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Neurocognitive insight in people with schizophrenia

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor
of Philosophy

in

Clinical Psychology

by

Cynthia Zurhellen Burton

Committee in charge:

University of California, San Diego

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2015

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Chair

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2015

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Chapter 2, in full, is a reprint of the material as it appears in the American Journal of Psychiatric Rehabilitation 2011. Burton, Cynthia Z.; Vella, Lea; Twamley, Elizabeth W., Routledge Press, 2011. The dissertation author was the primary investigator and author of this paper.

Chapters 3 and 4 are currently being prepared for submission for publication of the material. The dissertation author was the primary investigator and author of this material.

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ABSTRACT OF THE DISSERTATION

Neurocognitive Insight in People with Schizophrenia

by

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Doctor of Philosophy in Clinical Psychology

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Cognitive impairment is a core component of schizophrenia. Cognitive training is a promising behavioral treatment, with current research examining factors influencing treatment utilization and effectiveness. Insight is one proposed moderator that includes awareness of mental illness (clinical insight), self-certainty about beliefs (cognitive insight), and awareness of neuropsychological impairment (neurocognitive insight). Despite the known cognitive dysfunction associated with schizophrenia, individuals' awareness of impairment and whether that affects treatment use and outcome is unclear.

This research explored metacognitive abilities (cognitive and neurocognitive insight) among individuals diagnosed with schizophrenia, the relationships between insight and objective cognitive performance, and whether insight affects treatment adherence and/or outcome.

This project encompassed three studies. The first study investigated clinical and cognitive insight in 69 individuals enrolled in a compensatory cognitive training intervention. The second study ($n=214$) examined neurocognitive insight among participants with objectively measured cognitive impairment, and its relationship to executive functioning, functional capacity, and psychiatric symptoms. The third study evaluated the relationship between neurocognitive insight and treatment utilization and outcome in 69 cognitive treatment-seeking participants.

Study 1 demonstrated that better clinical insight was related to better executive functioning and less severe negative symptoms; cognitive insight was not related to any measures. Study 2 found that 54% of participants with cognitive impairment showed impaired neurocognitive insight. Those individuals reported significantly fewer positive symptoms and depressive symptoms; the groups did not significantly differ on other measures. Study 3 found a lower percentage of participants with impaired neurocognitive insight (28%); participants did not differ on treatment utilization variables. Moreover, participants with impaired neurocognitive insight in the treatment condition showed improvements in verbal memory and functional capacity.

These studies supported the multidimensional nature of insight and differential relationships with cognition, functioning, and symptoms. A substantial number of cognitively impaired participants minimally reported cognitive problems. Neurocognitive

insight was not related to executive functioning and was equivocally related to positive and depressive symptoms. As there were no differences between the neurocognitive insight groups on treatment utilization, and participants with impaired neurocognitive insight showed gains in verbal memory and functional capacity, clinicians need not exclude people with impaired insight from cognitive training treatment.

CHAPTER 1: GENERAL INTRODUCTION

The Oxford Dictionary defines insight as “the capacity to gain an accurate and deep understanding of someone or something”. In psychiatry, clinicians and researchers alike have struggled to provide a consistent definition of insight and a means by which it is assessed (Marková, 2005). Marková and Berrios (1992) offered a narrower but similarly vague description: “insight is a form of self-knowledge which includes not only information on problems and personality traits as applied to the self, but also an understanding of their effect on the way in which the self interacts with the world” (p. 857). Historically, insight was a unidimensional and dichotomous concept involving a person’s awareness of having a mental illness and attributing symptoms to that illness (Amador et al., 1993; Birchwood et al., 1994; Kay, Fiszbein, & Opler, 1987). Contemporary formulations acknowledge that insight is a complex and multidimensional construct, and have proposed a wider scope to define insight, including “clinical” insight, “metacognition”, “cognitive” insight, and “neurocognitive” insight.

Clinical insight

Clinical insight is the most studied type of insight and involves the awareness of having a mental disorder or symptoms of a mental disorder (Amador et al., 1993). It was frequently measured as a categorical variable, with patients rated as having “good” or “poor” insight based on whether they acknowledge or deny mental disturbance. This approach was limited because it failed to account for differing degrees of awareness, or partial insight (e.g., a patient acknowledges some symptoms but not others; Amador et al., 1993). Contemporary measures of clinical insight are more continuous and often incorporate awareness of multiple psychiatric symptoms as well as the need for treatment

and the effects of medication (Amador et al., 1993; Birchwood et al., 1994; David, Buchanan, Reed, & Almeida, 1992).

Metacognition

Metacognition is a broad term that generally refers to “thinking about thinking”; conceptually, it is related to but not synonymous with neurocognition (Lysaker et al., 2011). Metacognition is described more specifically as a range of semi-independent functions that allow people to think about their own thoughts and feelings, and to use their ideas about mental states to respond to distress and the challenges of social life (Lysaker et al., 2011a). This umbrella term includes two more novel types of insight: cognitive insight and neurocognitive insight.

Cognitive insight

Cognitive insight has been described in the last decade and involves a person’s capacity to evaluate unusual experiences and question their own potentially faulty conclusions, which relies on distancing oneself from misguided beliefs and re-evaluating misinterpretations (Beck, Baruch, Balter, Steer, & Warman, 2004). The capacity to reflect on experiences and recognize incorrect conclusions is reduced by impaired objectivity about cognitive distortions, loss of ability to gain perspective on these experiences, resistance to corrective information, and overconfidence in conclusions (Beck et al., 2004). Previous research has demonstrated modest to moderate convergence between a measure of cognitive insight and measures of clinical insight, supporting the notion that the concepts of cognitive and clinical insight are related but distinct (.24-.64 range; Beck et al., 2004; Pedrelli et al., 2004).

Neurocognitive insight

Another even more recent type of metacognitive insight is neurocognitive insight, defined as awareness of neuropsychological dysfunction (e.g., impaired attention, memory, problem-solving; Medalia & Thysen, 2008). Instruments to measure neurocognitive insight have been created to assess insight into cognitive deficits in comparison to actual performance on cognitive tests (Medalia & Thysen, 2010), as well as to allow reliable measurement of patients' or caregivers' opinions about a patient's degree of neurocognitive deficit (Keefe, Poe, Walker, Kang, & Harvey, 2006). Although the literature on neurocognitive insight is scant, there is some evidence that individuals with psychiatric disorders have poorer insight into their neurocognitive symptoms than their clinical symptoms, prompting researchers to encourage that they be addressed separately in treatment (Medalia & Thysen, 2010).

Insight in the context of schizophrenia

The concepts of clinical, cognitive, and neurocognitive insight are especially relevant in psychotic disorders like schizophrenia. Individuals with psychosis are prone to thought disorder and delusions (fixed false beliefs), which can interfere with the ability to recognize symptoms of psychiatric illness and discourage the pursuit of treatment. "Jumping to conclusions" and the inability to appraise erroneous thoughts are also common features of psychosis, leading to rigid and concrete thinking that impacts daily living as well as treatment adherence. By definition, the formation and maintenance of delusions are accompanied by steadfast conviction in the truth of such beliefs, even in the presence of contradictory evidence. This feature of psychosis often precludes the use of corrective feedback, complicating treatments for psychotic disorders that involve medication maintenance or therapeutic intervention (Beck et al., 2004). Even if clinical

insight is intact, lack of cognitive insight may limit cognitive skills like problem-solving, gathering evidence, and hypothesis testing, which are among the cornerstones of evidence-based psychotherapies for psychosis (Gaudiano, 2006; McCann, 2001). Aside from the awareness/appraisal of positive and negative symptoms of psychosis, unawareness of cognitive impairments can have devastating consequences. The inability to appreciate deficits in attention, memory, planning, and problem-solving can adversely affect everyday functioning, limit interest in treatments for cognitive impairment, and interfere with individuals' capacity to achieve rehabilitation goals.

Thus, the treatment implications of limited insight are profound. Antipsychotic medications have proven helpful in reducing the positive symptoms of psychosis, but residual cognitive and negative symptoms and side effects significantly decrease treatment adherence (Kane, 2001; Lieberman et al., 2005); this may be especially true for people with restricted insight. Furthermore, there is little evidence to date that antipsychotic medications can effectively address negative and cognitive symptoms (Keefe et al., 2007; Miyamoto, Miyake, Jarskog, Fleischhacker, & Lieberman, 2012). Numerous psychosocial treatments for schizophrenia are available, but the utility of such interventions may be reduced if poor insight discourages people with psychotic disorders from adhering to the treatment or agreeing to participate at all. It is well accepted in psychiatric research and practice that limited clinical insight affects a person's willingness to seek and accept treatment; it is less well understood how diminished cognitive and neurocognitive insight may impact a person's willingness to participate in treatment.

Cerebral function in schizophrenia

Cognition and functioning in schizophrenia

Little doubt remains regarding the significance of cognitive dysfunction in schizophrenia. Although this severe mental illness was previously conceptualized as a psychiatric disorder with co-occurring cognitive deficits, it is now increasingly recognized as a neurodevelopmental cognitive disorder that produces psychiatric symptoms (Gur, Ragland, & Gur, 1997; Heaton et al., 2001; Heinrichs, 2005; Kurtz, 2005). Cognitive impairment, therefore, is a central feature of schizophrenia that includes stable, enduring deficits in attention, processing speed, working memory, learning, memory, and executive function (Heaton et al., 2001; Heinrichs & Zakzanis, 1998). Although it is possible to have schizophrenia without neuropsychological impairment (Palmer et al., 1997), empirical evidence has consistently demonstrated that a large proportion of schizophrenia patients is impaired on standard neurocognitive tests, and that domain-specific deficits are relative and exist against a backdrop of generalized dysfunction (Heinrichs & Zakzanis, 1998). Furthermore, a critical link has been identified between cognitive impairment and functional outcome; that is, neuropsychological dysfunction is reflected in performance of real-world everyday activities that are necessary to live independently in the community (Green, Kern, Braff, & Mintz, 2000). In fact, cognitive symptoms explain more variation in daily functioning than do positive or negative symptoms of the illness (Green, 1996; Velligan et al., 1997). Cognitive impairment is also considered a rate-limiting factor for benefit from psychiatric rehabilitation programs (Kurtz & Tolman, 2011; McGurk, Mueser, Walling, Harvey, & Meltzer, 2004; Harding et al., 2008; Walsh, Wu, Mitchell, & Berkman, 2003).

Therefore, pharmacological and psychosocial treatments to improve cognition and ultimately everyday functioning are urgently needed.

Neurobiology of schizophrenia

Various investigations have sought to characterize the neurobiology of schizophrenia and the putative neurocognitive correlates of observed brain pathology. Among the preliminary structural findings decades ago were enlarged cerebral ventricles in patients with schizophrenia, suggesting a reduction in brain tissue (Jindal & Keshavan, 2008). Meta-analytic magnetic resonance imaging (MRI) studies have demonstrated reduced whole brain and hippocampal volume and increased ventricular volume in first-episode psychosis patients relative to healthy controls (Steen, Mull, McClure, Hamer, & Lieberman, 2006; Vita, De Peri, & Dieci, 2006). Further, reductions in grey matter volume in the prefrontal region and hippocampus have been shown to correlate with symptom severity and cognitive function (Gur et al., 2000a; Gur et al., 2000b). Abnormalities in white matter tracts have also been observed in schizophrenia, which appear to be present in the early stages of illness and even in neuroleptic-naïve patients (Kyriakopoulos & Frangou, 2009). Despite the abundance of studies on brain morphology in schizophrenia since the advent of neuroimaging techniques, there remains considerable inconsistency in the published literature; structural brain abnormalities are not universal among patients, the effects are often moderated by sex, and whether observed pathology represents a neurodevelopmental or neurodegenerative process is disputed (Andreasen et al., 1990; Gur et al., 2000a, Gur et al., 2000b; Jindal & Keshavan, 2008; Nopoulos et al., 1995; Puri, 2010). There does appear to be a general consensus, however, that schizophrenia is marked by structural brain abnormalities that occur early

in the course of illness and in neuroleptic-naïve patients, and that some deficits are inherited (Gur et al., 2000a; Kyriakopoulos & Frangou, 2009; Nopoulos et al., 1995; Puri, 2010; Whalley, Harris, & Lawrie, 2007).

Neurobiology of insight in schizophrenia

The neural correlates of insight deficits in schizophrenia remain poorly understood. Similar to the findings in schizophrenia in general, there is some evidence of an association between poor clinical insight and reduced total brain volume, ventricular enlargement, frontal lobe atrophy, reduced frontal lobe volume, and distributed gray matter deficits (Larøi et al., 2000; Morgan et al., 2010). There is considerable inconsistency among published studies though, with occasional failure to find any brain deficits related to poor insight (Morgan et al., 2010). Some authors maintain that poor insight may not simply be a function of structural or functional abnormalities within different areas of cerebral cortex, but rather may be a lack of communication between those areas (Shad, Keshavan, Tamminga, Cullum, & David, 2007). Further, there is some evidence of reduced right dorsolateral prefrontal cortex (DLPFC) volume in schizophrenia patients but not reduced left DLPFC volume, which is consistent with the idea that lack of insight may be similar to anosognosia reported in right parietal and/or frontal cortical lesions in right-handed subjects (Shad, Muddasani, Prasad, Sweeney, & Keshavan, 2004). Another study provided evidence that white matter deficits in frontotemporal brain regions are linked to unawareness of symptoms, and abnormalities in temporal and parietal white matter regions are involved in the misattribution of symptoms (Antonius et al., 2011).

Clinical Insight

Relationship with psychiatric symptoms

Meta-analytic data show that better clinical insight is modestly but statistically significantly associated with less severe positive and negative symptoms ($r = -.25$ and $-.23$, respectively; Mintz, Dobson, & Romney, 2003; see also McEvoy et al., 2006; Saeedi, Addington, & Addington, 2007; Wiffen, Rabinowitz, Lex, & David, 2010), but more severe depressive symptoms ($r = .18$; Mintz et al., 2003; see also Drake et al., 2004; McEvoy et al., 2006; Mutsatsa, Joyce, Hutton, & Barnes, 2006; Wiffen et al., 2010). Thus, awareness of psychotic illness may result in hopelessness and depression; alternatively, those with more severe depressive symptoms may have more intact affect, which could be related to insight. Only a small percentage of variance in clinical insight is accounted for by the severity of psychiatric symptoms, however, which limits interpretations about the practical significance of such findings (Mintz et al., 2003). There is little consensus regarding the relationship between changes in clinical insight and outcome, but some evidence suggests that improving clinical insight leads to reduced psychotic symptoms (Saeedi et al., 2007; but also see Wiffen et al., 2010).

