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Association between schizophrenia symptoms and neurocognition on mobility in older adults with schizophrenia

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INTRODUCTION

The number of older adults with a serious mental illness, such as schizophrenia, is predicted to more than double to 15 million by the year 2030 (Bartels, 2004). Those with schizophrenia comprise the largest non-dementia group of older people with severe psychiatric problems (Cohen et al., 2000). Data from these studies suggest that the physical health status of older adults with schizophrenia is poor (Folsom et al., 2009; Jeste, Wolkowitz, & Palmer, 2011; Kilbourne et al., 2005; Parks, Svendsen, Singer, & Foti, 2006). Although there are increasingly better psychiatric treatment options and better responses to these treatments, age-adjusted mortality rates for people with schizophrenia are more than twice those in the general population (Folsom et al., 2002). Despite the obvious need for

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research to improve the health of this vulnerable population, less than 10% of published research in schizophrenia focuses on older adults (Mittal et al., 2006).

Contributing factors to poor physical health include sociodemographic characteristics (Chafetz et al., 2005; Leutwyler, Chafetz, & Wallhagen, 2010), iatrogenic effects of medication (Allison et al., 2009), smoking (Gupta & Craig, 2009; Kelly et al., 2011; Kilbourne et al., 2009a), poor diet (McCreadie, 2003; McKibbin et al., 2006; Peet, 2004), and sedentary lifestyles (Leutwyler, Hubbard, Jeste, Miller, & Vinogradov, 2013; Lindamer et al., 2008). In addition, inadequate medical care also plays a role. Data suggest that individuals with schizophrenia receive less than optimal screening, prevention, and treatment services (Folsom et al., 2002; Leutwyler & Wallhagen, 2009). Acute and chronic care differences are also apparent. People will schizophrenia have higher post-stroke mortality rates(Kisely, Campbell, & Wang, 2009), post-myocardial infarction mortality rates(Druss, Bradford, Rosenheck, Radford, & Krumholz, 2001), and receive fewer medical and surgical interventions (Druss et al., 2001; Kisely et al., 2009). Moreover, when compared with age-matched peers in the general community, older adults with schizophrenia may receive less adequate medication treatment for certain chronic conditions (Vahia et al., 2008). These data all support that older adults with schizophrenia have poor physical health and experience multiple factors that contribute to their poor health. Yet, the relationships between neurocognition, schizophrenia symptomatology, and mobility of older adults with schizophrenia have not been adequately explored.

Mobility is an important aspect of physical function that may be a critical component to target in order to improve the overall physical health of older adults with schizophrenia. Functional limitations impair the ability of older adults to live independently (Covinsky et al., 2003). Optimizing mobility may help delay disability and maintain independent life in older adults (Tirodkar, Song, Chang, Dunlop, & Chang, 2008). Mobility is defined as the ability to move independently around the environment and is a critical part of many basic and instrumental activities of daily living (Shumway-Cook, Ciol, Yorkston, Hoffman, & Chan, 2005). In addition to severe mental health issues, people with schizophrenia often have multiple chronic medical conditions such as cardiovascular disease and diabetes(Chafetz, White, Collins-Bride, Nickens, & Cooper, 2006; Kilbourne et al., 2005; Kilbourne et al., 2009b). The multitude of chronic medical conditions experienced by people with schizophrenia can jeopardize optimal mobility. Furthermore, older adults with schizophrenia are susceptible to limitations in physical mobility due to the aging process (Shumway-Cook et al., 2005). Ample data support that gait speed, one aspect of mobility, is associated with survival in older adults (Studenski et al., 2011). Research among younger people with schizophrenia shows that their mobility is poor (Viertio et al., 2009) and their physical function may resemble that of someone 10 to 20 years older (Chafetz et al., 2006). Multiple factors play a role in the poor mobility of older adults with schizophrenia such as chronic medical conditions, limited access to physical activity, and sedentary lifestyles (Druss, Zhao, Von Esenwein, Morrato, & Marcus, 2011; Leutwyler, Hubbard, Jeste, D., et al., 2013; Leutwyler, Hubbard, Slater, & Jeste, 2013). However, the relationship of psychiatric symptoms and neurocognitive impairment to mobility are not known.

