to behaviour in everyday life. To assess this prediction, the Breakfast Task, a simulated ecologically relevant task that mimics a real-world activity that draws heavily

on executive functioning (i.e., cooking) was administered to patients with schizophrenia, in addition to commonly used measures of intellectual functioning (i.e., the WASI-II) and disability (i.e., the WHODAS).

Administration of the Breakfast Task to patients and controls revealed that, similar to patients with ABI (Tanguay et al., 2014), patients were impaired relative to controls in their ability to ensure all of the foods finish cooking at the same time (Range Score). This suggests that patients with schizophrenia demonstrated reduced planning ability and working memory in their completion of this task. Performance on this task, specifically performance on the Range Score, increased the ability to predict disability (i.e., WHODAS scores) beyond that provided by standard cognitive (i.e., WASI-II) and symptom (i.e., BPRS) measures, with the complete model accounting for 23.3% of the variance in disability scores.

There has been limited research on the incremental validity of more functionally relevant tasks in predicting real-world outcomes in schizophrenia above and beyond standard cognitive measures. Similar to the current results, performance on the COALS, a functional competence measure, added additional validity beyond that offered by symptoms, intellectual ability, and cognitive performance (McDermid Vaz et al., 2012). However, Heinrichs et al. (2010) observed conflicting results with a different measure of functional competence, the UPSA. Efforts to identify ecologically valid measures among patients with schizophrenia have found that tasks such as the Virtual Action Planning – Supermarket (Aubin, Béliveau, & Klinger, 2018), Computerized Digit Vigilance Test (Lin et al., 2018), and the Behavioural Assessment of Dysexecutive Syndrome (Katz, Tadmor, Felzen, & Hartman-Maeir, 2007) demonstrate ecological validity among

patients with schizophrenia. However, according to Spooner and Pachana (2006), clinicians and researchers remain reluctant to move beyond traditional neuropsychological measures to more ecologically valid measures. Further, there are limitations inherent in the ecological validity of some measures, such as social cognitive measures, when applied to schizophrenia research (Vaskinn, Sergi, & Green, 2009).

Recall that none of the three definitions of cognitive normality applied in the current studies provided promising functional outcome validity. When considering that cognition only accounts for 6% of the variance in functional outcome (Fett et al., 2011), and the increasing evidence that more functionally relevant tasks predict functioning or disability above and beyond standard cognitive tasks, the inclusion of tasks such as the Breakfast Task may be a promising approach to better assessing and predicting disability. Future research should focus on assessing if there is a subset of patients that performs within the normal range on more naturalistic measures, such as the Breakfast Task. Perhaps normal-range performance on a task such as this would have greater functional validity than classifications of normality based on classic standardized cognitive tasks.

Limitations

A notable limitation of the current investigation was that participants were assigned to the patient group according to criteria from an older version of the DSM (i.e., DSM-IV), as the current edition of the DSM (i.e., DSM-5) was not available at the outset of the studies. Despite the updates made to the new edition of the DSM, a recent study found that the majority of patients (99.5%) who met DSM-IV criteria for schizophrenia also met DSM-5 criteria (Mattila et al., 2015). Therefore, it is reasonable to conclude that the diagnostic criteria applied in the present investigations are currently valid based on

DSM-5 criteria. In addition to updates made to the DSM, the WRAT-3 has been updated to the WRAT-4 since the conception of the current study. The WRAT-3 continued to be used in the study to maintain data homogeneity. The WRAT-4 includes updated norms, and to my knowledge, no studies have been conducted that assess if WRAT-3 premorbid ability estimates are comparable to WRAT-4 estimates. Notably, however, Keefe et al. (2005) used the WRAT-3 in their study. Given that one of the aims of the study was to replicate methods conducted by Keefe et al. (2005) to assess a cognitive decrement, the use of the WRAT-3 in present investigations is supported.

With respect to inconsistences in measures, the MSIF was used as an assessment of daily functioning in Studies 1 and 2, whereas the WHODAS 2.0 was used in Study 3. Data from studies 1, 2, and 3 are from three separate grants, each with its own unique aims and methods. Therefore, the measures employed across the three studies are not identical. The MSIF was also administered as part of the measures in Study 3, yet there was inadequate training received by the test administrators to ensure appropriate reliability, and the results of the WHODAS were therefore reported instead. Further, the sample sizes, in particular among the cognitively normal-range (Studies 1 and 2) and above average-range (Study 2) patient groups were modest. This may have limited the statistical power of the findings and contributed to null findings (in particular with respect to normal-range compared to below-normal range group differences in ratings on the MSIF, as well as the PANSS).