Relationship with cognition

Several lines of evidence suggest that clinical insight and cognitive functioning are related in schizophrenia. Better clinical insight is related to better cognition in general (Aleman, Agrawal, Morgan, & David, 2006; Keshavan, Rabinowitz, DeSmedt, Harvey, & Schooler, 2004; McEvoy et al., 2006; Ritsner & Blumenkrantz, 2007), better executive functioning in general (Aleman et al., 2006; Larøi et al., 2000), and better performance on specific executive functioning tests (Wisconsin Card Sorting Test, Aleman et al., 2006; Monteiro, Silva, & Louzã, 2008; Mysore et al., 2007; Shad et al., 2004; Simon, De

Hert, Wampers, Peuskens, & van Winkel, 2009; Tower of London test, Medalia & Thysen, 2010). Drake and Lewis (2003) showed that the executive skills of set-shifting and abstraction were not significantly related to clinical insight, but less perseveration was associated with better insight. The abundant but variable findings regarding clinical insight and executive functioning have led some researchers to support the view that poor clinical insight in schizophrenia may be a function of specific prefrontally-mediated neurocognitive deficits rather than a global deficit in neuropsychological functioning (Shad et al., 2004).

Relationship with functional outcome

People with schizophrenia who demonstrate good clinical insight are more likely to adhere to treatment and less likely to suffer prolonged psychotic symptom exacerbations (Lysaker, Buck, Salvatore, Popolo, & Dimaggio, 2009; McEvoy et al., 2006). In addition, good clinical insight is associated with better functional outcomes, including improvement in global assessment of functioning ratings and functional skills ratings after long-term inpatient treatment (Schwartz, Cohen, & Grubaugh, 1997), ability to benefit from cognitive behavioral social skills training (Emmerson, Granholm, Link, McQuaid, & Jeste, 2009), social functioning (Saeedi et al., 2007), and subjective quality of life (Kurtz & Tolman, 2011). Finally, one study indicated that improved clinical insight led to improved functioning and greater rate of remission (Saravanan et al., 2010).

Cognitive Insight

Relationship with psychiatric symptoms

Some data suggest that good cognitive insight is related to less severe positive symptoms (Bora, Erkan, Kayahan, & Veznedaroglu, 2007; but see also Greenberger &

Serper, 2010), and greater reductions in positive symptoms following treatment (Perivoliotis et al., 2010). A recent study found that the occurrence of delusions specifically was associated with poor cognitive insight, but the occurrence of solitary hallucinations (i.e., no accompanying delusions) was related to good cognitive insight (Engh et al., 2010). Improvement in cognitive insight may also predict reduction in positive symptoms (Granholm et al., 2005; but see also Bora et al., 2007).

Relationship with cognition

Better cognitive insight as measured by the Beck Cognitive Insight Scale (BCIS) has been associated with better basic neurocognitive functions such as visual working memory, executive functioning (Orfei, Spoletini, Banfi, Caltagirone, & Spalletta, 2010), and verbal learning and memory (Lepage et al., 2008). Greater self-certainty (one indicator of poor cognitive insight) may be modestly associated with poorer executive functioning, but there appears to be no relationship between self-reflectiveness (an indicator of good cognitive insight) and neuropsychological performance (Cooke et al., 2010).

Relationship with functional outcome

Cognitive insight may be particularly important for psychosocial interventions to improve cognition and daily functioning, but the existing literature is limited, with no published studies examining the direct relationship between cognitive insight and functional outcome. One study reported that following a cognitive behavioral and social skills intervention, participants demonstrated improved cognitive insight as well as social functioning, though these were separate findings and it was not examined whether cognitive insight mediated change in social functioning (Granholm et al., 2005).

Neurocognitive Insight

Relationship with psychiatric symptoms

Numerous studies have demonstrated that greater self-report of cognitive problems is significantly related to increased depression (Medalia, Thysen, & Freilich, 2008; Moritz, Ferahli, & Naber, 2004). Further investigation revealed that greater awareness of neurocognitive dysfunction was significantly associated with more psychiatric symptoms, particularly anxiety and depression, but not thought disorder or activation (Saperstein, Thysen, & Medalia, 2012).

Relationship with cognition

In one study, 95% of participants were cognitively impaired, though more than half of the sample had no awareness of cognitive dysfunction; further, of those who had some awareness, cognitive deficits were only partially attributed to mental illness (Medalia & Thysen, 2008). Neurocognitive insight appears to relate differently than clinical insight to neuropsychological performance; Medalia and Thysen (2010) demonstrated that neuropsychological variables were significantly associated with clinical insight but not neurocognitive insight, and that participants had significantly less insight into their neurocognitive symptoms than their clinical symptoms. To date, no consistent evidence has emerged to suggest that neurocognitive insight converges with objective cognitive performance (Keefe, Poe, Walker, Kang, & Harvey, 2006; Medalia & Lim, 2004; Medalia, Thysen, & Freilich, 2008; Moritz, Ferahli, & Naber, 2004; Poletti et al., 2012; Saperstein, Thysen, & Medalia, 2012).

Relationship with functional outcome

A recent study showed that higher rates of self-reported cognitive complaints were associated with lower treatment utilization, suggesting that clinicians may need to target those at risk for drop out with more intensive follow-up care, compensatory strategies, and psychoeducation (Gooding, Saperstein, Rivera Mindt, & Medalia, 2012). Other authors have demonstrated differential relationships between metacognition and functional capacity performance, raising the possibility that the ability to use metacognitive knowledge to respond to daily life is uniquely linked with certain types of functional competence (Lysaker et al., 2011b).

Competing hypotheses of impaired insight in schizophrenia

There is a long-standing debate in the psychiatric literature about whether unawareness of illness in schizophrenia represents cerebral dysfunction, a psychological defense, or some combination. Osatuke, Ciesla, Kasckow, Zisook, and Mohamed (2008) outlined several different etiological models of insight, including lack of insight as (1) a positive symptom, (2) a negative symptom, (3) a disorganized symptom, (4) a neurological or neuropsychological deficit, (5) impaired metarepresentation or theory of mind, (6) a neuroanatomic deficit, and (7) a psychological defense. Their conclusion: “at present, the etiology of insight or awareness of illness in psychotic disorders remains uncertain. Multiple theories draw support from a variety of studies, with a comprehensive conceptual model yet unavailable” (Osatuke et al., 2008, p. 75). Indeed, there are a number of studies with strikingly variable conclusions. For example, some investigations have supported the “neurological or neuropsychological deficit” theory; one study provided evidence that unaware participants demonstrate significantly poorer performance on neurocognitive assessments linked to the integrity of the prefrontal

cortex (Lysaker et al., 2009), and another demonstrated that awareness of illness increased with clozapine treatment and was associated with an increase in P300 amplitude after clozapine (Pallanti, Quercioli, & Pazzagli, 1999). Conclusions supporting alternative pathways are mostly drawn from studies with negative findings on the relationship between insight and cognition; one study showed that executive function did not significantly contribute to the prediction of insight (Pruß, Wiedl, & Waldorf, 2012), and another concluded that symptoms explained a greater amount of the variance in insight than did executive functioning (Simon et al., 2009). Still other studies have supported combined etiological models. For example, one study evaluated alternative theories that poor insight in schizophrenia results from deficits in executive function and a preference for denial as a coping strategy (Lysaker, Lancaster, Davis, & Clements, 2003). Cluster analysis yielded both a poor insight and average executive functioning group who endorsed a greater preference for denial, and a poor insight and poor executive functioning group who made no such endorsement. These results appear to support both theories of poor insight in schizophrenia. Further, Subotnik and colleagues (2005) found that unawareness that persisted during remission of psychosis was associated with a neurocognitive deficit that also persisted, and not with psychological defensiveness. Unawareness during an acute phase of psychosis, however, was associated with psychological defensiveness and not neurocognitive dysfunction. Despite a growing body of literature and increasingly sophisticated imaging and assessment techniques, at present an integrated model of impaired insight in schizophrenia remains out of reach.

Aims and Hypotheses

Despite the known cognitive dysfunction associated with schizophrenia, the extent to which affected individuals show awareness of such impairment and whether that affects treatment-seeking behavior and treatment outcome is unclear. The general aims of the proposed research, therefore, were to explore the range of clinical, cognitive, and neurocognitive insight among individuals diagnosed with schizophrenia, the resulting relationships between insight and objective cognitive performance, and whether insight affects treatment adherence and/or outcome. Three studies addressed these questions:

(1) Clinical and cognitive insight in Compensatory Cognitive Training. The main aim of this study was to investigate the role of clinical and cognitive insight in a Compensatory Cognitive Training (CCT) intervention.

Hypothesis 1. Better clinical and cognitive insight will be associated with better executive functioning, less severe positive symptoms, and more severe depressive symptoms.

Hypothesis 2. Receiving CCT will result in improved cognitive but not clinical insight.

Exploratory analysis: To examine the relationships between clinical and cognitive insight at baseline and later neuropsychological and clinical treatment outcomes.

(2) Neurocognitive insight and objective cognitive functioning in schizophrenia. The aim of this study was to evaluate cross-sectional relationships between neurocognitive insight and objective cognition, functional capacity, and psychiatric symptoms in a schizophrenia sample.

Hypothesis 1. Participants with impaired neurocognitive insight will demonstrate domain-specific impairment in executive functioning.

Hypothesis 2. Participants with impaired neurocognitive insight will demonstrate poorer functional capacity.

Hypothesis 3. Individuals with impaired neurocognitive insight will have more severe negative symptoms but less severe depressive symptoms.

(3) Neurocognitive insight, treatment utilization, and treatment outcome in schizophrenia. The aims of this study were to examine awareness of cognitive dysfunction among cognitive treatment-seeking psychiatric patients who participated in a longitudinal randomized controlled trial, and whether that awareness was related to treatment utilization or treatment outcome.

Hypothesis 1. Participants with impaired neurocognitive insight (i.e., few self-reported cognitive symptoms despite evidence of objective cognitive impairment) will demonstrate poorer treatment utilization, including attendance, satisfaction with the intervention, and self-reported strategy use at post-treatment.

Hypothesis 2. Impaired neurocognitive insight will negatively affect treatment outcome as measured by cognitive and functional capacity performance.

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CHAPTER 2: CLINICAL AND COGNITIVE INSIGHT IN A COMPENSATORY COGNITIVE TRAINING INTERVENTION

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ABSTRACT

The impact of limited insight is a crucial consideration in the treatment of individuals with psychiatric illness. In the context of psychosis, both clinical and cognitive insight have been described. This study aimed to evaluate the relationships between clinical and cognitive insight and neuropsychological functioning, psychiatric symptom severity, and everyday functioning in patients with a primary psychotic disorder participating in a cognitive training intervention. Sixty-nine individuals diagnosed with a primary psychotic disorder were randomized to a 3-month cognitive training intervention (CT) or to standard pharmacotherapy, and completed a comprehensive neuropsychological, clinical, and functional battery at baseline, 3 months, and 6 months. The CT intervention focused on habit formation and compensatory strategy learning in four domains: prospective memory, attention and vigilance, learning and memory, and problem-solving/cognitive flexibility. At baseline, better clinical insight was significantly related to better executive functioning and less severe negative symptoms. There was no significant association between cognitive insight and cognitive functioning, symptom severity, or everyday functioning ability. The CT intervention did not have an effect on clinical or cognitive insight, but better cognitive insight prior to participation in CT significantly predicted decreased positive and depressive symptom severity at post-treatment, and better clinical insight predicted improved self-reported quality of life. Although clinical insight is related to executive functioning, the correlates of cognitive insight remain elusive. Intact insight appears to be beneficial in ameliorating clinical symptomatology like positive symptoms and depression, rather than augmenting cognition. It may be valuable to develop brief interventions aimed at improving clinical

and cognitive insight prior to other psychosocial rehabilitation, in order to maximize the benefit of treatment.

Introduction

Insight is considered a crucial component of psychiatric illness. Historically, insight was a unidimensional construct defined as awareness of having a mental disorder and recognition of the need for treatment (Amador et al., 1993; Birchwood, Smith, & Drury, 1994; Kay, Fiszbein, & Opler, 1987a). This is similar to the relevant neurological disorder anosognosia, a condition in which a person is unable to be aware of his or her impairment as a result of neurocognitive dysfunction resulting from brain injury (Rickelman, 2004). Recently, the concept of insight has expanded to include clinical insight as well as metacognition or “thinking about thinking” (see Lysaker et al., 2010), a broad term that encompasses both cognitive insight and neurocognitive insight.

Clinical insight

Clinical insight relates primarily to treatment outcomes in disordered populations and involves “the awareness of having a mental disorder or symptoms of a mental disorder” (Amador et al., 1993, pg. 873). It has often been measured as a dichotomous variable, with patients rated as having “good” or “poor” insight based on whether the patient acknowledged or denied mental disturbance. This approach was limited because it failed to account for differing degrees of awareness, or partial insight (e.g., a patient acknowledges some symptoms but not others; Amador et al.). Contemporary measures of clinical insight are more continuous and incorporate awareness of multiple psychiatric symptoms as well as the need for treatment and the effects of medication.

Cognitive insight

Cognitive insight is a recently defined aspect of metacognition (Beck, Baruch, Balter, Steer, & Warman, 2004). As described by Beck's research group (2004), cognitive insight involves a person's capacity to evaluate unusual experiences and question potentially flawed conclusions, which relies on distancing oneself from misguided beliefs and re-evaluating misinterpretations. The capacity to reflect on experiences and recognize incorrect conclusions is reduced by impaired objectivity about cognitive distortions, loss of ability to gain perspective on these experiences, resistance to corrective information, and overconfidence in conclusions (Beck et al). Previous research has demonstrated modest to moderate convergence between a measure of cognitive insight and measures of clinical insight, supporting the claim that cognitive and clinical insight are related but distinct concepts (.24-.64 range; Beck et al.; Pedrelli et al., 2004).

Neurocognitive insight

Another type of metacognitive insight is neurocognitive insight, defined as the awareness of neuropsychological dysfunction in schizophrenia-spectrum disorders (e.g., impaired attention, memory, problem-solving; Medalia & Thysen, 2008). Instruments to measure neurocognitive insight have been created to assess insight into cognitive deficits in comparison to actual performance on cognitive tests (Medalia & Thysen, 2010), as well as to allow reliable measurement of patients' or caregivers' opinions about a patient's degree of neurocognitive deficit (Keefe, Poe, Walker, Kang, & Harvey, 2006).

