The Cognitive Functioning of Comorbid Psychotic and Substance Use Disorder Patients

by Xi Sheng

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Rolf A. Peterson
Professor of Psychology and Psychiatry and Behavioral Sciences

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Xi Sheng

Dissertation Research Committee:

Rolf A. Peterson, Professor of Psychology and Psychiatry Behavioral Sciences, Dissertation Co-Director

Sidney W. Binks III, Neuropsychologist, D.C. Department of Mental Health St. Elizabeths Hospital, Committee Member

Lawrence A. Rothblat, Professor of Psychology and Anatomy, Committee Member

Dedication

The author wishes to dedicate this dissertation to her family, who has always supported her and encouraged her to aim high.

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Abstract of Dissertation

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and Substance Use Disorder Patients

The purpose of this study is to compare the cognitive functioning of comorbid psychotic disorder and substance use disorder (CO; n = 81) patients to that of psychotic disorder (PD; n = 30) and substance use disorder (SUD; n = 59) patients. Performances on cognitive domains of processing speed, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, and reasoning/problem solving were evaluated between: 1) CO vs. PD and SUD and 2) PD vs. SUD groups. Results show that CO patients did not perform significantly worse than PD and SUD patients on the cognitive domains. CO patients even performed significantly better than PD and SUD patients on reasoning/problem solving tasks. SUD patients performed better than PD patients on verbal memory. These findings are congruent with the enhancement model, indicating that psychotic disorder patients' cognition may be strengthened from substance use. One may suggest that it is the cognitively stronger psychotic disorder patients who are interested in or successful at finding substances. More surprisingly, results demonstrate that SUD patients may have cognitive impairments as severe as PD patients.

Table of Contents

List of Tables

Chapter 1: Cognitive Functioning of Comorbid Psychotic and Substance Use Disorder Patients

Comorbidity of multiple psychiatric disorders is common (Greenfield, Weiss, & Tohen, 1995). Particularly, the comorbidity of psychotic disorders such as schizophrenia and substance use disorder is frequent and on the rise (Westermeyer, 2006). There is extensive research showing the cognitive sequelae and functional outcome of these disorders, given the significant changes in brain morphology associated with psychosis and substance use (Liu, Matochick, Cadet, & London, 1997; Pettegrew et al., 1991; Pfefferbaum, Sullivan, Mathalon, & Lim, 1998; Robinson, Gorny, Milton, & Kolb, 2001). However, most research on the cognitive profile of psychotic disorder and substance use disorder patients did not examine the combined effects of these disorders and use either disorder as an exclusion criterion (Tracy, Josiassen, & Bellack, 1995). Thus, the cognitive status of dually diagnosed psychotic and substance use disorder patients remains to be determined. Understanding the cognitive effects of concurrent psychotic and substance use disorders can have implications for the treatment and cognitive rehabilitation of comorbid patients. Therefore, the purpose of this study is to examine the cognitive function of comorbid psychotic disorder and substance use disorder patients by comparing their cognitive performance to that of psychotic disorder patients and substance use disorder patients. This review will first provide an overview, including definition and prevalence, of psychotic disorders and substance use disorders, followed by a review of cognitive deficits associated with these disorders in studies that examined the disorders separately or

together. Most of the information is derived from literature on schizophrenia, alcohol, cannabis, and cocaine given that schizophrenia is a prevalent psychotic disorder and that alcohol, cannabis, and cocaine are frequently used by schizophrenia patients. Finally, the rationale for and a description of the current study will be provided.

Psychotic Disorders

Psychotic disorders are a group of psychopathologies with symptoms that result in a distortion of reality (Wood, Yücel, Yung, Berger, Velakoulis, & Pantelis, 2004). According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000), the term "psychotic" includes a variety of symptoms (e.g., delusions, hallucination, disturbed speech and behavior, inappropriate affect) that vary with diagnosis. The diagnoses are schizophrenia, schizophreniform disorder, schizoaffective disorder, brief psychotic disorder, delusional disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, substance-induced psychotic disorder, and psychotic disorder not otherwise specified (NOS; American Psychiatric Association, 2000).

In schizophrenia, schizophreniform disorder, schizoaffective disorder, and brief psychotic disorder, psychotic symptoms primarily include hallucinations, delusions, and disorganized speech or behavior. Schizophrenia is characterized by two or more positive symptoms (e.g., delusions, hallucinations, disorganized speech, disorganized behavior) and negative symptoms (e.g., flat affect, avolition, alogia, catatonic behavior) for a significant portion of the time for at least one month. Signs of disturbance must last at least six months with impaired social or occupational functioning. Schizophrenia has a lifetime

prevalence of about 1%. Schizophreniform disorder presents symptoms equivalent to schizophrenia. However, the duration of psychological disturbance need only to persist one to six months. This disorder has a lifetime prevalence rate of approximately .2%. Schizoaffective disorder is a psychotic disorder that includes features of both schizophrenia and a mood disorder, with lifetime prevalence ranging from .5% to .8%. Brief psychotic disorder includes acute and transient symptoms of psychosis that last from one day to one month. The number of incidences of this disorder is unknown but is considered rare (American Psychiatric Association, 2000; Sadock & Sadock, 2003).