As previously discussed, a second limitation involves the assessment of premorbid intellectual ability in Study 2. Given the cross-sectional, rather than longitudinal, nature of the study, premorbid IQ scores were not obtained directly and

were instead estimated using WRAT-3 Reading scores and parental education. Despite strong support for the use of both of these estimates (Bright et al., 2002; Bright & van der Linde, 2018; Kareken et al., 1995; Plomin, 1986; Resnick, 1992), the most accurate assessment of an intellectual decrement following the onset of schizophrenia would be direct observation through a longitudinal study design, where premorbid IQ was obtained through clinic-based testing. As well, despite the support of using participants' levels of parental education as an estimate of their intellectual potential, a limitation inherent in this approach, in schizophrenia specifically, is that schizophrenia or related phenotypes in the family may, in fact, be associated with reduced parental education (Keefe et al., 1994). Therefore, when interpreting the results of the second study, it is important to consider that parental education, as well as WRAT Reading scores, are simply estimates of premorbid intellectual ability, and that the term "discrepancy" is more appropriate than the term "decrement".

An additional limitation was that not all data were corrected for education (e.g., WASI-II). Although normal-range and non-normal range patient groups did not differ from one another in terms of educational achievement in Studies 1 and 2, education has been shown to have an impact on different cognitive tasks (Brooks, Sherman, Iverson, Slick, & Strauss, 2011). As well, while a goal of the second study was to assess the replicability of Keefe et al. (2005), the current study and that by Keefe et al. (2005) did not use identical measures (although measures assessed similar cognitive domains), and inclusion criteria of the two studies differed (e.g., Keefe included inpatients and outpatients). Therefore, while the current investigation is one of the first to apply and

evaluate the definition of a cognitive decrement as proposed by Keefe et al., a direct comparison of the results of the two studies must be interpreted with caution.

Conclusions

The present investigation revisited the ongoing debate surrounding the existence of cognitively normal patients in schizophrenia, and the role of cognition in daily functioning. Collectively, the results of the current studies provided evidence that even though cognitive impairments are highly prevalent in schizophrenia, it is still possible to be schizophrenic and cognitively normal. That is, even when the most stringent criteria were applied, consisting of having not experienced a cognitive decrement based on premorbid estimates of parental education and reading scores, and performing within the average range across a comprehensive battery of neuropsychology assessments, a subset of patients meeting these criteria emerged (9.3% of patients, to be precise). As was expected, the less stringent the criteria for normality, the greater the proportion of cognitively normal patients that emerged. Critically, when all classifications of cognitively normal patients were compared to controls, they continued to remain functionally disadvantaged in terms of community independence, and they rarely differed from impaired patients in terms of clinical symptom severity. Therefore, there is insufficient evidence supporting the functional or clinical validity of any of the definitions of cognitive normality included in the present investigation, suggesting that the role of cognition in functioning has been largely over-emphasized in the literature. Given the prevalent and severe levels of disability in schizophrenia, the findings have implications for rehabilitation efforts aimed to improve daily functioning in schizophrenia. That is, efforts to enhance daily functioning through cognitive remediation

may be met with limited generalizability to real-world functioning, consistent with previous studies in the area (Kidd et al., 2014; Lin et al., 2014). There is an urgent need to identify and ultimately remediate other factors that are driving impaired functioning in schizophrenia.

Data from the present investigation support the use of more ecologically valid, naturalistic measures that provide the advantages of experimental control inherent to traditional tasks of executive function, with the varying demands of real-world situations that draw largely on executive functions. We have shown for the first time that the Breakfast Task, a cognitive rehabilitation measure, provides incremental validity above and beyond that provided by standard clinical and cognitive measures in predicting disability among patients with schizophrenia. Therefore, in addition to focusing our efforts on identifying other factors that may account for functional impairment in schizophrenia, we should continue to focus our efforts on more ecologically valid ways of assessing cognition in schizophrenia. As it is well-established that cognition is one of the primary predictors of daily functioning identified to date, we must not ignore the role that cognition plays, but instead explore novel ways to assess it that are more relevant to the daily functioning difficulties experienced by patients with schizophrenia.