The concepts of clinical and cognitive insight are especially relevant in psychotic disorders. Individuals with psychosis are prone to disorganized and delusional thinking, which can interfere with the ability to recognize symptoms of psychiatric illness and discourage the pursuit of treatment (clinical insight). The ability to appraise erroneous

beliefs (cognitive insight) is also affected by psychosis, leading to rigid and concrete thinking that impacts daily living as well as treatment adherence. By definition, the formation and maintenance of delusions are accompanied by steadfast conviction in the truth of such beliefs, even in the presence of contradictory evidence. This feature of psychosis precludes the use of corrective feedback, complicating treatments for psychotic disorders that involve medication maintenance or therapeutic intervention (Beck et al., 2004). Even if clinical insight is intact, lack of cognitive insight may limit cognitive skills like problem-solving, gathering evidence, and hypothesis testing, which are among the cornerstones of psychosocial therapy for psychosis (Gaudiano, 2006; McCann, 2001). Thus, the treatment implications of limited insight are profound. Antipsychotic medications have proven useful in reducing some symptoms of psychosis, but residual symptoms and negative side effects decrease treatment adherence (Kane, 2001); this may be especially true for people with restricted insight. Numerous psychosocial treatments for psychotic disorders are available, but the utility of such interventions may be reduced if poor insight discourages people with psychotic disorders from adhering to the treatment or agreeing to participate at all. Therefore, clarification of the role of clinical and cognitive insight in psychosocial interventions is vital to the advancement of treatment for psychosis. Of particular importance is whether targeted cognitive training in self-monitoring and hypothesis testing might improve cognitive insight in those diagnosed with psychotic disorders.

Previous research has identified a link between clinical insight and neuropsychological functioning: better clinical insight has been related to better cognition in general (McEvoy et al., 2006), better executive functioning in general (Aleman,

Agrawal, Morgan, & David, 2006), and better performance on specific executive functioning tests (Wisconsin Card Sorting Test, Aleman et al.; Tower of London test, Medalia & Thysen, 2010). Meta-analytic data show that better clinical insight is associated with less severe positive and negative symptoms ($r = -.25$ & $-.23$, respectively; Mintz, Dobson, & Romney, 2003; see also McEvoy et al.; Saeedi, Addington, & Addington, 2007; Wiffen, Rabinowitz, Lex, & David, in press), but more severe depressive symptoms ($r = .18$; Mintz et al.; see also Drake et al., 2004; McEvoy et al.; Wiffen et al.). Thus, intact clinical insight may result in hopelessness, shame, and depression. People with schizophrenia who demonstrate good clinical insight are more likely to adhere to treatment and less likely to suffer prolonged psychotic symptom exacerbations (Lysaker, Buck, Salvatore, Popolo, & Dimaggio, 2009; McEvoy et al.). Finally, good clinical insight is associated with better functional outcomes, including improvement in global assessment of functioning ratings and functional skills ratings after long-term inpatient treatment (Schwartz, Cohen, & Grubaugh, 1997), ability to benefit from cognitive behavioral social skills training (Emmerson, Granholm, Link, McQuaid, & Jeste, 2009), and social functioning (Saeedi et al.). There is little consensus regarding the relationship between changes in clinical insight and outcome, but some studies have found that improving insight leads to reduced psychotic symptoms (Saeedi et al.; but also see Wiffen et al.), improved functioning, and greater rate of remission (Saravanan et al., 2010).

Because the concept of cognitive insight is relatively novel, its relationship to cognition, symptom severity, and functioning has been less extensively investigated. Better cognitive insight as measured by the Beck Cognitive Insight Scale (BCIS) has

been associated with better basic neurocognitive functions such as visual working memory, executive functioning (Orfei, Spoletini, Banfi, Caltagirone, & Spalletta, 2010), and verbal learning and memory (Lepage et al., 2008). Greater self-certainty (one indicator of poor cognitive insight) may be modestly associated with poorer executive functioning, but there appears to be no relationship between self-reflectiveness (an indicator of good cognitive insight) and neuropsychological performance (Cooke et al., 2010). Some data suggest that good cognitive insight is related to less severe positive symptoms (Bora, Erkan, Kayahan, & Veznedaroglu, 2007; but see also Greenberger & Serper, 2010), and greater reductions in positive symptoms following treatment (Perivoliotis et al., 2010). A recent study found that the occurrence of delusions specifically was associated with poor cognitive insight, but the occurrence of solitary hallucinations (i.e., no accompanying delusions) was related to good cognitive insight (Engh et al., 2010). Improvement in cognitive insight may also predict reduction in positive symptoms (Granholm et al., 2005; but see also Bora et al.). Cognitive insight may be particularly important for psychosocial interventions to improve cognition and daily functioning, but the existing literature is limited, with no published studies examining the relationship between cognitive insight and functional outcome.

Given the variable conclusions and variable effects across studies in the published literature, further investigation of clinical and cognitive insight and their relationship to neuropsychological performance, psychiatric symptoms, and everyday functioning is necessary. In addition, the effect of insight on treatment outcome requires further investigation, particularly as non-pharmacological interventions for psychosis continue to

accumulate. This study aimed to evaluate clinical and cognitive insight in patients with a primary psychotic disorder participating in a cognitive training intervention.

Consistent with previous literature and the idea that executive functioning (self-monitoring, hypothesis testing) might be especially related to insight, we hypothesized that better clinical and cognitive insight would be associated with better executive functioning, less severe positive symptoms, and more severe depressive symptoms. Secondly, because the intervention targeted specific domains of cognition (e.g., self-monitoring of strategy use) but not other clinical features of psychosis (e.g., self-monitoring of psychiatric symptoms), we hypothesized that the cognitive training intervention would improve cognitive, but not clinical, insight. In addition, cognitive insight may reflect flexibility and openness to trying new strategies, so we believed it would be associated with CT-related improvement more so than clinical insight.

We also explored the relationships between clinical and cognitive insight at baseline and later neuropsychological and clinical treatment outcomes, to examine whether initial level of insight leads to differential impact of treatment (via, e.g., willingness to try new strategies).

Method

Participants

Participants included 69 individuals receiving outpatient psychiatric care who were enrolled in a study of compensatory cognitive training for psychosis, described in a previous report (Twamley, Savla, Zurhellen, Heaton, & Jeste, 2008; 38 of the 69 participants' data was included in this report, but no analyses related to insight were previously reported). Participants were diagnosed with a primary psychotic disorder

(schizophrenia, schizoaffective disorder, psychosis not otherwise specified, or major depression with psychotic features); they completed a baseline assessment and were randomized to the treatment or control group. A subsample of 23 participants received the cognitive training intervention and completed at least one post-treatment assessment. A CONSORT diagram (Figure 1) is included to indicate sample size and attrition. The study was IRB approved and all participants provided written informed consent to participate. Demographic and clinical characteristics of both samples are included in Table 1. Overall, participants in the main sample (completed baseline assessment and randomized to treatment or control) had a mean age of 46 and completed 13 years of education. A majority of the sample were men, Caucasian, never married, and living independently in the community. Participants were chronically ill (mean duration of psychotic illness was 23 years) and most were prescribed atypical antipsychotic medication. Schizophrenia and schizoaffective disorder diagnoses were roughly equal. The characteristics of the subsample were similar; there were no significant demographic or clinical differences between the 23 cognitive training participants who completed a post-treatment assessment and the 46 participants who completed a baseline assessment only (i.e., lost to follow-up before 3-month assessment; $n=18$), or who completed a follow-up assessment as part of the control group and were not included in the cognitive training subsample analyses ($n=28$; all $ps \geq .188$).

Procedure

Potential participants were referred to the study by treating clinicians or self-response to recruitment flyers posted in psychiatric care centers. Following a detailed description of the study, participants provided written informed consent to a research

assistant. Participants' diagnoses were confirmed via structured diagnostic interview (Mini International Neuropsychiatric Interview; Sheehan et al., 1998) or diagnostic chart review. Inclusion criteria were: (a) DSM-IV (American Psychiatric Association, 1994) diagnosis of schizophrenia, schizoaffective disorder, or primary diagnosis of psychosis NOS or major depression with psychotic features, (b) English-speaking, (c) 18 years of age or older. Individuals were excluded from the study if they had: (a) substance use disorder in the past 30 days, (b) a history of neurological disease or injury, (c) mental retardation, or (d) concurrent enrollment in another treatment research protocol. Ongoing therapeutic interventions were permitted. Following baseline assessment, participants were randomly assigned to standard pharmacotherapy plus the cognitive training intervention (CT) or to standard pharmacotherapy alone. A comprehensive neuropsychological, clinical, and functional battery was administered at baseline, 3 months (immediate post-treatment), and 6 months (follow-up); raters were blinded to group assignment. The CT intervention is a 12-week, 2 hour per week class that focuses on habit formation and compensatory strategy learning in four cognitive domains: prospective memory, attention and vigilance, learning and memory, and problem-solving/cognitive flexibility. Examples of compensatory strategies include the use of calendars, paraphrasing important information, brainstorming solutions to a problem, self-monitoring progress, and gathering pro and con evidence to test hypotheses. The cognitive flexibility module of CT includes strategies for heightening cognitive awareness, for example self-monitoring or thinking about strategies one is using and modifying them as necessary. The primary targets of the CT intervention were cognition and everyday functioning; insight was examined as a secondary outcome. The main

outcomes of the randomized controlled trial are reported elsewhere (Twamley et al., under review), but briefly, the CT intervention appears to improve cognition, negative symptoms, functional capacity, and quality of life.

Measures

Premorbid intellectual functioning was measured with the American National Adult Reading Test (ANART; Grober & Sliwinski, 1991). Cognitive functioning was measured with a battery including domains targeted in CT and domains not targeted in CT. Targeted domains and measures included:

1. Prospective memory: Memory for Intentions Screening Test (total score; Raskin, 2004)
2. Attention and vigilance: Wechsler Adult Intelligence Scale, third edition (WAIS-III) Digit Span forward (Wechsler, 1997)
3. Verbal learning and memory: Hopkins Verbal Learning Test - Revised (HVLTR, total immediate recall and percent retained; Brandt & Benedict, 2001)
4. Executive Functioning: Wisconsin Card Sorting Test (WCST; total correct; Kongs, Thompson, Iverson, & Heaton, 2000)

Domains and measures not targeted by the CT intervention included:

1. Processing speed: WAIS-III Digit Symbol total correct (Wechsler, 1997)
2. Working memory: WAIS-III Letter-Number Sequencing total correct (Wechsler, 1997)
3. Language: Controlled Oral Word Association Test (AFV total; Benton & Hamsher, 1989)

Psychotic symptom severity was measured with the Positive and Negative Syndrome Scale, using the positive symptom total (sum of items P1-P7) and the negative symptom total (sum of items N1-N7; PANSS; Kay et al., 1987a). Depressive symptom severity was measured with the Hamilton Depression Rating Scale (HAMD; sum of items 1-17; Hamilton, 1960), and quality of life was measured with the Quality of Life Interview (QOLI; Global Subjective Life Satisfaction score; Lehman 1988). Everyday functioning ability was measured with the UCSD Performance-Based Skills Assessment (UPSA; total score; Patterson, Moscona, McKibbin, Hughs, & Jeste, 2001) and the Social Skills Performance Assessment (SSPA; total score; Patterson, Moscona, McKibbin, Davidson, & Jeste, 2001), both role-play tests of real-world living and social skills, as well as the self-report Independent Living Skills Survey (ILSS; mean of all subscales; Wallace, Liberman, Tauber, & Wallace, 2000).

Clinical insight was measured with the “Lack of Judgment and Insight” item from the PANSS interview. The description of this clinician-rated item is “impaired awareness or understanding of one’s own psychiatric condition and life situation. This is evidenced by failure to recognize past or present psychiatric illness or symptoms, denial of need for psychiatric hospitalization or treatment, decisions characterized by poor anticipation of consequences, and unrealistic short-term and long-range planning” (Kay, Opler, & Fiszbein, 1987b). Interviewers rate insight on a 1 (absent) to 7 (severe) scale using self-report information elicited directly from the interviewee; lower scores indicate better clinical insight. Raters for this study demonstrated good interrater reliability on the PANSS ($ICC \geq 0.80$).

Cognitive insight was measured with the Beck Cognitive Insight Scale (Beck et al., 2004), a 15-item self-report questionnaire that assesses both self-reflectiveness and self-certainty. Respondents rate their agreement with various statements on a 0-3 scale. Items that comprise the self-reflectiveness (SR) subscale measure objectivity, reflectiveness, and openness to feedback (e.g., “At times I have misunderstood other people’s attitudes towards me,” “Some of my experiences that have seemed very real may have been due to my imagination”). The self-certainty (SC) subscale assesses decision-making and dogmatic certainty about beliefs and conclusions (e.g., “I know better than anyone else what my problems are,” “I cannot trust other people’s opinion about my experiences”). Additional sample items from the BCIS are listed in the appendix. Scores for each subscale are summed; higher scores on the SR subscale are considered favorable (i.e., more self-reflective), and higher scores on the SC subscale are considered poor (i.e., more overconfidence). The authors of the BCIS hypothesized that higher levels of self-certainty would diminish a person’s capacity for self-reflection, so a composite index score (SR-SC index) is calculated by subtracting the self-certainty total from the self-reflectiveness total and is used as the principal indicator of cognitive insight. The possible score range of the BCIS SR-SC index is -18 through 27; higher scores indicate better cognitive insight.

Data analyses

All variables were inspected for normality; the variable for change in digit span score and the variable for change in SSPA total were found to have leptokurtic distributions. Use of log transformed variables did not change the results, so for ease of interpretation, the non-transformed results are reported. The first hypothesis was tested

with Pearson correlations ($n=69$) between the insight measures and neuropsychological test scores, symptom severity ratings, and everyday functioning measures. The second hypothesis was tested with repeated measures ANOVA of BCIS SR-SC index score using participants who completed at least one post-treatment assessment ($n=47$; 20 CT [3 participants had missing baseline BCIS data] and 27 SP [1 participant had missing baseline BCIS data]). Pearson correlations were used for the exploratory analyses ($n=23$), testing baseline PANSS insight item as a predictor of change scores on neuropsychological measures, as well as clinical and functional outcomes; the same analysis was used for the baseline BCIS SR-SC index score. Alpha for significance was set at 0.05; data were analyzed using PASW Statistics for Windows (Version 18).