Schizophrenia symptoms may be categorized as positive, negative, depressive/anxious, disorganized, excitatory, and other (Poole, Tobias, & Vinogradov, 2000). These varying symptoms can be problematic for the patients and significantly impact their physical health. For example, an association was found between more severe schizophrenia symptoms and greater number of medical problems (Friedman et al., 2002). In addition to psychiatric symptoms, people with schizophrenia have impaired neurocognitive function (Keefe et al., 2006). Cognitive impairment is a central aspect of schizophrenia and is distinct from the psychotic symptoms of the disease. Neurocognition links cognitive constructs, in theory, to particular brain regions, systems, and processes (Leutwyler, Hubbard, Jeste, D. et al., 2013). The fundamental dimensions of neurocognitive impairment in schizophrenia are: working memory, attention/vigilance, verbal learning and memory, visual learning and memory, reasoning and problem solving, speed of processing, and social cognition (Nuechterlein, 2004). Previous work showed an association between greater severity of symptoms and worse neurocognition with lower levels of physical activity in older adults with schizophrenia (Leutwyler, Hubbard, Jeste, D., et al., 2013).

Schizophrenia symptoms and neurocognitive deficits may also impact mobility. The UCSF Theory of Symptom Management (TSM) (Dodd et al., 2001) provides a theoretical framework for exploring the associations between schizophrenia symptoms, neurocognition, and mobility. The TSM is predicated upon the idea that management of a symptom or group of symptoms demands that the symptom experience, symptom management strategy, and outcomes all be considered. The outcomes dimension specifies that outcomes emerge from the symptom management strategies as well as from the symptom experience. Symptom management is viewed as a dynamic process that is modifiable by both individual outcomes and the influences of the nursing domains of person, health/illness, or environment.

The symptom experience dimension can include an evaluation of severity of schizophrenia symptoms and neurocognitive function. Individuals perceive their psychiatric symptoms, evaluate the meaning of their symptoms, and respond to these meanings in their own unique ways that are influenced by factors such as environment, socio-cultural contexts, personality, biology, and age. The TSM purports that the perception, evaluation, and response to symptoms are iterative and may occur simultaneously. When individuals report their perceptions, such as during a psychiatric symptom assessment, these reports are informed by their evaluation and response. For example, patients may be reluctant to report hallucinations during an interview if they are distressed and are concerned others will also be frightened.

In addition to psychiatric symptoms, neurocognitive functions, such as speed of processing, are needed to modulate behavior, anticipate outcomes, and adapt to changing situations; all of which can be critical to optimal mobility. The symptom management dimension begins with assessment followed by identifying a focus for intervention. This is a dynamic process that can require changes in strategies over time. For the older adult with schizophrenia, symptom management may include activities such as a medication regimen and psychosocial treatment. Both the symptom experience and the symptom management dimensions are linked to the third dimension, outcomes. Understanding the relationships between the symptom experience (which includes symptoms and neurocognitive function)

and outcomes is necessary to be able to design symptom management strategies, such as mobility enhancing interventions, that are tailored specifically for older adults with schizophrenia.

Only three studies(Chwastiak et al., 2006; Lallart, Jouvent, Herrmann, Beauchet, & Allali, 2012; Viertio et al., 2009) have explored the relationship between schizophrenia symptoms, neurocognitive functioning and/or mobility in people with schizophrenia. The previous studies suggest more severe symptoms and impaired neurocognition negatively impact aspects of physical mobility. A major limitation to previous studies is the lack of an objective measure of mobility. Exploring these associations with an objective measure of mobility can provide more insight into a loss of functional status that can be quantified and potentially followed over time. This is the first study to explore these associations with a comprehensive neurocognitive and psychiatric assessment, using an objective measure of mobility in an older group of patients with schizophrenia. With the TSM (Dodd et al., 2001) as the theoretical framework, the purpose of this study was to test the following hypothesis in a sample of older adults with schizophrenia: 1. More severe schizophrenia symptoms and more severe neurocognitive deficits would be associated with lower levels of mobility.

METHODS

Design

A cross sectional design was used to examine the hypotheses. Institutional review board approval was obtained from the University's Committee on Human Research. Anonymity and confidentiality were maintained according to ethical guidelines.

Participants and Settings

Inclusion criteria were that participants be English-speaking adults older than or equal to 55 with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder (based on the Structured Clinical Interview for DSM-IV). A 7-item capacity to consent evaluation was conducted prior to enrollment to ensure that participants had sufficient understanding of their involvement in the study. Participants were given a total of 3 trials to correctly answer a missed question. If a participant answered more than 2 questions incorrectly, they were deemed ineligible for study participation at that time. If the potential participant that failed the capacity to consent test wanted to go through the consent process again on another day, the PI or her staff re-administered the consent and the capacity to consent evaluation.