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Appendices

Appendix A. Study 1 Group Assignment: MCCB *T* scores between 43 and 57

Methods

A second approach to participant assignment to the Broad Normal-Range (BrNR) group was based on the following criteria: MCCB composite *T* score equal to or between 43 and 57, with those *T* score parameters set in order to achieve psychometric equivalence with the WASI IQ score criterion for average-range performance (based on Wechsler Classification). If participants met criteria for both NaNR and BrNR, they were classified as BrNR for the purpose of subsequent statistical analysis to ensure that no participants were included in both cognitive subtype groups for group comparisons. Based on this broad measure, cognitively below-normal range was defined as an MCCB composite *T* score ranging from 20 to 42. This classification yielded 10 BrNR patients (11%), 0 above BrNR patients (0%), and 85 patients falling below the BrNR (89%) when applying these criteria to the entire sample of patients (n = 95). The classification yielded 42 BrNR controls (54%), one above BrNR control (1%), and 35 below BrNR Controls (45%) when applying these criteria to the entire sample of controls (n = 78). Recall the following prevalence rates were obtained when the MCCB composite score criterion was based on *T* scores equal to or between 40 and 60: 13 BrNR patients (14%), 0 above BrNR patients (0%), and 82 patients falling below the BrNR (86%), 52 BrNR controls (65%), one above BrNR control (1%), and 26 below BrNR Controls (33%).

Given the low prevalence (11%) of BrNR patients (MCCB *T* scores between 43 and 57), and to ensure demographic similarity with comparison subgroups, these patients' age range and sex proportion were used as criteria in assigning controls to a normal range

(NR) ability group, patients to the NaNR ability group, and patients to the below-normal range group for statistical analyses. Hence, inclusion criteria for the normal range control group were: 1) age 20 – 46; 2) sex ratio 65-85% male; and 3) MCCB composite T score between 43 and 57 or IQ between 90 – 109. There were only three controls within the NaNR group who met age-range criteria, as the majority of controls also met criteria for the BrNR group. Therefore, NaNR and BrNR controls were combined to form one normal-range control group, rather than separating controls into their NaNR and BrNR groups for analyses. A total of n = 22 controls met these criteria and were assigned to a normal-range (NR) group. For patients, inclusion criteria for the NaNR group were: 1) age 20 – 46; 2) sex ratio 65-85% males; and 3) WASI Two-Subtest IQ score equal to or between 90 and 109. These requirements were met by n = 25 patients who were therefore assigned to the NaNR category. The cognitively below-normal range (BNR) patient group was defined as an MCCB composite score less than or equal to 42 and an IQ score less than or equal to 89. Applying the age, sex, IQ, and MCCB criterion to the pool of patients yielded n = 13 patients falling into the BNR group (see Table 11).

Results

Demographic characteristics of the NaNR, BrNR patient groups (MCCB *T* scores between 43 and 57), the BNR patients, and the NR comparison controls are presented in Table 11. Patient and control subgroups did not differ significantly in terms of age, sex distribution, or proportion for whom English was their first language. Groups did differ in terms of years of education; the NR controls reported significantly higher levels of education compared to the three patient groups (ps < .05), however patient groups did not differ from one another in terms of years of education.

Table 11

Descriptive and Criterion Data for Below Normal Range (BNR) Patients, Narrow Normal Range (NaNR) Patients, Broad Normal Range (BrNR) Patients, and Normal Range (NR) Controls, with MCCB BrNR Criteria Set at 43 ≥ T ≤ 57

Variable	BNR Patients (n = 13)	NaNR Patients (n = 25)	BrNR Patients (n = 10)	NR Controls (n = 22)	Statistic
Age, yrs *(M, SD)*	35.31 (6.46)	34.96 (6.54)	31.60 (7.66)	30.91 (8.77)	F(3,66) = 1.65
Sex (males %)	85	76	70	68	FET = 1.39
Years Education *(M, SD)*	11.69 (1.25)	13.08 (2.64)	13.90 (2.08)	16.45 (2.43)	F(3,) = 14.06 **
First Language English (%)	83	84	80	52	FET = 6.30
MCCB Composite *T (M, SD)*	20.62 (8.64)	30.04 (7.17)	50.00 (3.39)	47.00 (6.96)	F(3,65)= 58.12 **
WASI 2-Subtest IQ *(M, SD)*	78.22 (7.42)	99.44 (5.28)	119.20 (6.51)	107.00 (18.84)	F(3,66) = 26.15**

Note: FET = Fisher's Exact Test; *M* = mean; MCCB = MATRICS Consensus Cognitive Battery; SD = standard deviation; WASI = Wechsler Abbreviated Intelligence Scale.

Functional Implications of NaNR and BrNR Subtypes (MCCB *T* Scores Between 43 and 57)

Assumptions for ANOVA were assessed. Based on the interquartile range and boxplot, there were no outliers among MSIF scores. Results of the Shapiro-Wilk test (p = .01) indicate that the distribution of the residuals of MSIF scores was not normal, and residuals remained non-normally distributed following log transformation. Therefore, the non-parametric Kruskal-Wallis test was performed to compare the effect of group (i.e.,

BNR patients, NaNR patients, BrNR patients, and NR Controls) on community outcome (i.e., MSIF global scores), with post-hoc Mann-Whitney tests conducted with Bonferroni correction.