In delusional disorder and shared psychotic disorder, the hallmark of these psychotic disorders is delusions. A delusional disorder is diagnosed when the person exhibits nonbizzare delusions for at least 1 month and does not experience other psychotic symptoms of schizophrenia. Shared psychotic disorder involves having a delusion that belongs to another person. Compared to schizophrenia, both disorders are considered rare, with a lifetime morbidity ranging from .05% to .1% for delusional disorder (American Psychiatric Association, 2000).

Psychotic disorder due to a general medical condition and substance-induced psychotic disorder feature psychotic symptoms similar to other psychotic disorders, and patients lack the insight that their psychoses are induced by a medical condition or by substances. Because psychotic symptoms result from medical conditions or substance use, these two disorders are considered to be secondary psychotic disorders. There is a lack of information on the epidemiology of these disorders given the wide range of medical and

substance use etiologies (American Psychiatric Association, 2000; Sadock & Sadock, 2003).

The diagnosis psychotic disorder NOS is used when psychotic symptoms do not meet criteria for other psychotic disorders or when there is limited information or contradictory information to make a diagnosis. For instance, psychotic disorder NOS is appropriate when a patient experiences persistent visual hallucinations in the absence of other psychotic symptoms (American Psychiatric Association, 2000).

Most research on psychotic disorders has focused on schizophrenia, possibly due to its high prevalence rate compared to other psychotic disorders. Therefore, most information presented in this introduction is based on studies conducted with schizophrenia patients.

Comorbid Psychotic Disorders and Substance Use Disorders

Patients with psychotic disorders may also engage in substance use to alleviate their symptoms (Cleghorn, Kaplan, Szechtman, Szechtman, Brown, & Franco, 1991). Psychosis has been identified as a significant factor in the cause and maintenance of substance use (Tracy et al., 1995). Patterns of substance use may also qualify for a diagnosis of substance use disorder in addition to psychotic disorder. Substance use disorders can be diagnosed as either abuse or dependence. A substance *abuse* disorder requires a maladaptive pattern of substance use resulting in at least one of the following within one year: failure to fulfill social responsibilities, involvement in legal problems, continued use in physically hazardous situations and despite social or interpersonal problems. A substance *dependence* disorder involves a maladaptive pattern of use of at least one year that is characterized by

three or more of the following: tolerance, withdrawal, increase in quantity or duration of substance use, unsuccessful efforts to reduce substance use, significant amount of time is spent related to substance use, impairment in social or occupational functioning, and continued substance use despite knowledge of negative effect (American Psychiatric Association, 2000).

Recent estimates indicate that the rates of comorbid psychotic disorders and substance use disorders are on the rise. For instance, the life-time prevalence of comorbid schizophrenia and substance use disorder ranges from 70% to 80%, which is a 20% to 30% increase over the last 12 years (Westermeyer, 2006). Psychotic disorder patients use a variety of substances (e.g., depressants, stimulants, opiods, and hallucinogens; Herman, 2004). Excluding the wide use of nicotine, most common types of substances used by psychotic disorder patients are alcohol, cannabis, and cocaine (Pencer & Addington, 2003; Tracey et al., 1995; Westermeyer, 2006).

Alcohol is a depressant that is widely used because of its availability and legality (Fisher & Harrison, 2005). Alcohol slows down the overall functioning of the central nervous system and can have a significant impact on mood and behavior. Alcohol can reduce anxiety, tension, and inhibition, but it can also facilitate inappropriate behaviors, mood lability, and impaired judgment (American Psychiatric Association, 2000; Society for Neuroscience, 2002). Among individuals experiencing psychosis, alcohol may relieve hallucinations (Mueser & Gingerich, 1994). In a study with first-episode psychosis patients, Pencer and Addington (2003) found that 12% of their sample had an alcohol abuse or dependence disorder. Additionally, alcohol is the most frequently used substance

among schizophrenia patients. Alcohol abuse or dependence is three times more likely in schizophrenia patients than in the general population, with a prevalence rate of approximately 20% to 26% (Herman, 2004; Regier et al., 1990; Thoma, Wiebel, & Daum, 2007). Additionally, Westermeyer & Schneekloth (1999) reported that the lifetime prevalence rate of an alcohol use disorder to be as high as 79% in schizophrenia patients.