Results

At baseline, the mean PANSS insight item score was 1.8 (range 1-6); the mean BCIS SR-SC index score was 6.6 (range -3-25; Table 1). This cognitive insight score is fairly consistent with, but slightly higher, than that previously been reported in psychosis samples (Beck et al., 2004; Colis, Steer, & Beck, 2006; Martin, Warman, & Lysaker, 2010; Pedrelli et al., 2004). Table 2 includes mean post-treatment PANSS insight item score and BCIS SR-SC index score for the CT and the SP groups. The PANSS insight item score and the BCIS SR-SC index score were modestly, but not significantly correlated at any time point (Baseline $r=-.27$; $p=.070$; immediate post-treatment $r=-.22$; $p=.160$; follow-up $r=-.29$; $p=.053$), although the strength of the correlations was similar to that reported previously (Beck et al.; Pedrelli et al.).

The first hypothesis was partially supported. Better clinical insight was significantly related to better executive functioning as measured by the WCST ($r=-.25$;

$p=.037$), and less severe negative symptoms ($r=.27$; $p=.027$), but was not related to positive symptoms ($p=.105$). There were no significant baseline correlations between cognitive insight and neuropsychological test scores, symptom severity ratings, or functional outcomes (all $ps \geq .144$; see Table 3).

Contrary to our second hypothesis, participation in the CT intervention did not produce any significant changes in cognitive insight in comparison to the control group ($F[1,45]=.03$; partial $\eta^2=.001$; $p=.856$).

With regard to our exploratory analyses, neither baseline clinical insight nor cognitive insight predicted change on neuropsychological measures (Table 4). Higher cognitive insight at baseline significantly predicted lower positive symptom severity ($r=-.46$; $p=.040$), as well as decreased depressive symptom severity ($r=-.54$; $p=.014$) at post-treatment. In addition, better clinical insight at baseline significantly predicted increased subjective quality of life at post-treatment ($r=-.46$; $p=.036$; Table 4).

Discussion

In contrast to our expectation, these results suggest minimal association between cognitive insight and cognitive functioning. Better clinical insight, however, appears to be related to better executive functioning and less severe negative symptoms. Although the CT intervention did not have an effect on clinical or cognitive insight, we found that better insight prior to participation in the CT intervention predicted decreased positive and depressive symptom severity, as well as improved self-reported quality of life at post-treatment.

This study was unable to replicate previous cross-sectional findings linking clinical and cognitive insight to general cognitive ability, positive symptoms, depression,

and everyday functioning (Aleman et al., 2006; Bora et al., 2007; McEvoy et al., 2006; Mintz et al., 2003; Saeedi et al., 2007; Schwartz et al., 1997; Wiffen et al., 2010). However, our non-significant findings on the relationship between baseline BCIS and symptom severity replicate those of a recent study comparing BCIS self-reflectiveness and self-certainty on multiple PANSS domains (Greenberger & Serper, 2010). In addition, although other studies have found a relationship between cognitive insight and executive functioning (Cooke et al., 2010; Orfei et al., 2010), our results suggest instead that better *clinical* insight is related to better executive abilities. This is consistent with other findings that individuals with schizophrenia who showed better clinical insight performed better on measures of executive functioning (Aleman et al., 2006; Medalia & Thysen, 2010). It could be that individuals who acknowledge their psychiatric illness and identify a need for treatment exercise their problem-solving abilities by seeking intervention. Our results also replicated other findings that those with better clinical insight demonstrated less severe negative symptoms (Mintz et al., 2003); although this finding was not hypothesized, the effect could be driven by overall illness severity or by a specific link between cognition and negative symptoms (Harvey, Koren, Reichenberg, & Bowie, 2006).

Whereas other treatment studies have shown evidence that insight can improve over time (Granholm et al., 2005; Saeedi et al., 2007), the CT intervention failed to demonstrate any effect on clinical or cognitive insight. This is not necessarily surprising, as CT does not specifically target insight. Our hypothesis, however, was that the hypothesis testing and self-monitoring strategies included in the CT intervention might improve cognitive insight. It is possible that those who enroll in treatment programs are

more insightful to begin with, because they self-selected into a study targeting improvement in cognitive functioning. Indeed, this sample started out with relatively good insight, which resulted in a restricted range of insight scores and could have limited potential for improvement in insight. Nonetheless, this study was conducted with a sample of individuals interested in rehabilitation, so the results should generalize to similar, rehabilitation-seeking samples.

Finally, these results extend previous findings by showing that better clinical insight at baseline predicts improved quality of life, and better cognitive insight at baseline predicts decreased severity of positive and depressive symptoms following CT. It may be the case that intact insight allows for more flexible appraisal of one's life situation, enabling a more interactive approach to rehabilitation. Better insight did not predict improvement across all domains, however, which may suggest that intact insight is not a necessary condition to benefit from cognitive training, but rather that the CT intervention can be effective regardless of baseline insight level.

Limitations of this study include small sample size in the CT post-treatment subsample, which limited power to detect significant change in clinical or cognitive insight and accordingly increased the chance of Type II error. In addition, no corrections were made for multiple comparisons, which may impact the statistical significance of the results. Further, clinical insight was only measured with one item of the PANSS interview. Previous research has supported the convergent validity of the PANSS insight item with other measures of clinical insight such as awareness of mental disorder on the Scale to Assess Unawareness of Mental Disorder (SUMD; $r=0.66$; $p<0.001$; Tranulis, Lepage, & Malla, 2008) and the Birchwood Insight Scale (IS; $r=-0.65$; $p<0.001$; Cooke et

al., 2007). Nevertheless, it would have been beneficial to include another more comprehensive instrument of clinical insight like the SUMD (Amador et al., 1993) or the IS (Birchwood et al., 1994). Our measure of cognitive insight has limitations as well: the BCIS is more likely to be related to flexibility about maladaptive thoughts and may not accurately reflect flexibility in trying new strategies (e.g., flexibility in examining thoughts may not be the same process as flexibility in strategy use for medication adherence or appointment attendance.) Also, because the BCIS is a relatively new instrument, its psychometric properties are still under evaluation and its use remains limited to research samples. Finally, this study did not evaluate neurocognitive insight, which is a more recently developed concept; future cognitive remediation studies would benefit from measurement of neurocognitive insight because it may predict treatment acceptance and engagement.

Despite these limitations, the current study is among the first to investigate clinical and cognitive insight during the course of a cognitive intervention. Although numerous studies have examined cross-sectional relationships between insight and cognitive and clinical domains, few have demonstrated the influence of insight in longitudinal designs. Also, this study included a comprehensive battery of neuropsychological measures, psychiatric symptom ratings, and everyday functioning measures, capturing the broad applicability of insight to treatment outcomes.

If these results remain consistent in larger, more diverse samples, the implications for treatment are informative. First, level of cognitive and clinical insight may be immaterial to interventions targeting cognition exclusively. Successful cognitive remediation appears possible despite poor insight, as long as an individual is willing to

enroll in and adhere to a treatment protocol. However, limited cognitive insight may reduce interest in cognitive remediation interventions. Second, intact insight appears to be beneficial in ameliorating clinical symptomatology such as positive symptoms and depression. If this is the case, it would be valuable to include awareness-heightening strategies as part of the rehabilitation readiness process for individuals in the pre-contemplation stage (Prochaska & Velicer, 1997) who may not be ready to enroll in a treatment program. Also, it may be possible to develop brief interventions aimed at improving clinical and cognitive insight prior to other psychosocial rehabilitation, in order to maximize the benefit of treatment. Further, because the impact of limited insight has profound treatment implications, patients and families may benefit from psychoeducational resources to encourage adherence to treatment (e.g., Amador, 2000). Ultimately, the goal of any intervention is to improve everyday functioning for those who suffer from psychiatric illness. Demonstrating improvement in psychiatric symptoms and quality of life may be a first step, but further investigation is warranted to explore how these benefits may extend to everyday functioning and successful community integration in individuals with psychosis.

Chapter 2, in full, is a reprint of the material as it appears in the American Journal of Psychiatric Rehabilitation 2011. Burton, Cynthia Z.; Vella, Lea; Twamley, Elizabeth W., Routledge Press, 2011. The dissertation author was the primary investigator and author of this paper.

Table 2.1: Demographic and Clinical Characteristics of the Samples

	Randomized Sample (n=69)	CT post- treatment Sample (n=23)
	Mean (SD) or %	Mean (SD) or %
Age (years)	46.3 (9.7)	44.4 (10.4)
Duration of Illness (years)	23.3 (12.3)	20.5 (14.2)
Education (years)	12.9 (1.7)	13.3 (1.8)
ANART estimated IQ	106.9 (10.0)	106.0 (9.4)
Male	65.2	65.2
Caucasian, non-Hispanic	63.8	73.9
Diagnosis		
Schizophrenia	53.6	43.5
Schizoaffective	43.5	52.2
Psychosis NOS	1.4	4.3
MDD + psychotic features	1.4	0.0
Antipsychotic Medication		
None	6.0	0
Atypical only	85.1	90.5
Typical only	4.5	4.8
Both Atypical and Typical	4.5	4.8
Living Situation		
House or apartment	80.7	86.9
Board and care	16.4	13.0
Homeless	3.0	0
Marital status		
Single, never married	55.9	60.9
Divorced/separated	29.4	34.8
Married	13.2	4.3
Widowed	1.5	0
PANSS insight item score	1.8 (1.4)	1.9 (1.5)
BCIS index score	6.6 (5.6)	7.6 (5.5)

Note. ANART=American National Adult Reading Test; MDD=Major Depressive Disorder; PANSS=Positive and Negative Syndrome Scale; BCIS=Beck Cognitive Insight Scale.

Table 2.2: Post-treatment Clinical and Cognitive Insight Scores by Group

	Immediate Post-treatment						Follow-up					
	CT			SP			CT			SP		
	n	mean (sd)	range	n	mean (sd)	range	n	mean (sd)	range	n	mean (sd)	range
PANSS insight item	20	2.0 (1.3)	1-5	24	2.1 (1.7)	1-6	21	1.9 (1.3)	1-4	25	2.1 (1.7)	1-6
BCIS SR-SC index	20	6.4 (6.8)	-9-17	24	5.6 (6.0)	-13-17	22	7.6 (6.1)	-4-19	25	5.3 (5.3)	-10-16

Note. PANSS=Positive and Negative Syndrome Scale; BCIS=Beck Cognitive Insight Scale.

Table 2.3: Baseline Correlations between Clinical/Cognitive Insight and Neuropsychological Variables, Symptom Severity Ratings, and Everyday Functioning Variables

	PANSS insight item		BCIS SR-SC index	
	Pearson correlation	<i>p</i>	Pearson correlation	<i>p</i>
Neuropsychological variables				
MIST summary score	-.07	.565	.07	.588
Digit Span forward total score	-.02	.853	.06	.617
HVLT-R immediate recall total score	.03	.787	.12	.351
HVLT-R percent retained score	-.00	.987	.18	.155
WCST-64 total correct	-.25	.037	.13	.325
Digit Symbol total correct	-.05	.683	-.17	.167
Letter Number Sequencing total score	-.04	.747	-.01	.921
Animals/Fruits/Vegetables total correct	-.11	.360	.19	.144
Symptom severity variables				
PANSS positive total	.20	.105	.05	.684
PANSS negative total	.27	.027	-.08	.509
HAMD total	-.09	.477	.19	.187
QOLI global life satisfaction	.19	.125	.11	.388
Everyday functioning variables				
UPSA total	-.13	.281	.15	.248
SSPA total	-.17	.171	-.07	.565
ILSS mean of subscales	.05	.680	-.01	.971

Note. Significant correlations are indicated with bold font. MIST=Memory for Intentions Screening Test; HVLT-R=Hopkins Verbal Learning Test – Revised; WCST=Wisconsin Card Sorting Test; PANSS=Positive and Negative Syndrome Scale; HAMD=Hamilton Depression Rating Scale; QOLI=Quality of Life Interview; UPSA=UCSD Performance-Based Skills Assessment; SSPA=Social Skills Performance Assessment; ILSS=Independent Living Skills Survey.

Table 2.4: Baseline Clinical/Cognitive Insight as Predictors of Change in Neuropsychological Domains, Symptom Severity Ratings, and Everyday Functioning Measures

Change score	PANSS insight item		BCIS SR-SC index	
	Pearson correlation	<i>p</i>	Pearson correlation	<i>p</i>
Neuropsychological domains				
Prospective memory	-.16	.493	.05	.845
Attention	-.17	.443	.24	.302
Verbal learning	-.01	.975	.42	.063
Verbal memory	.06	.779	-.11	.643
Executive functioning	.21	.341	.23	.329
Processing speed	-.05	.821	-.15	.527
Working memory	-.28	.213	.19	.431
Language	.33	.136	.04	.876
Symptom severity ratings				
PANSS positive symptoms	-.07	.763	-.46	.040
PANSS negative symptoms	-.31	.166	.20	.394
HAMD depressive symptoms	-.17	.446	-.54	.014
QOLI global life satisfaction	-.46	.036	.05	.822
Everyday functioning measures				
UPSA	.36	.111	.10	.662
SSPA	.02	.923	-.13	.589
ILSS	-.11	.635	.06	.803

Note. Significant correlations are indicated with bold font. PANSS=Positive and Negative Syndrome Scale; HAMD=Hamilton Depression Rating Scale; QOLI=Quality of Life Interview; UPSA=UCSD Performance-Based Skills Assessment; SSPA=Social Skills Performance Assessment; ILSS=Independent Living Skills Survey.