The participants were recruited from three main sites: a transitional residential and day treatment center for older adults with severe mental illness; a locked residential facility for adults diagnosed with serious mental illnesses; and an intensive case management program. Participant referrals were also made from the community and other participants. Participants received $ 90 for their involvement in the study and a bonus payment of $ 20 if all of the study procedures were completed.

Measures

A trained member of the research staff administered all of the assessments.

Symptom Severity—Psychiatric symptoms were measured with the extended Positive and Negative Syndrome Scale (PANSS) (Poole et al., 2000). The extended PANSS contains six subscales measuring positive (e.g. delusions), negative (e.g. emotional and social withdrawal), excited (e.g. poor impulse control), depressed-anxious (e.g. depressed), disorganized (conceptual disorganization) and other symptoms (e.g. preoccupation, poor attention). The original PANSS (Kay, Fiszbein, & Opler, 1987) categorizes the symptoms into only 3 subscales: positive, negative, and general. One of the aims of our study was to understand how symptoms are associated with mobility. Therefore, we chose the extended PANSS because it provides more details about the variety of symptoms experienced. Lindenmayer et al. (2007) describe the scale to have demonstrated good-to-excellent reliability in assessing symptoms and their change during the course of treatment in clinical trials with participants diagnosed with schizophrenia. The scale takes approximately 60 minutes to administer. The items on the PANSS are summed to determine the scores on the six subscales and the total score (the sum of all six subscales).

Neurocognitive Functioning—The Matrics Consensus Cognitive Battery (MCCB) was used to assess neurocognitive functioning on each of the following seven domains identified as discrete, fundamental dimensions of cognitive impairment in schizophrenia, with a likely sensitivity to intervention (Nuechterlein, 2004): Speed of processing (SOP), Attention/ vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition. Speed of processing tests include: Trail Making Test: Part A, Brief Assessment of Cognition in Schizophrenia (BACS) Symbol Coding, and Category Fluency (animal naming). Attention/Vigilance tests include Continuous Performance Test-Identical Pairs (CPT-IP). Working memory tests include: Wechsler Memory Scale (WMS) -Spatial span and letter number span. Verbal learning tests include the Hopkins verbal learning test-revised. Visual Learning measures include the Brief Visuospatial Memory Test-revised. Reasoning and problem solving measures include Neuropsychology Assessment Battery (NAB) Mazes. Social Cognition consisted of the Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions. The MCCB scoring program produces seven domain scores and a composite score that are standardized to the same t-score measurement scale with a mean of 50 and an SD of 10 based upon the normative data collected from a sample of 300 community participants as part of the MATRICS psychometric and standardization study and published in the MCCB manual and the MCCB scoring program (Kern et al., 2008; Nuechterlein et al., 2008).

Mobility—Mobility was measured objectively with the Timed Get Up and Go (TGUG) test. The TGUG is a valid and reliable test for quantifying functional mobility and may be useful in following clinical change over time (Podsiadlo & Richardson, 1991). The test is quick, requires no special equipment, and is easy to administer. During the test, the person is observed and timed while s/he rises from an arm chair, walks 3 meters, turns, walks back, and sits down again. A time of 12 seconds or less to complete the TGUG can be used to identify normal mobility in community-dwelling adults and to differentiate fallers from non-fallers (Bischoff et al., 2003; Trueblood, Hodson-Chennault, Mc- Cubbin, & Youngclarke, 2001).

Data analysis

Statistical analyses were performed using SPSS (Version 20). Mobility data were analyzed descriptively for the entire sample. Pearson's bivariate correlations (two-sided) were conducted on the entire sample. Variables that were significant at $p < 0.10$ and had a correlation of greater than 0.30 in bivariate analysis were included in the simultaneous multiple regressions model. Variables that were highly correlated with one another ($r > .8$) were not included in same model. One simultaneous regression model was used to examine the relationship between mobility (TGUG) and neurocognition or symptoms. Alpha was set to $p < .05$. Timed get up and go score in seconds was the dependent variable. The significant schizophrenia symptom subscale and significant neurocognitive domain from the bivariate analyses were the independent variables. Age was also included as an independent variable.

RESULTS

A total of 46 participants were included in the analyses. Sociodemographic and clinical characteristics are presented in Table 1. The majority of participants were male and the average age was 61 years (range 55 to 78). More than half of the patients were current smokers. The mean BMI for the sample was 29.4 (overweight) and mean waist circumference was 111 centimeters.