Cannabis is the most widely used illegal drug and is a hallucinogen. It can alter one's perception of taste, touch, and smell and create auditory and visual hallucinations, as well as paranoid delusions, that may be pleasant or unpleasant to the user (Fisher & Harrison, 2005; Hannay, Howieson, Loring, Fischer, & Lezak, 2004). Prevalence of cannabis abuse or dependence has been found to be 13% among psychotic patients (Pencer & Addington, 2003) and 20% to 26% among schizophrenia patients (Herman, 2004; Thoma et al., 2007). Lifetime comorbidity of cannabis abuse or dependence has been estimated to be 41% in schizophrenia patients (Westermeyer & Schneekloth, 1999).

Cocaine is another illegal substance that is frequently used by psychotic disorder patients. It is a central nervous system stimulant that induces euphoria or flat affect, changes in sociability, hypervigilance, interpersonal difficulties, anxiety or irritability, stereotyped behaviors, and impaired judgment and occupational functioning (American Psychiatric Association, 2000). The incidence of cocaine abuse or dependence in psychotic disorder patients was found to be low, 2% (Pencer & Addington, 2003). However, 15% of schizophrenia patients have been found to use cocaine (Richard, Linskow, & Perry, 1985). Lifetime cocaine use disorder in schizophrenia patients is approximately 7% (Westermeyer & Schneekloth, 1999).

Similar to substance use patients, comorbid psychotic and substance use disorder patients may use more than one substance and meet diagnostic criteria for multiple substance use disorders (Westermeyer & Schneekloth, 1999). For instance, Pencer and Addington (2003) found that 14% of their patients with psychosis also met criteria for both cannabis and alcohol abuse or dependence and that 5% of their psychotic patients met criteria for cannabis, alcohol, and hallucinogen abuse or dependence. In schizophrenia patients, Thoma et al. (2007) found that almost half of their sample used both alcohol and cannabis or in combination with cocaine and hallucinogens. Moreover, Westermeyer & Schneekloth (1999) reported a lifetime prevalence of 3% for multiple substances abuse or dependence in comorbid schizophrenia and substance use patients.

Overall, the incidence of substance use disorders in psychotic disorders is high. The pattern of substances used in comorbid patients mostly involves alcohol, cannabis, cocaine, or various combinations of these and other substances (e.g., hallucinogens). Prevalence rates of substance use disorders appear to be lower in patients with mixed psychotic illnesses than when examining only schizophrenia patients (2% to14% versus 15% to ~50%), indicating that schizophrenia patients are highly vulnerable to substance use disorders. This vulnerability is also reflected in the high lifetime comorbidity of substance use disorders and schizophrenia, which ranges from 3% to 79%.

Cognitive Functioning in Psychotic Disorders and Substance Use Disorders

Cognitive functioning in psychotic disorders and substance use disorders has been separately studied. Research on the cognitive status of psychotic disorder and substance use disorder patients is conducted for several reasons. First, individuals with psychotic

disorders and substance use disorders have been shown to have altered the structure of the brain, which can have a significant impact on a person's cognitive function (Society for Neuroscience, 2002). Second, examining the cognitive profile of psychotic and substance use disorder patients may help to inform treatment. Cognitive deficits can interfere with patients' ability to participate and engage in treatment. For example, psychotherapies, such as insight related therapy, that requires the use of the learning and memory system is less effective if a patient exhibits significant deficits in learning and memory (Aleman , Hijman, de Haan, & Kahn, 1999). Additionally, cognitive impairments are related to rule violations, poor prognosis, and high rates of attrition from detoxification programs (cited in Bates, 2005; Verdejo-García, López-Torrecillas, Giménez, & Pérez-García, 2004). Third, cognitive functioning is important to study because of its relation to functional outcome. Cognitive deficits are associated with impairments in everyday living, from one's ability to take care of activities of daily living to obtaining employment (Twamly, Jeste, & Lehman, 2003). Specifically, memory, vigilance, and executive functioning are key cognitive domains that are significantly related to functional outcome (Green, Kern, Braff, & Mintz, 2000).

Cognitive Deficits in Psychotic Disorders. Cognitive deficits in psychotic disorders have mostly been studied with schizophrenia patients. There is evidence to suggest that the cognitive profile of patients without schizophrenia-type psychotic disorders is similar to that of schizophrenia patients. For instance, studies have shown that the cognitive performance of schizoaffective and delusional disorder patients do not differ significantly from that of schizophrenia patients (Evans, Paulsen, Harris, Heaton, & Jeste, 1996; Evans,

Heaton, Paulsen, McAdams, Heaton, & Jeste, 1999). Also, Gladsjo, McAdams, Palmer, Moore, Jeste, & Heaton (2004) reported that schizophrenia and related psychotic disorder patients exhibited the same pattern of cognition. Therefore, cognitive functioning of schizophrenia patients may be generalized to related psychotic disorders. The National Institute of Mental Health (NIMH)- Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS; Nuechterlein, Barch, Gold, Goldberg, Green, & Heaton, 2004) identified six separate cognitive dimensions that should be examined when studying schizophrenia: processing speed, attention/vigilance, reasoning/problem solving, working memory, verbal learning and memory, visual learning and memory.