MSIF scores were significantly affected by participant group ($H(3) = 34.94$, $p < .001$). Mann-Whitney tests were used to follow up on this finding based on the following comparisons: i) BNR patients vs. NaNR patients; ii) BNR patients vs. BrNR patients; iii) NaNR patients vs. NR controls; and iv) BrNR patients vs. NR controls, with only these select Mann-Whitney tests chosen to reduce the Type I error rate while addressing the primary study aims, and a Bonferroni correction applied with effects reported at a .0125 (.05/4) level of significance. Effect size values were calculated as follows: $r = Z/\sqrt{n}$, with r values above 0.1 representing a small effect size, values above 0.3 representing a medium effect size, and values above 0.5 representing a large effect size.

Results indicated that MSIF scores did not differ between the BNR patient group and both the NaNR patient group ($U = 128.50$, $p > .05$, $r = -.097$), and the BrNR patient group ($U = 50.50$ $p > .05$, $r = -.138$). When comparing the patients with the controls, results indicate that MSIF global scores were significantly higher among the NaNR patient group as compared to the NR control group ($U = 36.5$, $p < .01$, $r = -.76$), and MSIF scores were also significantly higher among the BrNR patient group as compared to the NR control group ($U = 14.50$, $p < .01$, $r = -.71$) (see Table 12).

Table 12

Community Independence and Clinical Data for Below Normal Range (BNR) Patients, Narrow Normal Range (NaNR) Patients, Broad Normal Range (BrNR) Patients, and Normal Range (NR) Controls, with MCCB BrNR Criteria Set at 43 ≥ T ≤ 57

Variable	1. BNR Patients (n = 13)	2. NaNR Patients (n = 25)	3. BrNR Patients (n = 10)	4. NR Controls (n = 22)	Statistic	Post hoc Comparisons
MSIF Global Scores, *(M, SD)*	4.17 (1.40)	3.88 (1.04)	3.80 (1.03)	1.77 (0.75)	H(3) = 34.94 **	2, 3 > 4 1 = 2 = 3
PANSS Positive *T (M, SD)*	47.46 (9.12)	46.36 (8.22)	44.90 (8.52)	n/a	λ = .93	n/a
PANSS Negative *T (M, SD)*	44.31 (10.16)	40.04 (6.96)	39.10 (9.77)	n/a	λ = .93	n/a

Note: MSIF = Multidimensional Scale of Independent Functioning; PANSS = Positive and Negative Syndrome Scale.
** $p < .001$

Clinical implications of NaNR and BrNR Subtypes (MCCB *T* Scores Between 43 and 57)

Assumptions for MANOVA were assessed. All observations were statistically independent, and data were randomly sampled from the population. Based on Mahalanobis distance ($df = 2$, cut off = 13.82), there were no multivariate outliers among the residuals (all values were less than 8.250). Multivariate normality was assessed in R Studio using Mardia's multivariate test of normality. Based on the residuals of PANSS Positive and Negative *T* scores, the Skewness (Mardia's = 5.22, $p = .27$) and Kurtosis (Mardia's = -.96, $p = .34$) indicate multivariate normality. Box's test of equality of covariance matrices was not violated (M = 12.81, F(6, 9106.633) = 1.97, $p = .066$).

The MANOVA, with patient group (i.e., BNR, NaNR, and BrNR) set as the independent variable, and the PANSS Positive and Negative *T* scores set as dependent variables, did not show a significant difference between patient groups in terms of symptom severity ($\lambda = .93$, $F(4, 88) = .934$, $\eta_P^2 = .034$, $p = .548$). Therefore, BNR, NaNR and BrNR patient groups did not differ in terms of their positive and negative symptom severity (Table 12).

Summary

Using the MCCB criterion of T scores between 43 and 57 to classify patients as BrNR, 11% of patients were identified, in contrast to 14% of patients when MCCB criterion was based on *T* scores between 40 and 60. Functional and clinical implications of the BrNR criterion of MCCB *T* scores between 43 and 57 are consistent with findings pertaining to BrNR criterion of MCCB *T* scores between 40 and 60. That is, regardless of the MCCB criterion applied, BrNR patients were functionally disadvantaged, based on MSIF scores, relative to cognitively normal controls. They demonstrated no advantage in functionality or clinical symptom severity, based on PANSS symptom scores, relative to cognitively impaired patients