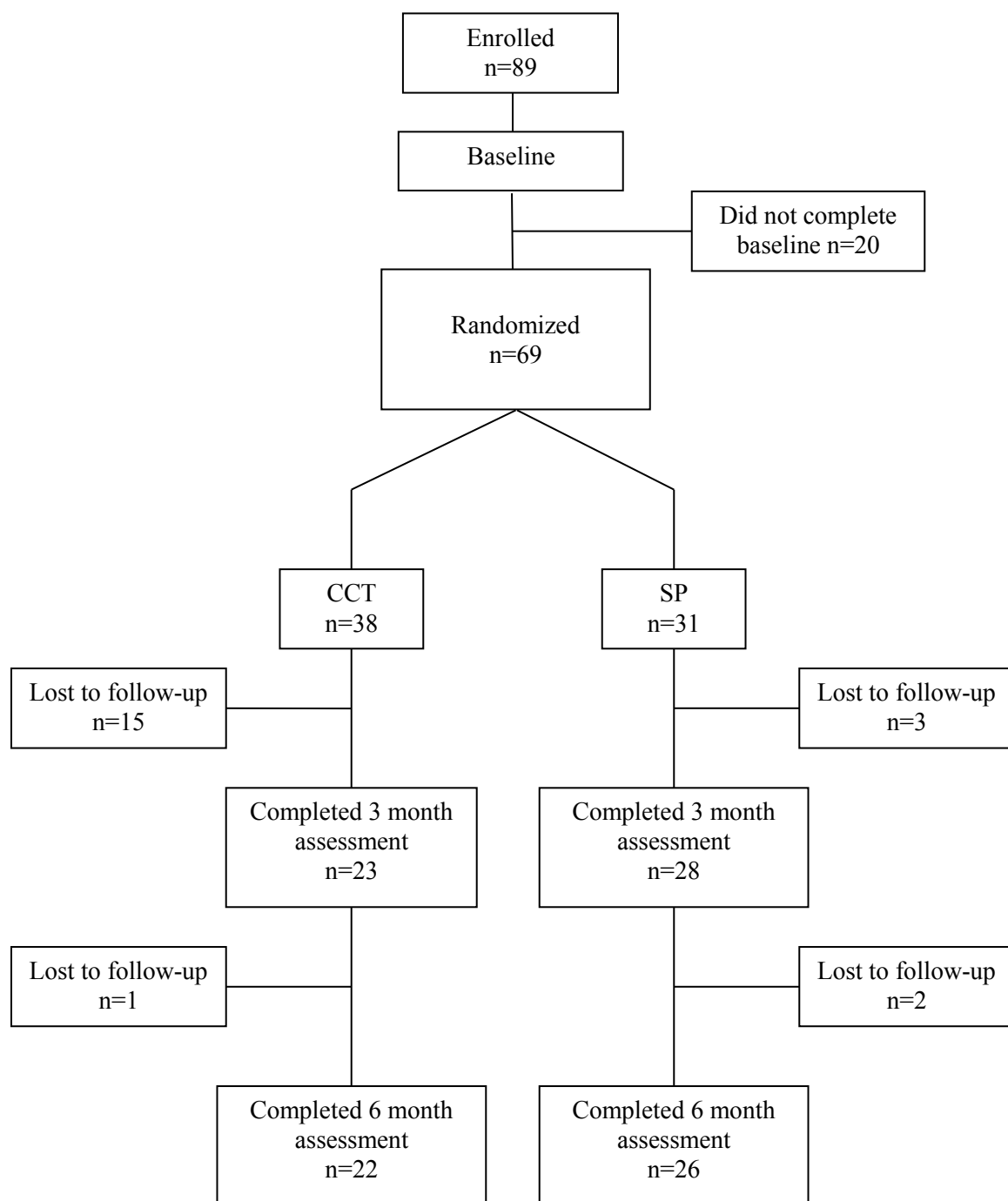


Figure 2.1: CCT CONSORT Diagram

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CHAPTER 3: NEUROCOGNITIVE INSIGHT AND OBJECTIVE COGNITIVE
FUNCTIONING IN SCHIZOPHRENIA

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ABSTRACT

Neurocognitive impairment is a core component of schizophrenia affecting everyday functioning; the extent to which individuals with schizophrenia show awareness of neurocognitive impairment (neurocognitive insight) is unclear. This study investigated neurocognitive insight and examined the cross-sectional relationships between neurocognitive insight and objective neurocognition and functional capacity performance in a large outpatient sample.

Two hundred and fourteen participants with schizophrenia-spectrum disorders completed measures of neurocognition, functional capacity, and self-reported neurocognitive problems. Latent profile analysis classified participants with regard to neuropsychological performance and self-report of neurocognitive problems. The resulting classes were then compared on executive functioning performance, functional capacity performance, and psychiatric symptom severity.

More than three quarters of the sample demonstrated objective neurocognitive impairment (global deficit score ≥ 0.50). Among the participants with neurocognitive impairment, 54% were classified as having “impaired” neurocognitive insight (i.e., reporting few neurocognitive problems despite having objective neurocognitive impairment). Participants with impaired vs. intact neurocognitive insight did not differ on executive functioning measures or measures of functional capacity or negative symptom severity, but those with intact neurocognitive insight reported higher levels of positive and depressive symptoms.

A substantial portion of individuals with schizophrenia and objectively measured neurocognitive dysfunction appear unaware of their deficits. Patient self-report of

neurocognitive problems, therefore, is not likely to reliably assess neurocognition.

Difficulty self-identifying neurocognitive impairment appears to be unrelated to executive functioning, negative symptoms, and functional capacity. For those with intact neurocognitive insight, improving depressive and psychotic symptoms may be a valuable target to maximize everyday functioning.

Introduction

Little doubt remains regarding the significance of cognitive dysfunction in schizophrenia. Empirical evidence has consistently demonstrated stable, enduring deficits in attention, processing speed, working memory, learning, and executive function, and that domain-specific deficits are relative and exist against a backdrop of generalized dysfunction (Heaton et al., 2001; Heinrichs & Zakzanis, 1998). Furthermore, a critical link has been identified between cognitive impairment and functional outcome; that is, neuropsychological dysfunction affects performance of real-world everyday activities that are necessary to live independently in the community (Green, Kern, Braff, & Mintz, 2000).

Three types of insight, or awareness of dysfunction, have been described in schizophrenia. Clinical insight refers to awareness of psychotic illness (Amador et al., 1993); cognitive insight refers to awareness of “mistakes in thinking” such as jumping to conclusions or catastrophizing (Beck, Baruch, Balter, Steer, & Warman, 2004); neurocognitive insight is defined as awareness of neuropsychological dysfunction (e.g., impaired attention, memory, problem-solving; Medalia & Thysen, 2008) expressed through subjective cognitive complaints (Stip, Caron, Renaud, Pampoulova, & Lecomte, 2003). Although the domains of clinical and cognitive insight in schizophrenia have been

extensively investigated (Burton, Vella, & Twamley, 2011; Nair, Palmer, Aleman, & David, 2014) there is less known about neurocognitive insight (Lysaker et al., 2011). Instruments to measure neurocognitive insight have been created to assess insight into cognitive deficits in comparison to actual performance on cognitive tests, as well as to allow reliable measurement of patients' or caregivers' opinions about a patient's degree of neurocognitive deficit (Keefe, Poe, Walker, Kang, & Harvey, 2006; Medalia & Thysen, 2010; Stip et al., 2003).

Although the literature on neurocognitive insight is limited, there is some evidence that individuals with schizophrenia have poorer insight into their neurocognitive symptoms than their clinical symptoms, prompting researchers to encourage that they be addressed separately in treatment (Medalia & Thysen, 2010). Indeed, a 2011 review indicated that 14 of 26 published studies found no correlation between objective cognitive performance and subjective cognitive complaints (Homayoun, Nadeau-Marcotte, Luck, & Stip, 2011). Another study reported that 95% of participants were cognitively impaired, though more than half of the sample had no awareness of cognitive dysfunction (Medalia & Thysen, 2008). Still other researchers have concluded that even when patients express cognitive difficulties, their specific complaints do not align with the cognitive domains tested (Prouteau et al., 2004). To date, no consistent evidence has emerged to suggest that neurocognitive insight converges with objective cognitive performance (Johnson, Tabbane, Dellagi, & Kebir, 2011; Keefe, Poe, Walker, Kang, & Harvey, 2006; Medalia & Lim, 2004; Medalia, Thysen, & Freilich, 2008; Moritz, Ferahli, & Naber, 2004; Poletti et al., 2012; Saperstein, Thysen, & Medalia, 2012). Despite the apparent lack of association between neurocognitive insight and objective cognitive

performance, numerous studies have demonstrated that greater self-report of cognitive problems is significantly related to increased depression and anxiety (Medalia et al., 2008; Moritz et al., 2004; Saperstein et al., 2012). Furthermore, a recent study showed that higher rates of self-reported cognitive complaints were associated with lower treatment utilization, suggesting that clinicians may need to target those at risk for drop out with more intensive follow-up care, compensatory strategies, and psychoeducation (Gooding, Saperstein, Rivera Mindt, & Medalia, 2012).

Despite the known cognitive dysfunction associated with schizophrenia, the extent to which affected individuals show awareness of such impairment is unclear. The aims of this study were to explore the range of neurocognitive insight among a large, multi-site sample of individuals diagnosed with schizophrenia, and evaluate cross-sectional relationships between neurocognitive insight and objective cognitive and functional capacity performance. The three hypotheses were as follows: (1) participants with impaired neurocognitive insight will demonstrate domain-specific impairment in executive functioning, (2) participants with impaired neurocognitive insight will demonstrate poorer functional capacity, and (3) individuals with impaired neurocognitive insight will have more severe negative symptoms but less severe depressive symptoms.

Method

Participants. These analyses were conducted as part of the larger Validating Everyday Real-World Outcomes study (VALERO) Phase II, which aimed to identify the determinants of impaired self-assessment in schizophrenia. Participants included 214 individuals diagnosed with schizophrenia or schizoaffective disorder receiving outpatient care at one of three sites: UCSD Outpatient Psychiatric Services ($n = 100$), the University

of Miami Miller School of Medicine ($n = 79$), and Skyland Trail Rehabilitation Services in Atlanta ($n = 35$). Participants were enrolled in the VALERO II parent study that was approved by each site's institutional review board. On average, participants were 41 years old and had completed 12 years of education; the majority of the sample was male, Caucasian, diagnosed with schizophrenia, and prescribed antipsychotic medication (Table 1).

Procedures. Potential participants were referred to the study by treating clinicians or self-response to recruitment flyers posted in psychiatric care centers; all participants provided written informed consent prior to any data collection. Participants' diagnoses were confirmed via structured diagnostic interview (Mini International Neuropsychiatric Interview; Sheehan et al., 1998). Inclusion criteria were: (a) age between 18 and 65, (b) DSM-IV diagnosis of schizophrenia or schizoaffective disorder, (c) English-speaking, and (d) minimum 8th grade reading level. Patients were excluded if they had (a) history of unconsciousness greater than 10 minutes, (b) a seizure disorder or other neurological condition affecting cognition, (c) current substance abuse or dependence, (d) for patients aged 55 or older, a score less than 27 on the Mini Mental State Exam (Folstein, Folstein, McHugh, & Fanjiang, 2001). Participants completed a one-time comprehensive neuropsychological, clinical, and functional battery.

Measures. Premorbid intellectual functioning was measured with the reading subtest of the Wide Range Achievement Test – Third Edition (Wilkinson, 1993). Psychiatric symptom severity was measured with the Positive and Negative Syndrome Scale (Kay, Fiszbein, & Opler, 1987) and the Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Neurocognitive insight was measured with the Measure of

Insight into Cognition – Self-Rated (MIC-SR; Medalia, Thysen, & Freilich, 2008). The MIC-SR consists of twelve statements about attention, executive functioning, and memory (e.g., “I have trouble listening and paying attention”; “I have difficulty thinking through possible solutions to problems”) rated by respondents in terms of frequency: never, once a week or less, twice a week, or almost daily (additional sample items are listed in the appendix). The maximum score is 36; higher scores indicate greater frequency of cognitive problems.

Current cognitive functioning was measured with a modified version of the MATRICS Consensus Cognitive Battery (MCCB; Nuechterlein et al., 2008); the social cognition measure was excluded due to concern that social cognition measures would differ from neurocognitive measures in terms of their relationship to everyday functioning. The other nine subtests of the MCCB measured six neurocognitive domains, as follows:

1. Speed of processing (Trail Making Test, Part A; Brief Assessment of Cognition in Schizophrenia Symbol Coding subtest; Category Fluency Test, animal naming)
2. Attention/vigilance (Continuous Performance Test-Identical Pairs Version [CPT-IP])
3. Working memory (Wechsler Memory Scale, 3rd edition, Spatial Span subtest; Letter-Number Span test)
4. Verbal learning (Hopkins Verbal Learning Test-Revised, immediate recall)
5. Visual learning (Brief Visuospatial Memory Test-Revised, immediate recall)

6. Reasoning and problem solving (Neuropsychological Assessment Battery, Mazes subtest)

Executive functioning was also measured with Koren and colleagues' metacognitive version of the Wisconsin Card Sorting Test (WCST; Koren et al., 2004). In this task, the WCST is administered following the standardized instructions; however, prior to receiving feedback about the accuracy of the sort, participants are asked to (1) rate their confidence in the correctness of that sort on a "0" (*guessing*) to "100" (*completely confident*) scale, and (2) decide whether they do or do not want that sort to be "counted" toward their overall performance score on the test (Koren et al., 2004). Several key metacognitive variables can be derived; for example, the accuracy score is calculated as the number of correct sorts out of the total number of volunteered sorts.

Everyday functional skills were evaluated with the UCSD Performance-based Skills Assessment, Brief version (UPSA-B; Mausbach, Harvey, Goldman, Jeste, & Patterson, 2007), in which participants perform everyday tasks related to finance (e.g., write a check to pay a utility bill), and communication (e.g., call a doctor to reschedule an appointment). The UPSA-B takes 10-15 minutes to administer and yields raw subscale scores as well as raw scores that are converted into a total score ranging from 0 to 100, with higher scores indicating better functional capacity.

Analyses. All continuous variables were normally distributed. To first identify participants with objective cognitive impairment, a global deficit score (GDS) was calculated for each participant (Heaton, Miller, Taylor, & Grant, 2007). To accomplish this, each of the nine t-scores calculated by the MCCB scoring program was assigned a numerical degree of deficit on a scale of 0 (t-score ≥ 40 ; no deficit) to 5 (t-score ≤ 19 ;

severe deficit) in five point decrements in the t-score. The GDS is the average deficit score across measures. In this sample, eight participants were missing at least one MCCB score (seven participants were missing one score, and one participant was missing three scores); for these participants, the GDS was calculated from all available data. The recommended cutoff for cognitive impairment is $GDS \geq 0.50$, which roughly corresponds to mild impairment on half of the component measures (Heaton et al., 2007).