Processing speed is the ability to quickly perform mental functions and motor activities (Lezak, Howieson, & Loring, 2004). Previous studies have found that slower reaction times are characteristic of schizophrenia patients (Binks & Gold, 1998; Rosofsky, Levin, & Holzman, 1982; Strauss, 1989). Furthermore, Hawkins et al. (2004) found that individuals who are at high risk for psychosis exhibited lower performances on a processing speed task when compared to the population norm, suggesting that a processing speed deficit may be characteristic of the prodromal phase of psychosis.

Attention/vigilance and reasoning/problem solving are domains that involve the frontal lobe, and frontal lobe dysfunction is a core feature of schizophrenia (Lezak et al., 2004). Attention/vigilance refers to the ability to receive incoming information with sustained effort while inhibiting irrelevant information. Schizophrenia patients have difficulty attending to relevant information and inhibiting irrelevant information. Reasoning/problem solving is related to executive functioning, which is the ability to solve

problems, use abstract reasoning, and coordinate other cognitive skills (Bowie & Harvey, 2005). Executive functioning deficit is consistent among schizophrenia patients (Bowie & Harvey, 2005; Velligan & Bow-Thoma, 1999) and has also been found in a sample of schizophrenia and schizoaffective disorder patients (Gooding, Braun, & Studer, 2006).

Deficits in working memory, verbal learning/memory, and visual learning/memory domains are also present in schizophrenia and related psychotic disorders. Working memory is the ability to manipulate information held in the short-term memory store and recalled from long-term memory. Schizophrenia patients have significant impairment in this cognitive domain. Verbal and visual learning/memory are associated with schizophrenia by moderate to large effect sizes on free recall, cued recall, and recognition tasks (Aleman et al., 1999). Specifically, schizophrenia patients show severe deficits in verbal learning and memory (Bowie & Harvey, 2005). However, Aleman et al. (1999) did not find any significant differences between verbal and visual learning and memory in a meta-analysis of memory impairment in schizophrenia. Similar to schizophrenia patients, deficits in working memory and verbal memory have been noted in schizophrenia spectrum disorder patients (González-Blanch, Álavez-Jiménez, Rodríguez-Sánchez, Pérez-Iglesias, Vázquez-Barquero, & Crespo-Facorro, 2006; Zabala et al., 2007).

Cognitive Deficits in Alcohol Use Disorders. Individuals with alcohol use disorders experience impairments in executive function (i.e., problem solving, abstract reasoning), short-term memory, complex visuospatial abilities, reaction time, and visual-motor integration (Hannay et al., 2004). However, significant recovery of most cognitive function usually occurs within the first year of abstinence, with the rate of recovery leveling off at

three to six weeks (Hannay et al., 2004; Crew et al., 2005). Spatial processing impairments are most often reported in abstinent individuals, suggesting that spatial processing deficits may be enduring and a long-term effect of alcohol use disorder (Crew et al., 2005; Sullivan, 2005). In addition, the magnitude of deficits in alcohol use disorder patients is typically above the clinically impaired range (Nixon et al., 1995).

However, marked cognitive deficits related to alcohol is associated with the Wernicke-Korsakoff syndrome, a condition from chronic, heavy drinking that results in a depletion of thiamine, leading to impaired neuronal function and cell death. Cognitively, Wernicke-Korsakoff patients perform similar to alcohol dependent patients; however, severe memory impairment is noted in Wernicke-Korsakoff patients. Specifically, Wernicke-Korsakoff patients exhibit defective encoding associated with severe retrieval and learning deficits. Additionally, Wernicke-Korsakoff patients demonstrate significant executive function impairment and disorientation for time and place (Hannay et al., 2004).

Cognitive Deficits in Cannabis Use Disorders. Cognitive effects of cannabis use are mostly associated with the residual effects of the substance. Acute effects of cannabis use include reduced memory efficiency related to storage of information, slowed visual processing speed, and time misperception (e.g., tendency to underestimate how much time has elapsed). Long-term effects of cannabis are subtle and centered in attention and memory problems, which are mostly related to chronic and heavy use (Hannay et al., 2004; Verdejo-Garcia et al., 2004).