The mean Total PANSS score of 81.2 (SD=25.7) indicated that the sample was moderately ill (Leucht et al., 2005). Higher scores on the PANSS reflect more severe symptoms. The MCCB global cognition composite score was 18.1 (SD=13.5). Lower scores on the MCCB tests reflect poorer neurocognitive function. A summary of the performance on the MCCB domains and the PANSS subscales is provided in Table 1. Global scores were calculated for 44 out of 46 participants with complete neurocognitive data. An Attention Vigilance score was not calculated for one participant because the participant refused to complete the CPT-IP. A working memory score was not calculated for one participant because the participant did not attempt the letter number span test. Average time to complete the TGUG was 12.3 seconds (SD=4.2; range=7-29).

There were significant bivariate correlations between TGUG and age, negative symptoms, working memory, speed of processing, and overall cognition. Older age ($p = .008$), higher scores on the negative symptom subscale ($p = .03$) and lower scores on working memory ($p = .04$), speed of processing ($p = .01$), and overall cognition ($p = .04$) were associated with slower timed get up and go scores. We did not find significant bivariate associations with the positive, disorganized, excited, depressed-anxious, or other symptom subscales.

Results of the simultaneous multiple regression are in table 2. Negative symptom subscale, speed of processing domain, and age were included as predictors in the model. Working memory was highly correlated with speed of processing therefore it was not included in the model. The global cognition score was not included as a predictor in the model in order to avoid including the speed of processing tests twice in the model. With three predictors in the model, we explained 34% of variation in TGUG score ($p = .001$). Speed of processing made a significant unique contribution to the model ($p = .019$). When controlling for age and negative symptoms, for every 1-point increase in speed of processing, there is a 0.1 second

decrease in TGUG score. Age also made a significant unique contribution to the model (p =. 003). When controlling for speed of processing and negative symptoms, for every 1-year increase in age, there is a 0.4 second increase in TGUG score.

DISCUSSION

Our data suggest that more severe negative symptoms, slower speed of processing, and being older have a negative impact on mobility. Our findings build on previous research in several ways. First, studies in samples without serious mental illness found a similar association between slower TGUG and poorer performance on speed of processing tests (Donoghue et al., 2012; Herman, Giladi, & Hausdorff, 2011) and memory tests (Donoghue et al., 2012). Second, after adjusting for covariates (including age), Donoghue et al. (2012) also reported significant associations between TGUG time and speed of processing. Furthermore, although there is a lack of research on the association of mobility and cognition in older adults with schizophrenia, a small (n=17) study in patients with early schizophrenia (mean age 30) showed a significant univariate association between TGUG time with cognitive function (measured with the MMSE and a Frontal Assessment Battery) (Lallart et al., 2012).

A consistent finding across previous research and our study is the association of slower speed of processing and slower TGUG time. Impaired speed of processing is a core cognitive deficit in schizophrenia (Knowles, David, & Reichenberg, 2010). Speed of processing usually indicates the number of correct responses an individual can make during a task within a certain amount of time (Knowles et al., 2010). Rosano et al. (2012) provide some rationale for the association between speed of processing and mobility by suggesting that walking requires perception and interpretation of the terrain's properties and obstacles in surrounding space. In our sample, it is possible that slower speed of processing may have impaired this interpretation process therefore slowing the TGUG time. For example, although participants watched staff preform the TGUG first and were given a practice trial, slower speed of processing could still make it difficult to initiate movement, to anticipate obstacles, and to navigate walking in an unfamiliar environment. Future research should evaluate mobility in more depth to better understand which particular aspects of mobility are linked to speed of processing.

Furthermore, our findings are similar to results in other studies that evaluated associations of schizophrenia symptoms to aspects of mobility. In one study(Chwastiak et al., 2006), the interrelationship between psychiatric symptoms and physical function was evaluated using baseline data from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) trial. The CATIE trial was a national multi-site trial of antipsychotic pharmacotherapy that collected data from more than 1,400 patients (age 18-65, mean age 40.6 years). Higher total PANSS scores as well as higher positive symptom scores were associated with significantly worse physical function scores (measured with the SF-12). We did not find a significant association with total or positive symptom scores but we did find an association with severity of negative symptoms and an objective measure of mobility. In another study (Viertio et al., 2009), a nationally representative sample of 6,927 persons in Finland self-reported mobility limitations and were examined in performance tests. Of this group, 185

participants were identified with a lifetime-ever diagnosis of a psychotic disorder. In the group with non-affective psychosis, similar to our findings, mobility difficulties were associated with greater severity of negative symptoms.