Latent profile analysis (LPA) was then used to group cases based on participants' similarities on two continuous observed variables: the GDS and the MIC-SR total score; only participants with objective cognitive impairment were included. Conceptually similar to cluster analysis, LPA is a multivariate approach that groups individuals based on shared characteristics that distinguish members of one group from members of another group. LPA determines class assignment through fit statistics and tests of significance, and uses probabilities to take uncertainty of membership (error) into account (Herman, Ostrander, Walkup, Silva, & March, 2007). For the descriptive fit indices, lower values are considered indicative of better fit for the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Adjusted BIC; higher values indicate better fit for Entropy. The Lo-Mendell-Rubin Test (LMRT) of significance indicates whether the model under consideration is statistically a superior fit to the lower-order model (e.g., if a 3-class model fits better statistically than a 2-class model). A cutoff of $<.05$ is used for significance.

The three hypotheses were tested using the resulting groups from the LPA. The groups were compared via t-tests for independent samples on the following variables: executive functioning (Koren WCST accuracy score; Mazes t-score), functional capacity

(UPSA-B total score), positive and negative symptom severity (PANSS positive total and negative total scores), and depressive symptom severity (BDI-II total score). To correct for multiple comparisons, alpha for significance was set at 0.008 (0.05/6).

Exploratory analyses examined domain-specific neurocognitive awareness using Pearson correlations between: MIC-SR attention score and CPT-IP t-score, MIC-SR executive function score and Mazes t-score/Koren WCST accuracy score, and MIC-SR memory score and MCCB HVLT total recall t-score. Data were analyzed using Mplus (Version 7.11) and SPSS (Version 21).

Results

Among all 214 participants, 168 (78.5%) were classified as cognitively impaired ($GDS \geq 0.5$), whereas 46 (21.5%) were classified as cognitively intact. The remainder of the analyses included only the 168 cognitively impaired participants (Table 1).

The LPA demonstrated that on two of the four descriptive fit indices as well on the statistical test of model fit, a 2-class model was preferable to both a 1- and 3-class solution (Table 2). According to this LPA, 77 (46%) of the participants demonstrated “intact neurocognitive insight” (mean $GDS=1.75$; mean $MIC-SR=27.89$), and 91 (54%) of the participants demonstrated “impaired neurocognitive insight” (mean $GDS=1.61$; mean $MIC-SR=9.49$). The groups did not statistically differ on any demographic variables (Table 3). The intact neurocognitive insight group reported significantly more severe positive symptoms (mean PANSS positive total score 17.58 versus 14.89; $t=-3.09$; $df=162$; $p=.002$) and depressive symptoms (mean BDI-II total score 20.25 versus 10.39; $t=-5.87$; $df=144.08$; $p<.001$). The groups did not differ significantly on Koren WCST accuracy score, Mazes t-score, UPSA-B, or PANSS negative symptom total score (Table

3). Follow-up item analysis of the PANSS positive symptoms subscale indicated that participants with intact neurocognitive insight were rated more highly on delusions, hallucinatory behavior, suspiciousness, and hostility (all $ps < .016$), though across items the mean ratings were “minimal” to “mild.”

Exploratory analyses of domain-specific neurocognitive awareness among all participants yielded no statistically significant correlations between the attention and memory domains of the MIC-SR and their objective cognitive counterparts (MIC-SR attention and CPT-IP $r = .069$; $p = .325$; MIC-SR memory and HVLT t-score $r = -.013$; $p = .854$). There was no significant relationship between MIC-SR executive function and Mazes ($r = -.123$; $p = .077$), though participants who reported more problems with executive functioning scored significantly higher on Koren accuracy ($r = .147$; $p = .038$).

Discussion

These results are consistent with previous research showing that the majority of people with schizophrenia demonstrate significant neuropsychological impairment (Palmer et al., 1997), and that a large proportion of those individuals minimally endorse cognitive problems (Medalia & Thysen, 2008). Indeed, more than half of participants with objectively measured cognitive impairment demonstrated impaired neurocognitive insight. This finding is consistent with previous literature suggesting that individuals with schizophrenia are poor raters of their own cognitive and everyday functioning (Johnson, Tabbane, Dellagi, & Kebir, 2011; Keefe, Poe, Walker, Kang, & Harvey, 2006; Medalia & Lim, 2004; Medalia, Thysen, & Freilich, 2008; Moritz, Ferahli, & Naber, 2004; Poletti et al., 2012; Sabbag et al., 2012; Saperstein, Thysen, & Medalia, 2012).

The first and second hypotheses, that impaired neurocognitive insight would be related to poorer executive functioning and functional capacity performance, were not supported. Our measures of executive functioning were not comprehensive, and included only a reasoning task and a speeded planning task; thus, constructs such as switching and inhibition were not measured. It is possible that these latter tasks are more related to neurocognitive insight, but it is also possible that neurocognitive insight is unrelated to executive skills and the ability to carry out tasks of daily living. We generally found no evidence of domain-specific neurocognitive insight; cognitive symptom complaints in specific domains were mostly unrelated to actual neurocognitive performance, except that greater executive functioning symptoms were weakly related to better executive performance.

The third hypothesis had mixed support; as hypothesized, participants with intact neurocognitive insight reported more severe depressive symptoms, which is consistent with numerous previous studies examining insight and depression (Medalia, Thysen, & Freilich, 2008; Moritz, Ferahli, & Naber, 2004; Sellwood et al., 2013). These findings are also in line with previous research demonstrating that more severe self-rated depression was associated with underestimation of functional abilities (Bowie et al., 2007) as well as higher self-reported disability (Sabbag et al., 2012). In the current study, participants with intact insight did not differ from those with impaired insight, however, on negative symptom severity. Unexpectedly, participants with intact neurocognitive insight reported more severe positive symptoms of psychosis. Item analysis demonstrated that the groups significantly differed on delusions, hallucinatory behavior, suspiciousness, and hostility, though on average the ratings were no greater than “mild.” As voices and related

delusional ideation are conceptualized in the cognitive-behavioral model as negative cognitions about oneself reflecting interpersonal vulnerability (Beck & Rector, 2005), perhaps those with intact awareness are more confronted with their cognitive problems via voices. Additional investigation is warranted to examine the relationship between neurocognitive insight and positive symptom severity.

This study is limited by characteristics of the sample (e.g., outpatient status, middle-age, chronic psychosis); these results may not generalize to inpatients and/or first-episode schizophrenia patients. The narrow measurement of executive functioning and functional capacity may have also limited our ability to detect significant differences between participants with impaired versus intact neurocognitive insight. In addition, although classification of participants into groups reflecting “intact” and “impaired” insight was conducted using a statistically sound technique and for the purpose of comparing groups on other relevant variables, we acknowledge that neurocognitive insight (like other types of insight) likely exists on a continuum and is not simply an all-or-none feature of schizophrenia.

Finally, as the concept of neurocognitive insight becomes better characterized and understood, investigation of its role in cognitive treatment adherence and outcome will be critical. Just as patients with low levels of clinical insight are less likely to adhere to their prescribed medication regimen (McEvoy et al., 2006), those with low levels of neurocognitive insight may be less likely to be interested in or adherent to cognitive training interventions. Because individuals tend to be poor raters of their own cognitive functioning, particularly when they show evidence of objective cognitive impairment, it may be helpful to provide education and feedback regarding cognitive performance, as

has been done by Medalia and colleagues in the Braincheck intervention to increase awareness of cognitive impairment (Medalia, Saperstein, Choi, & Choi, 2012). Future studies may emphasize clinical features of those lacking neurocognitive insight, as well as the relationship between neurocognitive insight at baseline and outcome following cognitive remediation treatment.

Chapter 3, in full, is in preparation for submission for publication. Burton, Cynthia Z.; Harvey, Philip D., Patterson, Thomas L.; Twamley, Elizabeth W. The dissertation author was the primary investigator and author of this paper.

Table 3.1: Demographic and Clinical Features of the Full Sample and the Neurocognitively Impaired Sample

	Full Sample (n=214)	Neurocognitively Impaired Sample (n=168)
	Mean (sd) or %	Mean (sd) or %
Age, years	41.2 (12.4)	42.7 (12.3)
Education, years	12.3 (2.2)	12.1 (2.1)
% Male	65.4	67.3
% Caucasian	54.7	51.2
% Hispanic ethnicity	23.4	21.4
% African American	36.0	40.5
% Schizophrenia (vs. Schizoaffective)	58.2	63.0
% Prescribed antipsychotic medication	98.1	98.2
% Living independently	73.3	72.6
% Employed	9.8	10.1
% Never married	53.2	50.3
PANSS positive symptoms total	15.7 (5.5)	16.1 (5.7)
PANSS negative symptoms total	15.7 (6.1)	16.2 (6.3)
BDI-II total	15.3 (11.7)	15.0 (11.6)

Note. BDI-II=Beck Depression Inventory, Second Edition; PANSS=Positive and Negative Syndrome Scale.

Table 3.2: Descriptive and Statistical Fit Indices

Cognitively Impaired (n=168)	1 class	2 classes	3 classes
AIC	1680.06	1663.97	1663.02
BIC	1692.55	1685.83	1694.26
Adjusted BIC	1679.89	1663.67	1662.60
Entropy	N/A	0.705	0.611
LMRT	N/A	0.001	0.8773

Note. Favorable values are indicated in bold font. AIC=Akaike Information Criterion; BIC=Bayesian Information Criterion; LMRT=Lo-Mendell-Rubin Test of significance

Table 3.3: Demographic, Clinical, and Cognitive Differences between Participants with Intact Versus Impaired Neurocognitive Insight (n=168)

	Intact		Impaired					
	n	Mean (sd) or %	n	Mean (sd) or %	t or χ^2	df	<i>p</i>	Cohen's <i>d</i>
Age, years	77	43.6 (12.0)	91	41.9 (12.5)	-0.91	166	0.364	
Education, years	77	11.9 (1.9)	90	12.3 (2.2)	1.33	165	0.185	
% Male	77	59.7	91	73.6	3.65	1	0.056	
% Caucasian	77	48.1	91	53.8	0.80	2	0.671	
% Hispanic ethnicity	77	16.9	91	25.3	1.74	1	0.187	
% Schizophrenia	73	57.5	89	67.4	1.68	1	0.195	
% Prescribed antipsychotic medication	76	97.4	88	98.9	0.51	1	0.476	
% Living independently	77	77.9	91	68.1	4.43	3	0.219	
% Employed	77	9.1	91	11.0	1.73	3	0.630	
% Never married	70	47.1	75	53.3	7.53	6	0.275	
WRAT-III reading total	77	43.2 (6.9)	89	44.6 (6.9)	1.26	164	0.210	
Koren accuracy score	73	0.5 (0.2)	86	0.5 (0.2)	-1.26	157	0.208	0.00
Mazes score	77	37.3 (7.9)	90	39.9 (8.2)	2.11	165	0.036	0.32
PANSS positive symptoms total	76	17.6 (5.7)	88	14.9 (5.5)	-3.09	162	0.002	0.49
PANSS negative symptoms total	76	16.9 (6.3)	89	15.6 (6.3)	-1.30	163	0.195	0.21
BDI-II total	76	20.3 (11.7)	88	10.4 (9.5)	-5.87	144.08	<0.001	0.94
UPSA-B total	75	67.9 (13.9)	89	68.0 (16.5)	0.04	162	0.966	0.01

Note. Significant differences are indicated in bold font. WRAT-III=Wide Range Achievement Test, third edition; PANSS=Positive and Negative Syndrome Scale; BDI-II=Beck Depression Inventory, second edition; UPSA-B=UCSD Performance Based Skills Assessment, Brief

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CHAPTER 4: NEUROCOGNITIVE INSIGHT, TREATMENT UTILIZATION, AND
COGNITIVE TRAINING OUTCOMES IN SCHIZOPHRENIA

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ABSTRACT

The degree to which people with schizophrenia show awareness of cognitive dysfunction and whether this neurocognitive insight affects treatment use or outcome is understudied. We aimed to examine neurocognitive insight among a treatment-seeking sample of patients with psychotic disorders, and whether neurocognitive insight affects treatment utilization or outcome.

Sixty nine individuals with schizophrenia-spectrum disorders enrolled in a trial comparing Compensatory Cognitive Training (CCT) to standard pharmacotherapy (SP). Participants with objective cognitive impairment were identified and grouped into “intact” vs. “impaired” neurocognitive insight groups. These groups were then compared via ANCOVA on three treatment utilization variables and six post-treatment cognitive/functional variables.

Forty three participants demonstrated objective cognitive impairment. Among those individuals, 31 were considered to have intact neurocognitive insight and 12 showed impaired neurocognitive insight. These two groups did not differ on CCT attendance, satisfaction with the intervention, or self-reported cognitive strategy use at post-treatment. There were significant treatment group by neurocognitive insight group interactions for verbal memory and functional capacity outcomes, in that individuals with impaired neurocognitive insight who received treatment performed better than those who did not receive treatment.

Even among individuals who self-select into a cognitive treatment study, many show minimal awareness of cognitive dysfunction. Impaired neurocognitive insight, however, was not associated with decreased treatment utilization, and was associated

with positive treatment outcomes in some cognitive domains as well as functional capacity. As cognitive training treatments become increasingly available, clinicians need not exclude patients with impaired neurocognitive insight.

Introduction

Cognitive impairment is a central feature of schizophrenia and affects everyday functioning more so than psychotic symptoms (Green, 1996; Velligan et al., 1997). Cognitive dysfunction is also considered a rate-limiting factor for benefit from psychiatric rehabilitation programs (Kurtz & Tolman, 2011; McGurk, Mueser, Walling, Harvey, & Meltzer, 2004; Harding et al., 2008; Walsh, Wu, Mitchell, & Berkman, 2003). Efforts are underway, therefore, to develop both pharmacological and psychosocial treatments to improve cognitive functioning in this population. Cognitive training or remediation is one such type of intervention, defined as “a behavioral training based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition or metacognition) with the goal of durability and generalization” (Wykes et al., 2011). Cognitive training has shown considerable promise, with a recent meta-analysis including 2,104 participants demonstrating an effect size of 0.45 on global cognition and 0.42 on functional outcome, with no evidence that different elements of treatment (e.g., approach, duration) affected cognitive outcome (Wykes et al., 2011). The authors further suggested that researchers examine predictors of treatment outcome and treatment adherence, as treatment acceptability may be a key issue for therapy implementation (Wykes et al., 2011). Thus, it is imperative to examine moderating factors that may influence treatment acceptability, adherence, and effectiveness.