Cognitive Deficits in Cocaine Use Disorders. Cognitive deficits in cocaine use disorders are more often associated with short-term effects than with long-term effects of

the substance. Problems with visuospatial ability, memory, attention, reasoning, and problem solving ability are residual effects related to cocaine use. However, long-term effects of cocaine are often reduced (for a review, see Verdejo-Garcia et al., 2004). For instance, Selby and Azrin (1998) reported that cocaine dependent patients showed cognitive performance comparable to that of normal controls three years after last cocaine use. In contrast, chronic cocaine use can result in impairments in memory, attention, and executive functioning (e.g., abstract reasoning; Hannay et al., 2004; Verdejo-Garcia et al., 2004). Other studies have found marked deficits in the verbal learning and memory in cocaine use disorder patients during both acute and prolonged cessation (10 days to 45 days; Beatty, 1995; van Gorp, 1999). Mildly impaired to intact functioning of executive, attention, and visual domains have been observed (cited in Serper, Bergman, Copersino, Chou, Richarme, & Causio, 2000).

Cognitive Deficits in Polysubstance Use. Studies on the cognitive performances of individuals who use multiple substances have been limited, with mixed results. In a review of neuropsychological correlates of substance use, Verdejo-Garcia et al. (2004) indicated more brain damage and reduced capacity to recover cognitive functions in polysubstance users than in individuals who only use one substance. On the same note, Simon, Domier, Sim, Richardson, Rawson, & Ling (2002) found that cocaine and methamphetamine users have significantly more impaired verbal memory than methamphetamine only users. In contrast, Sclafani, Tolou-Shams, Price, & Fein (2002) found that crack-cocaine dependent users and crack-cocaine and alcohol dependent users have the same magnitude and pattern of cognitive impairments. Overall, a pattern of impairments in processing speed, verbal

and visual memory, and verbal and visuoperceptual abilities has been noted in polysubstance users. However, verbal abstraction remains intact (Hannay et al., 2004).

Summary. In general, schizophrenia and related psychotic disorder patients show similar patterns of impairment in multiple cognitive domains. Schizophrenia patients frequently score 1.5 to 3 standard deviations below the norm on neuropsychological tests (Gold & Harvey, 1993; Nixon, 1995). Particularly, deficits in attention, working memory, and executive functioning are moderate, with most severe impairments in processing speed and verbal learning and memory (Binks III & Gold, 1998; Bowie & Harvey, 2005). With the exception of Wernicke-Korsakoff's nutrition related impairments in alcohol dependency, cognitive deficits reported in the substance use disorder literature have been less severe than those seen in schizophrenia. The most significant deficit in alcohol use disorders is related to visual-spatial processing. Cognitive effects of cannabis use include attention and memory effects which appear to be subtle. Verbal learning and memory, attention, and executive function deficits are related to cocaine use. Lastly, polysubstance use can lead to impairment in multiple cognitive domains (e.g., processing speed, memory, verbal and visual abilities).

Cognitive Functioning in Comorbid Psychotic and Substance Use Disorders

There is a lack of information on the cognitive functioning of patients with comorbid psychotic disorder and substance use disorder (Herman, 2004). This limitation in the literature is significant given the high rate of individuals who are diagnosed with both disorders (Westermeyer & Schneekloth, 1999; Westermeyer, 2006). Researchers consider that the cognitive functioning of comorbid patients is unique given the combined effects of

psychotic disorders and neurotoxic effects of substance use (Addington & Addington, 1997; Herman, 2004). Specifically in schizophrenia, a number of brain abnormalities have been identified. The neurotransmitter dopamine involved in movement, cognition, and emotion is dyregulated (Society for Neuroscience, 2003). Asymmetrical cerebral and ventricular volume, reduced hippocampus-amygdala complex, and changes in blood flow are present (Sadock & Sadock, 2003). In alcohol and cocaine dependent patients, researchers have observed smaller volumes of cortical areas and morphological changes in dendrites as well as in the prefrontal and frontal cortex (Liu, Matochick, Cadet, & London, 1998; Pettegrew et al., 1991; Pfeffer-baum et al., 1997; Robinson et al., 2001). These findings suggest that comorbid patients may possess neuroanatomical abnormalities from both psychotic and substance use disorders, which may further interfere with their cognitive functioning (Addington & Addington, 1997).