It is interesting to note that we did not find an association between mobility and positive symptoms in our sample. This may be due to the relatively stable psychiatric symptom level in our sample. It is also possible that participants were less willing to discuss their positive symptoms and may have under-reported their presence and severity. It was not surprising to find an association with negative symptom subscale because the symptoms that make up this subscale assess some aspects of slowed movement. The symptoms in the subscale include: emotional withdrawal, passive/apathetic/social withdrawal, lack of spontaneity/flow of conversation, poor rapport, blunted affect, motor disturbance, and disturbance of volition. In addition, greater severity of negative symptoms could also be associated with factors that contribute to poor mobility such as duration and amount of antipsychotic use.

Previous researchers (Donoghue et al., 2012; Herman et al., 2011) point out that the TGUG may be more complex than originally thought because it involves not only walking but also turning and transfers from sitting. In future work, it will be important to determine which aspects of the TGUG are most impaired (e.g. walking, turning, sitting) and if any of these aspects are most closely linked to specific cognitive domains. A small randomized controlled trial testing cognitive remediation as an intervention to improve gait velocity in sedentary seniors provides some preliminary evidence that targeting cognition may be an effective way to improve mobility (Verghese, Mahoney, Ambrose, Wang, & Holtzer, 2010). If we can tease out the particular aspects of mobility and cognitive domains that are most impaired and where the strongest associations are, then we can use this information to target future mobility and cognition enhancing interventions. Understanding the nuances in an especially vulnerable older adult sample such as ours may help us to also tailor interventions to meet the needs of other older adults with higher potential for cognitive or mobility limitations (e.g. patients with mild cognitive impairment, dementia, or Parkinson’s disease).

Limitations

Our study has several limitations—The cross-sectional nature of the study limits our ability to make an assessment of causation. In addition, we assessed mobility objectively only with the TGUG. A comprehensive assessment of mobility could help determine which specific aspects of mobility are most impaired and associated with aspects of neurocogntion and symptoms. We were unable to collect complete medication lists from the participants so we could not capture the effect of psychiatric medications on TGUG performance, such as the impact of tardive dyskinesia on mobility or akathisia on mobility. Despite the limitations, this is, to our knowledge, the first study to explore the associations of neurocognitive functioning and schizophrenia symptoms with mobility in older adults with schizophrenia. An understanding of these relationships is particularly important in order to design and implement mobility interventions effectively with this population.

Future Research

Future studies should explore these relationships longitudinally in a larger sample of patients. In addition, a comprehensive assessment of mobility should be conducted to better understand the various aspects of mobility associated with neurocognitive function and symptoms. It should also be determined if improved neurocognition and/or symptoms improves mobility in a sample of older adults with serious mental illness.

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Table 1

Sociodemographic and Clinical Characteristics of the Sample

Characteristic	Mean or ratio (+/− sd),
Age (in years)	61.0 (4.4)
BMI	29.4 (5.7)
Waist Circumference (in inches)	111.4 (14.7)
Timed Get Up and Go Test (in seconds)	12.3 (4.2)
Male	29/46
Current smoker	26/46
Past smoker	9/46
Never smoker	11/46
Psychiatric symptoms	
Panss Total	81.2 (25.7)
Panss Positive	17.0 (8.1)
Panss Negative	15. 0 (5.9)
Panss Depressed/Anxious	10.5 (3.8)
Panss Disorganized	9.1 (4.3)
Panss Excited	7.7 (3.0)
Panss Other	22.0 (8.0)
Neurocognition	
Speed of processing	22.5 (16.7)
Attention/vigilance	26.0 (13.2)
Working memory	26.9 (12.9)
Verbal learning	33.4 (8.9)
Visual learning	36.5 (12.9)
Reasoning and Problem solving	39.5 (5.8)
Social cognition	31.5 (8.8)
Trails Making Test	24.5 (16.9)
BACS Symbol Coding	25.2 (13.3)
WMS-Spatial Span	34.6 (10.4)
Global	18.1 (13.5)

Table 2

Effect of Schizophrenia Symptoms and Neurocognition on TGUG

Source	R^2	B	95% CI UB	95% CI LB	R^2 Change (sr^2)	df	F	p
Overall	.34					3,42	7.09	<.01
Intercept		−10.75	4.05	−25.55				
Age		.38	.62	.14	.16	1,42	10.32	<.01
Negative Symptoms		.12	.32	−.08	.02	1,42	1.47	.23
Speed of Processing		−.08	−.01	−.15	.09	1,42	5.90	.02