Awareness of cognitive impairment, or neurocognitive insight, may be one such moderator. It is well accepted in psychiatric research and practice that limited clinical insight (i.e., unawareness of illness and need for treatment) negatively affects treatment adherence (Lysaker, Buck, Salvatore, Popolo, & Dimaggio, 2009; McEvoy et al., 2006), but the available literature exploring whether neurocognitive insight affects treatment adherence and outcome is scant. One recent study demonstrated that higher rates of self-reported cognitive complaints were associated with lower treatment utilization, a counterintuitive finding prompting the authors to assert that clinicians may need to target individuals at risk for drop out with more intensive psychoeducation and follow-up care (Gooding, Saperstein, Rivera Mindt, & Medalia, 2012). Another study found that cognitive complaints generally decreased from baseline to post-treatment, though there was no difference in cognitive complaints between treatment and control conditions (Lecardeur et al., 2009).

Given the extant literature regarding the relationship between neurocognitive insight and cognitive treatment, this study aimed to examine awareness of cognitive dysfunction among cognitive treatment-seeking psychiatric patients who participated in a longitudinal randomized controlled trial, and whether that awareness was related to treatment utilization or treatment outcome. We hypothesized that (1) participants with impaired neurocognitive insight (i.e., few self-reported cognitive symptoms despite evidence of objective cognitive impairment), compared with those with intact neurocognitive insight, would demonstrate poorer treatment attendance, lower satisfaction with the intervention, and less self-reported strategy use at post-treatment,

and (2) impaired neurocognitive insight would negatively affect treatment outcome as measured by cognitive and functional capacity performance.

Method

Participants. Participants included 69 individuals diagnosed with a primary psychotic disorder (schizophrenia $n=37$; schizoaffective disorder $n=30$; psychosis not otherwise specified $n=1$; major depression with psychotic features $n=1$) and receiving outpatient psychiatric care who enrolled in a study of Compensatory Cognitive Training (CCT) for psychosis (Twamley, Vella, Burton, Heaton, & Jeste, 2012). This study was approved by the UCSD Institutional Review Board and all participants provided written informed consent. On average, participants were 46 years old and had completed 13 years of education; the majority of the sample were men, Caucasian, never married, and living independently in the community (Table 1). Participants were chronically ill (mean duration of psychotic illness was 23 years) and most were prescribed atypical antipsychotic medication.

Procedures. Candidates for the study were referred by clinicians or self-response to recruitment flyers posted in psychiatric care centers. The following inclusion criteria were used: (a) DSM-IV (American Psychiatric Association, 1994) diagnosis of schizophrenia, schizoaffective disorder, or primary diagnosis of psychosis NOS or major depression with psychotic features, (b) English-speaking, (c) 18 years of age or older. Individuals were excluded from the study if they had: (a) substance use disorder in the past 30 days, (b) a history of neurological disease or injury, (c) mental retardation, or (d) concurrent enrollment in another treatment research protocol (ongoing therapeutic interventions were permitted). Following completion of written informed consent,

participants' diagnoses were confirmed via structured diagnostic interview (Mini International Neuropsychiatric Interview; Sheehan et al., 1998) or diagnostic chart review. Participants then completed a baseline assessment and were randomly assigned to standard pharmacotherapy plus CCT (treatment condition) or to standard pharmacotherapy alone (control condition). A comprehensive neuropsychological, clinical, and functional battery was administered at baseline, 3 months (immediate post-treatment), and 6 months (follow-up); raters were blinded to group assignment. The CCT intervention is a 12-week, 2 hour per week class that emphasizes new habit formation and compensatory strategy learning in four cognitive domains: prospective memory, attention and vigilance, learning and memory, and problem-solving/cognitive flexibility. Compensatory strategies include, for example, calendar use, paraphrasing important information, taking notes, brainstorming solutions to a problem, and gathering pro and con evidence to test hypotheses. The main outcomes of the randomized controlled trial are reported elsewhere (Twamley, Vella, Burton, Heaton, & Jeste, 2012), but in summary, the CCT intervention appears to improve aspects of cognition, negative symptoms, functional capacity, and quality of life.

Measures. Premorbid intellectual functioning was measured with the American National Adult Reading Test (ANART; Grober & Sliwinski, 1991). Cognitive functioning was measured with a battery including the following domains and measures:

1. Prospective memory: Memory for Intentions Screening Test (total score; Raskin, 2004)
2. Attention and vigilance: Wechsler Adult Intelligence Scale, third edition (WAIS-III) Digit Span total score (Wechsler, 1997a)

3. Verbal learning and memory: Hopkins Verbal Learning Test - Revised (HVLT-R, total immediate recall and total delayed recall; Brandt & Benedict, 2001); Wechsler Memory Scale, third edition (WMS-III) Logical Memory subtest (LM, total immediate recall and total delayed recall; Wechsler, 1997b)
4. Executive Functioning: Wisconsin Card Sorting Test (WCST; total errors; Kongs et al., 2000); Trail making test, part B minus part A (Reitan, 1992)
5. Processing speed: WAIS-III Digit Symbol total correct and Symbol Search total correct (Wechsler, 1997a), Trail making test, part A (Reitan, 1992)
6. Working memory: WAIS-III Letter-Number Sequencing total correct (Wechsler, 1997a)
7. Visual learning and memory: Brief Visuospatial Memory Test – Revised (BVMTR, total immediate recall and total delayed recall; Benedict, 1997)

Psychotic symptom severity was measured with the Positive and Negative Syndrome Scale, using the positive symptom total (sum of items P1-P7) and the negative symptom total (sum of items N1-N7; PANSS; Kay et al., 1987a). Depressive symptom severity was measured with the Hamilton Depression Rating Scale (HAMD; sum of items 1-17; Hamilton, 1960). For both the PANSS and HAMD, higher scores indicate greater severity of psychiatric symptoms. Functional capacity was measured with the UCSD Performance-Based Skills Assessment (UPSA; total score; Patterson, Moscona, McKibbin, Hughs, & Jeste, 2001), a role-play measure that assesses skills in recreation planning, financial management, communication, transportation planning, and shopping. Higher UPSA scores indicate better everyday functional ability.

Self-reported cognitive problems were measured with the Cognitive Problems and Strategies Assessment (CPSA), created for the study. The CPSA consists of multiple self-report items assessing the frequency of cognitive problems and use of cognitive strategies. The “cognitive problems” section contains thirty statements (e.g., “I have difficulty remembering to do things that I have scheduled”; “I have trouble staying focused during conversations”) rated by the respondent as occurring rarely/never (0 points), sometimes (1 point), often (2 points), and always (3 points); higher sums indicate greater frequency of cognitive problems (additional sample items are listed in the appendix). The “cognitive strategies” section also includes thirty statements (e.g., “I keep a written list of things I need to do”; “When I’m having trouble solving a problem, I switch to a different strategy”) rated on the same 0-3 scale as the problems section; higher sums indicate greater frequency of cognitive strategy use.

Analyses. All continuous variables were found to be normally distributed. To identify participants with objective cognitive impairment, a global deficit score (GDS) was calculated for each participant (Heaton et al., 2007). To accomplish this, each of the thirteen baseline cognitive t-scores was assigned a numerical degree of deficit on a scale from 0 (t-score ≥ 40 ; no deficit) to 5 (t-score ≤ 19 ; severe deficit) in five point decrements in the t-score, and then averaged to create the GDS. The recommended cutoff of $\text{GDS} \geq 0.50$ was used to indicate cognitive impairment, which roughly corresponds to mild impairment on half of the component measures (Heaton et al., 2007).

Latent profile analysis (LPA) was then used to group cases based on participants’ similarities on two continuous observed variables: baseline GDS and CPSA problems total score. LPA is a multivariate approach that groups individuals based on shared

characteristics that distinguish members of one group from members of another group; class assignment is determined through fit statistics and tests of significance. For the descriptive fit indices, lower values are considered indicative of better fit for the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Adjusted BIC; higher values indicate better fit for Entropy. The Lo-Mendell-Rubin Test (LMRT) of significance indicates whether the model under consideration is statistically a superior fit to the lower-order model (e.g., if a 3-class model fits better statistically than a 2-class model). A cutoff of $<.05$ is used for significance.

The main hypotheses were tested using the resulting groups from the LPA. To examine treatment utilization, the neurocognitive insight groups were compared via t-tests for independent samples on three variables: adherence (percent of CCT classes attended), satisfaction (overall rating of the CCT class on a 1-10 scale), and post-treatment cognitive strategy use (post-treatment mean CPSA strategies). Alpha for significance was set to 0.05. To evaluate whether neurocognitive insight affects treatment outcome, Analysis of Covariance (ANCOVA) was conducted using two dichotomous independent variables: treatment group (CCT versus SP) and neurocognitive insight group (intact versus impaired), and six continuous dependent variables: immediate post-treatment MIST total raw score, WAIS-III digit span total score, HVLT total recall raw score, HVLT delayed recall raw score, WCST total errors raw score, and UPSA total raw score. Baseline scores were entered as covariates, and the list of dependent variables was limited to domains and measures targeted by the CCT intervention to minimize the number of comparisons and reduce the chance of Type I error. Due to the small sample

size, omega squared was calculated as a measure of effect size. Data were analyzed using Mplus (Version 7.11) and SPSS (Version 21).

Results

Among all 69 participants, 43 (62.3%) were classified as cognitively impaired ($GDS \geq 0.5$) while 26 (37.7%) were classified as cognitively intact. The remainder of the analyses included only the 43 cognitively impaired participants.

The LPA demonstrated that on all four of the descriptive fit indices, a 2-class model was preferable to both a 1- and 3-class model, though the LMRT test was not significant (Table 2). According to this LPA, 31 participants demonstrated “intact neurocognitive insight” (mean $GDS=0.95$; CPSA mean total=27.15), and 12 participants demonstrated “impaired neurocognitive insight” (mean $GDS=2.29$; CPSA mean total=38.02). There were some demographic and clinical differences between these two groups: the intact neurocognitive insight participants had significantly higher levels of education ($M=13.1$ [1.8] versus $M=12.0$ [0.9]; $t=2.61$; $df=39.1$; $p=0.013$) and estimated premorbid IQ ($M=107.2$ [9.1] versus $M=98.7$ [10.0]; $t=2.66$; $df=39$; $p=0.011$), and less severe positive symptoms ($M=14.8$ [5.8] versus $M=20.7$ [6.1]; $t=-2.89$; $df=41$; $p=0.006$) and depressive symptoms ($M=9.7$ [5.4] versus $M=15.4$ [9.1]; $t=-2.50$; $df=39$; $p=0.017$).

For the treatment utilization analysis, t-tests for independent samples comparing those with intact versus impaired neurocognitive insight in the treatment condition only yielded no statistically significant group differences on CCT attendance, satisfaction with the intervention, or self-reported strategy use at post-treatment (all $ps>0.187$; Table 3).

With regard to treatment outcome, the 2x2 ANCOVA yielded two statistically significant interactions between treatment group and neurocognitive insight group (Table

4): HVLT delayed recall (Figure 1) and UPSA total score (Figure 2). For HVLT delayed recall, participants with intact neurocognitive insight improved comparably across treatment groups, whereas those with impaired neurocognitive insight and in CCT improved more than those with impaired neurocognitive insight in the control condition. For the UPSA, SP participants showed no improvement, while CCT participants with impaired neurocognitive insight improved more than CCT participants with intact neurocognitive insight. These interactions remained significant when GDS was added as an additional covariate, suggesting that the effects are not simply due to the impaired neurocognitive insight group having more room for cognitive improvement. For the non-statistically significant interactions, a medium effect size was observed for HVLT total recall; the other three dependent variables (MIST total score, WMS-III digit span total, and WCST errors) showed no effect (Table 4).

Discussion

Consistent with the general literature on cognition in schizophrenia, these results indicated that approximately two-thirds of individuals diagnosed with schizophrenia-spectrum disorders demonstrate objectively measured cognitive impairment (Heinrichs & Zakzanis, 1998; Palmer et al., 1997). Among participants with impaired cognition, many minimally reported cognitive problems in their everyday life, though the percentage of cognitively impaired individuals with impaired neurocognitive insight was lower in this study than in previous reports (28% in this sample, compared to 54% in Burton et al., under review and 50% in Medalia & Thysen, 2008). The main difference between these samples is that participants in the current study were treatment-seeking patients who self-selected into a cognitive training research program; this likely explains the difference and

suggests that those who volunteer for cognitive treatment generally may be more aware of their deficits. As psychosocial treatment to improve cognition becomes more widely available, perhaps recruitment efforts could be maximized by broadly targeting and educating patients with psychotic disorders, many of whom would not otherwise be interested or engaged in treatment.

Although nearly a third of participants in this sample had impaired neurocognitive insight, they did not attend fewer classes, report less satisfaction with the intervention, or report less strategy use following treatment. These results suggest that even individuals with poor awareness of their cognitive dysfunction can adhere to a cognitive treatment, which is contrary to our expectation and the general clinical notion that those unaware of a problem would not be motivated to engage in treatment. Further, although there were no differences between intact and impaired neurocognitive insight groups on treatment utilization, treatment outcome was significantly affected by level of neurocognitive insight for verbal memory and functional capacity. Receiving the CCT intervention appears to improve performance in these domains among those with impaired neurocognitive insight to a level comparable to those with intact neurocognitive insight in either condition. These results suggest that patients with impaired neurocognitive insight need not be excluded from cognitive training; rather, they may be excellent candidates in that they appear to show substantial gains compared to those with impaired neurocognitive insight that do not receive treatment.

Taken together, these results indicate that among individuals with schizophrenia-spectrum disorders who self-selected into a cognitive treatment study, approximately one-third demonstrated impaired awareness of objective cognitive dysfunction. Despite

their apparent lack of neurocognitive insight, these individuals were no different from those with intact neurocognitive insight in terms of treatment utilization, and in fact they demonstrated good treatment outcomes in the domains of verbal memory and functional capacity.