Another rationale to suggest that comorbid patients may have a unique cognitive status is their pattern of outcome. Compared to schizophrenia patients, dually diagnosed schizophrenia and substance use disorder patients have poorer quality of life, are unemployed, homeless, and often live in poverty. They also require more treatment episodes and exhibit lower treatment compliance. Moreover, comorbid patients have more suicide attempts and higher incidences of violent behavior (Westermeyer, 2006; Thoma et al., 2007). Related to the course of these comorbid disorders, dually diagnosed patients tend to have earlier onset of schizophrenia compared to schizophrenia only patients, which is related to poor prognosis (Sadock & Sadock, 2003). Additionally, comorbid patients show deterioration in their functioning over time; whereas, schizophrenia patients' function

remains relatively stable (Choulgian, Shumway, Balancio, Dwyer, Surber, & Jacobs, 1995), suggesting that "substance use undermines specific psychological functions in schizophrenia, reducing the patients' ability to cope" (cited in Westermeyer, 2006, p. 351). When compared to substance use only patients, dually diagnosed patients do not appear to be more different on variables such as marital status and employment (Westermeyer & Schneekloth, 1999). To the best of our knowledge, no studies to date have compared the functional outcome and quality of life between comorbid patients and substance use disorder patients.

Overall, these findings of functional outcome indicate that comorbid patients show more deficits than psychotic disorder patients. Since cognitive functioning is closely related to functional outcome (Green et al., 2000; Twamly et al., 2003), the more impaired outcome of comorbid patients suggests that comorbid patients may have cognitive deficits that are different from, or more severe than, that of non-comorbid patients. If the cognitive functioning of comorbid patients is unique from that of non-comorbid patients, then there are implications for treatment and functional outcome of dually diagnosed patients. As previously described, treatment rehabilitative interventions and daily functioning are related to cognitive abilities such as attention, memory, and executive function (Green et al., 2000). If there are significant differences in the cognitive abilities of non-substance using psychotic disorder patients and dually diagnosed patients, then it would be important to tailor treatment strategies to address the different cognitive capacities of dually diagnosed patients to maximize treatment effects and to improve functioning (Herman, 2004).

Previous Research on Cognitive Functioning of Comorbid Patients

Previous studies on comorbid psychotic disorder and substance use disorder patients mostly examined the combined effects of schizophrenia and alcohol, schizophrenia and cannabis, schizophrenia and cocaine, and schizophrenia/psychosis and substance use disorders. These studies have shown mixed results regarding the cognitive profile of comorbid patients.

Allen, Goldstein, and Aldarondo (1999) compared demographically matched schizophrenia patients with alcohol abuse or dependence disorder, schizophrenia only patients, alcohol abuse or dependent patients, and hospital patients on cognitive measures of intelligence, processing speed, working memory, verbal and visual ability, executive function, and sensory and perception. The hospital patient group performed significantly better than the two schizophrenia groups. Alcohol abuse or dependent patients performed consistently better than schizophrenia with and without alcohol use disorder. The combined effect of alcohol and schizophrenia was significant but subtle, with comorbid patients performing significantly worse than schizophrenia patients on sensory and perception.

While Allen et al. (1999) found a unique cognitive status in comorbid patients with alcohol use disorders, Nixon, Hallford, & Tivis (1996) did not produce similar findings. They examined the effects of comorbid schizophrenia and alcohol in a study that compared dually diagnosed schizophrenia and alcohol dependent patients, schizophrenia patients, alcohol abuse or dependent patients, and community volunteers. Comparison groups were matched on demographic variables such as age, education, years of alcohol use, and length

of hospitalization. Participants were compared on measures that assessed facial recognition and executive function. The study found that the control group performed better than the clinical groups. Within the clinical groups, alcoholic patients' cognitive status was comparable to that of schizophrenia patients. Furthermore, dually diagnosed patients performed similar to schizophrenia and alcoholic groups, indicating that comorbid patients were not more cognitively impaired than schizophrenia and alcohol dependent patients on facial recognition and executive tasks.

Cannabis use in psychotic disorder patients was studied by Sevy et al. (2007). This study only examined the effects of cannabis abuse or dependence in schizophrenia and schizoaffective patients. Comorbid patients were compared with schizophrenia only patients and healthy controls on measures of premorbid intelligence, attention, working memory, verbal learning and memory, verbal fluency, processing speed, and executive function. Comparison groups were not significantly different on age or gender; however, schizophrenia patients had significantly less years of education than control participants. Overall, the study found that all psychotic disorder patients were inferior in their performance compared to healthy controls on all measures. No significant differences were found between the two clinical groups, except on a test of attention (Digit Span forward), with the comorbid group performing worse than the non-substance abusing group. This finding suggests the compounding effects of cannabis use and psychotic disorder on the domain of attention.

The effects of comorbid schizophrenia and cocaine use were examined by Serper et al (2000) and Sevy, Kay, Opler, and Praag (1990). Serper et al. compared verbal learning

and memory functioning between dual diagnosis, schizophrenia, and cocaine dependent patients. No significant demographic (e.g., age, gender, number of prior hospitalizations, medication status) differences were found between the groups. Serper et al. discovered that cocaine patients performed as poorly as schizophrenia only patients and that comorbid patients exhibited significant learning and memory deficits beyond what is expected for schizophrenia and cocaine patients. Sevy et al. examined schizophrenia patients with and without cocaine dependence on measures of attention, verbal learning and memory, abstract reasoning, and intelligence. The study noted that comorbid patients also used other substances (e.g., alcohol, cannabis, opiates, hallucinogens) in addition to cocaine. Participants from two groups were not significantly different in age, gender, education, intelligence, premorbid adjustment, medication, onset of schizophrenia, and length of hospitalization. Results of the study indicate that comorbid patients were more impaired in abstract reasoning and verbal memory but were superior in the attention domain than schizophrenia only patients. Together these studies suggest that schizophrenia patients with cocaine use disorder exhibit deficits in cognitive domains of reasoning and verbal learning and memory that are more severe than that of schizophrenia patients who do not use cocaine and other substances.

A number of studies have been conducted to explore the cognitive functioning of comorbid patients by examining dually diagnosed patients with a variety of substance use disorders. Herman (2004) studied schizophrenia patients with and without substance use disorders (mostly alcohol, cannabis, and polysubstance) on cognitive domains of intelligence, verbal and visual memory, and executive function. The two clinical groups

were not significantly different in their educational attainment, but the comorbid group was younger and had more males than the comparison group. This study discovered that comorbid patients performed better than schizophrenia only patients on measures of executive function and that there were no significant differences between the two groups on other measures. Thoma et al. (2007) examined aspects of executive function related to inhibition and mental flexibility in comorbid schizophrenia and substance use disorder patients (mostly alcohol, cannabis, and polysubstance), schizophrenia patients, alcohol abuse/dependent patients, major depression patients, and healthy controls. Thoma et al. found that dual diagnosis patients did not differ significantly from schizophrenia only and alcohol patients, although they performed significantly worse than depression patients and healthy controls. However, the authors noted a trend that the schizophrenia only group showed the most pronounced deficits relative to the control group and that there was a trend suggesting that the dual diagnosis group performed better than the schizophrenia group on executive function tasks. Together, these studies suggest more intact executive function in comorbid patients than in non-substance using schizophrenia patients.

Although Herman et al. (2004) and Thoma et al. (2007) found that comorbid patients performed better than patients without comorbid substance use disorder on executive functioning, other studies did not report similar findings. Addington & Addington (1997) compared substance (alcohol and/or cannabis) abuse/dependent schizophrenia patients and demographically matched non-substance abuse/dependent schizophrenia patients on measures of verbal ability, attention, executive functioning, and verbal and visual memory. The study showed a lack of cognitive difference between the

two clinical groups. Likewise, Cleghorn et al. (1991) assessed demographically similar comorbid schizophrenia and substance use patients (mostly alcohol and LSD), non-substance using schizophrenia patients, and normal controls. Results of the study suggest no significant difference between comorbid patients and schizophrenia patients on cognitive measures of intelligence, verbal ability, memory and learning, and executive function (problem-solving).

Pencer & Addington (2003) studied the cognitive function of substance abuse or dependent individuals in early psychosis. Comorbid patients in this sample primarily used alcohol and cannabis, and a minority of patients used cocaine, hallucinogens, or various combinations of substances (e.g., cannabis and alcohol; cannabis, alcohol, and hallucinogens). Participants in this study were all experiencing their first episode of psychosis and were divided into four comparison groups: 1) no substance use disorder, 2) alcohol abuse or dependence, 3) drug abuse or dependence, 4) both alcohol and drug abuse or dependence. Demographic information regarding the group participants was not compared. The four clinical groups were evaluated on tests of verbal ability, processing speed, attention, verbal and visual learning and memory, and executive function at baseline and one year into the study. Researchers reported that comorbid patients did not show cognitive impairment worse than those who did not use substances and that no significant group differences were found at both time points.

Limitations of Previous Research

Mixed Results. Previous research on the cognitive status of comorbid psychotic and substance use disorder patients has produced diverse results. When examining the

combined effects of substance use disorder and schizophrenia by the type of substance, cannabis and cocaine appear to have compounded the cognitive deficits present with schizophrenia in areas of attention for cannabis and verbal learning and memory and abstract reasoning for cocaine. However, comorbid cocaine and schizophrenia patients exhibited superior attentional functioning to schizophrenia patients. On the other hand, the cognitive effects of alcohol have been mixed (e.g., Allen et al., 1999; Nixon et al. 1996). In addition, there are inconsistent findings regarding how executive function is impacted, with no clear evidence regarding whether comorbid patients have better executive function abilities than schizophrenia/psychotic disorder patients.