The limitations of this study must be considered. In particular, the full sample size of 69 and the cognitively impaired sample size of 43 are small and limit power to detect significant group differences. In an effort to preserve power, neither correction for multiple comparisons nor use of additional covariates were employed. However, although the neurocognitive insight groups significantly differed on education, estimated premorbid IQ, positive symptom severity, and depressive symptom severity, their correlations with the dependent variables were modest and mostly not significant, supporting their exclusion as covariates. The problem of multicollinearity (i.e., highly significant relationship between education and premorbid IQ) also precluded use of additional covariates in the statistical models. Finally, it is natural to assume that those with impaired insight might be less educated or more symptomatic, so by design it may not be reasonable to covary variables that might hide otherwise significant relationships. Nevertheless, replication of these results in a larger sample would be beneficial to support and extend our conclusions. Finally, dichotomization of participants into intact and impaired neurocognitive insight may not reflect the more continuous conceptual nature of insight; although for this study LPA was suitable to allow for group comparisons on treatment utilization and outcome variables, other approaches (e.g., a continuous variable reflecting the degree of discrepancy between objective and subjective cognitive

dysfunction) may also be a sensible method of examining neurocognitive insight in this population.

These results are a first step in determining the importance of neurocognitive insight in both cognitive training utilization and outcome; future studies with larger samples may further explore neurocognitive insight among treatment-seeking patients, and whether any intervention prior to participation in cognitive training may be helpful. For example, clinicians may wish to specifically target individuals with impaired awareness, both to promote insight per se and to communicate that cognitive training can benefit people who perceive very few cognitive problems.

Chapter 4, in full, is in preparation for submission for publication. Burton, Cynthia Z.; Twamley, Elizabeth W. The dissertation author was the primary investigator and author of this paper.

Table 4.1: Demographic and Clinical Features of the Full Sample (n=69)

	Mean (sd) or %
Age, years	46.3 (9.7)
Education, years	12.9 (1.7)
Duration of illness, years	23.3 (12.3)
% Male	65.2
% Caucasian	76.8
% Hispanic ethnicity	17.4
% African American	11.6
% Schizophrenia	53.6
% Prescribed antipsychotic medication	91.3
% Living independently	78.3
% Never married	55.0
PANSS positive symptoms total	16.7 (6.3)
PANSS negative symptoms total	15.0 (5.7)
HAMD 1-17 total	11.7 (7.0)

Note. HAMD=Hamilton Depression Rating Scale; PANSS=Positive and Negative Syndrome Scale.

Table 4.2: Descriptive and Statistical Fit Indices

Cognitively Impaired (n=43)	1 class	2 classes	3 classes
AIC	450.21	442.00	448.00
BIC	457.25	454.33	465.61
Adjusted BIC	444.72	432.40	434.29
Entropy	N/A	0.84	0.45
LMRT	N/A	0.30	0.50

Note. Favorable values are indicated in bold font. AIC=Akaike Information Criterion; BIC=Bayesian Information Criterion; LMRT=Lo-Mendell-Rubin Test of significance

Table 4.3: Group Differences in Treatment Utilization Variables

	n	Intact Neurocognitive Insight Mean (sd)	Impaired Neurocognitive Insight Mean (sd)	t	df	p
CCT attendance (%)	20	52.5 (41.9)	69.1 (42.0)	-0.84	18	0.411
Satisfaction (1-10)	10	9.3 (1.0)	8.3 (1.2)	1.44	8	0.187
Mean self-reported strategy use at post-treatment	8	1.8 (0.7)	1.4 (1.0)	0.66	6	0.533

Table 4.4: Interaction Effects of Treatment Group and Insight Group on Cognitive and Functional Outcomes

Dependent variable	interaction F	df	p	% variance accounted for (omega squared*100)
MIST total score	0.043	1	0.838	0
WMS-III digit span total	0.315	1	0.580	0
HVLT-R total recall	3.708	1	0.066	5.5
HVLT-R delayed recall	9.776	1	0.005	11.4
WCST total errors	0.031	1	0.863	0
UPSA total score	6.085	1	0.022	9.2

Note. HVLT-R=Hopkins Verbal Learning Test, Revised Version; MIST=Memory for Intentions Screening Test; UPSA=UCSD Performance-Based Skills Assessment; WCST=Wisconsin Card Sorting Test; WMS-III=Wechsler Memory Scale, Third Edition.

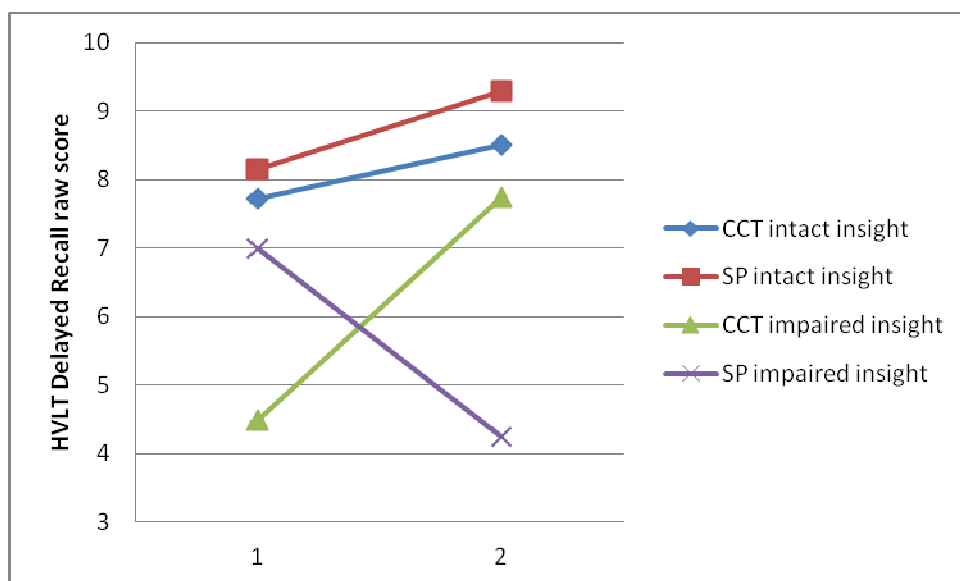


Figure 4.1: Baseline and Post-treatment Scores by Group on HVL-T-R Delayed Recall

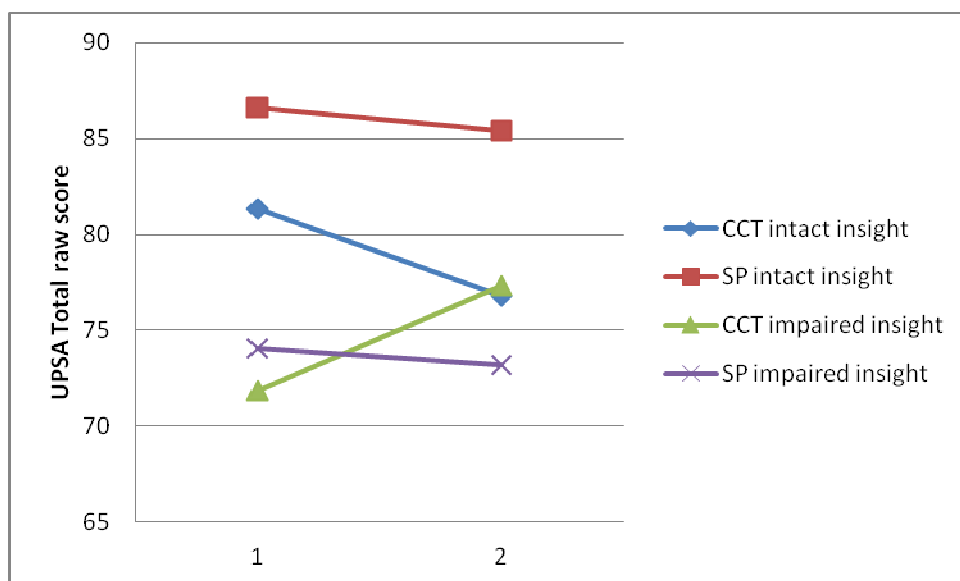


Figure 4.2: Baseline and Post-treatment Scores by Group on UPSA Total Score

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CHAPTER 5: GENERAL DISCUSSION

This series of studies investigated metacognitive abilities, including cognitive and neurocognitive insight, in people diagnosed with schizophrenia, and their relationships to cognition, functioning, and psychiatric symptoms, as well as treatment utilization and outcome. Broadly, these studies supported the multidimensional nature of insight and differential relationships with cognition, functional capacity, and psychiatric symptoms. For example, Study 1 indicated that clinical insight was related to executive functioning and negative symptom severity, whereas cognitive insight showed no significant correlation with any cognitive or symptom measures. Study 2 failed to demonstrate a significant relationship between neurocognitive insight and executive functioning or functional capacity. These results are consistent with the ideas that insight is a complex construct, that it can be appropriately divided into subtypes, and it may need to be addressed separately in treatment. Clinical insight, for instance, is known to affect psychiatric treatment engagement and adherence, whereas we found no evidence that neurocognitive insight affects cognitive treatment adherence.

These studies also added to the limited existing literature on neurocognitive insight among people with schizophrenia. Consistent with previous research, a substantial number of participants demonstrated impaired neurocognitive insight, meaning they minimally endorsed cognitive problems despite evidence of objective cognitive impairment. Interestingly, the percentage of participants with impaired neurocognitive insight was considerably higher (54%) in a cross-sectional, non-treatment-seeking sample compared to a sample of participants who self-selected into a research protocol investigating the efficacy of Compensatory Cognitive Training (28%). This suggests that

individuals with schizophrenia who elect to participate in cognitive treatment may be more aware of their deficits. It also implies, though, that a large portion of individuals with cognitive impairment (and who may well benefit from treatment) are not being captured by current approaches to enrollment. Clinicians are therefore faced with the challenge of determining how to target and engage patients with few perceived cognitive difficulties. Because neuropsychological impairment in schizophrenia is more the rule than the exception, it is reasonable to assume that each client would demonstrate impaired cognition to a degree, and it may be beneficial to initiate a discussion about available treatments early and often regardless of the person's self-report of cognitive or everyday problems.

In addition to examining the rates of impaired neurocognitive insight in people with schizophrenia, these studies also investigated the cognitive and symptom correlates of neurocognitive insight. Specifically, executive functioning is a domain often implicated in impaired insight, which makes sense given that self-monitoring is a critical frontally-mediated executive skill. Study 2, however, found no differences on executive functioning measures between participants with impaired versus intact neurocognitive insight. As mentioned in the discussion of Study 2 results, it is possible that the included executive function measures were not sufficiently comprehensive to capture group differences, or it could be that neurocognitive insight is not related specifically to executive skills. With regard to psychiatric symptom severity and its relationship to neurocognitive insight, the results of these studies were equivocal; Study 2 found that participants with impaired neurocognitive insight reported less severe positive and depressive symptoms, and in Study 3 the opposite pattern was observed (participants with

impaired neurocognitive insight reported *more* severe positive and depressive symptoms). The depression severity findings for Study 2 are most consistent with the abundant available literature linking insight and depression; it is unclear what produced the inconsistent results in Study 3. It is possible that differences in the samples (e.g., the impaired neurocognitive insight group in Study 3 was quite a bit more cognitively impaired, and perhaps simply more symptomatic than those in Study 2), or the depression measures (the self-report BDI-II and the clinician-rated HAMD) may have contributed to this discrepancy. Nevertheless, additional research is warranted on the relationship between neurocognitive insight specifically and depressive symptoms. The same is true for the relationship between neurocognitive insight and positive symptom severity; with conflicting findings across Study 2 and 3, the exact nature and direction of their relationship remains ambiguous.

With Study 1 and 2 providing a foundational examination of metacognition, Study 3 investigated the effect of neurocognitive insight on treatment utilization and outcome. There were no differences between those with impaired versus intact neurocognitive insight on cognitive treatment utilization, and participants with impaired neurocognitive insight who completed CCT showed greater improvement in verbal memory and functional capacity than those in the control condition or those who received treatment with intact neurocognitive insight. These results suggest that clinicians need not exclude people with impaired insight from cognitive training treatment. Rather, psychoeducation about the benefits of cognitive training even among those who perceive minimal cognitive problems may be helpful when engaging patients in treatment. Normalization of everyday problems like forgetting information or difficulty paying attention, as well as

emphasizing the practical strategy use inherent in many training programs, may also be beneficial.

Limitations of these studies, although described fully in their respective chapters, include small sample size and resulting decrease in power in Study 1 and 3, general characteristics of the samples that may limit generalizability to other populations (e.g., outpatient status, chronic psychosis, predominantly male and Caucasian), and relatively narrow measurement of executive functioning. For Study 2 and 3, dichotomization of participants into “intact” and “impaired” insight, although conducted using an appropriate multivariate statistical technique, may somewhat artificially represent the construct of neurocognitive insight. Like other types of insight, the neurocognitive subtype likely exists on a continuum and is not an all-or-none feature of psychotic illness. Future studies may wish to examine neurocognitive insight as a continuous variable rather than a dichotomous variable.

These studies extend the existing knowledge base on clinical insight in schizophrenia, and augment the limited literature on cognitive and neurocognitive insight in this population. To summarize the major conclusions of this research: outpatients diagnosed with schizophrenia present with a range of insight and metacognitive abilities, which appear to have differential relationships with cognition, everyday functioning, and psychiatric symptom severity. Many people with objective cognitive impairment minimally endorse cognitive problems, but such individuals appear able to adhere to a cognitive training intervention and benefit similarly if not more so than individuals who report frequent cognitive problems. Cognitive gains did not occur across all domains, however, so researchers and clinicians must be careful to adopt a domain-specific

approach in evaluating treatment outcome in cognitive training trials. With these results in mind, additional research is warranted to further elucidate the relationship between neurocognitive insight, depression, and positive symptom severity; future studies with larger samples would also be helpful to confirm these findings on treatment utilization and outcome. As cognitive training becomes more widely adopted and part of routine treatment offerings within psychiatric rehabilitation centers, it will be increasingly important to identify the individuals who are most likely to adhere to and benefit from treatment. These results suggest that people with intact and impaired neurocognitive insight alike are appropriate candidates.

Appendix

Table 5: Sample Items from the BCIS, MIC-SR, and CPSA

BCIS	Some of the ideas I was certain were true turned out to be false.
	My interpretations of my experiences are definitely right.
	Even though I feel strongly that I am right, I could be wrong.
MIC-SR	I have trouble listening and paying attention.
	I have trouble working on more than one task at a time.
	I have trouble remembering information like names, directions, and/or dates.
CPSA Problems	I have difficulty remembering to do things that I have scheduled.
	I have trouble staying focused while I work on a task.
	My thinking gets stuck in a rut.

Note. BCIS=Beck Cognitive Insight Scale; MIC-SR=Measure of Insight into Cognition, Self-Rated; CPSA=Cognitive Problems and Strategies Assessment.