Results that show superior functioning in dually diagnosed patients or no difference between comorbid and non-comorbid patients are unexpected for several reasons. One, comorbid patients suffer from neuroanatomical abnormalities from disorders that are known to interfere with the neurobiology of the brain and to change the morphology of the brain to produce cognitive deficits (Liu et al., 1997; Pettegrew et al., 1991; Pfeffer-baum et al., 1998; Robinson et al., 2001). Second, comorbid patients have an earlier onset of schizophrenia, which is related to poor prognosis (Sadock & Sadock, 2003). Lastly, findings indicating that comorbid patients may have better executive function abilities are contrary to expectation given that comorbid patients have more negative functional outcomes than schizophrenia patients, and executive function is significantly related to functional outcome in psychotic disorder patients (Green et al., 2000; Twamly et al., 2003). Therefore, the cognitive status of comorbid patients remains to be elucidated.

Another area of uncertainty is related to the cognitive status of substance use disorder patients and schizophrenia patients. Allen et al. (1999) reported that their alcohol abuse or dependent patients exhibited superior cognitive functioning relative to their schizophrenia patients. However, other studies have shown that substance use disorder patients' cognitive abilities are comparable to those of schizophrenia patients (Nixon et al., 1996; Serper et al., 2000; Thoma et al., 2007). This inconsistency is unexpected given that previous studies have suggested that substance use disorder patients usually show significant cognitive deficits compared to community controls but with better cognitive functioning than schizophrenia patients. Generally, substance use disorder patients have cognitive deficits above the clinically impaired range; whereas, schizophrenia patients tend to score in clinically impaired range (Nixon, 1995). More research is needed to clarify whether substance use disorder patients' cognitive status is more intact than that of psychotic disorder patients.

Inadequate Comparison Groups. Another limitation that emerges from previous studies is related to comparison groups. Comorbid patients who use substances may have deficits that are different from either psychotic disorder patients or substance abuse patients due to a combination of insults on the brain from two different psychiatric disorders. In order to assess the cognitive profile of dually diagnosed patients, adequate comparison groups are needed. Most previous studies lacked a substance use group for comparison; they mostly compared comorbid patients and psychotic disorder patients or compared comorbid patients, psychotic disorder patients, and controls (e.g., Addington & Addington, 1997; Cleghorn et al., 1991; Herman, 2004; Pencer & Addington, 2003; Sevy, 1990; Sevy,

2007). Leaving out a direct comparison with a substance use disorder group may not be informative of the combined effects of psychotic and substance use disorders, given that any differences between comorbid patients and psychotic disorder patients may be only related to substance use.

Gender Differences. Different cognitive performances have been described for male and female patients in studies of schizophrenia and substance use disorders. Studies have shown that female schizophrenia patients performed worse than male patients on tasks that require attention and abstract reasoning (Perlick, Mattis, Stastny, & Teresi, 1992). In the substance use disorder literature, female alcohol dependent patients showed more cognitive deficits than male patients, even if the female alcoholic patients have less severe drinking history (Acker, 1986). Given these cited gender differences in cognitive functioning, gender should be considered when evaluating or conducting research in this area. A number of studies in this literature review did not examine the number of participants by gender (e.g., Allen et al., 1999; Pencer & Addington, 2003, Sevy et al., 2007). For studies that did examine gender differences, Herman (2004) reported that the study had more male schizophrenia patients in the dual diagnosis group (87%) than in the schizophrenia only group (53%). This discrepancy may explain the lack of difference between comorbid patients and schizophrenia patients and the greater performance of the comorbid patients on executive function tasks. Having more female patients may have lowered the performance of the schizophrenia only groups if they performed poorly on tests of attention and abstract reasoning, thus, possibly reducing the cognitive discrepancy between the groups or even causing the schizophrenia only groups to perform worse than comorbid groups.

Premorbid Functioning. Premorbid cognitive function has been cited as a mediator in the evaluation of cognitive function of psychotic disorder and substance use disorder patients (Tracey et al., 1995). If premorbid cognitive status is not controlled, it would be difficult to ascertain the cognitive ability of comorbid patients. The lack of cognitive differences observed between dually diagnosed patients, schizophrenia patients, and substance use disorder patients may be related to differences in premorbid level of cognitive functioning. For instance, if comorbid patients have greater initial intellectual ability than non-substance using schizophrenia patients, then comorbid patients may be performing at a level that is similar to them even if the comorbid patients have experienced greater cognitive loss from the combined effects of substance use and psychosis. Previous studies tried to address this issue by matching groups on level of education or using education as a covariate in analyses (Allen et al., 1999; Sevy et al., 1990). However, education may not be the best indictor of premorbid cognitive function. For instance, Kramen et al. (1996) found that chronic schizophrenia patients performed better on tests of estimated premorbid ability than education equivalent normal controls, indicating that demographically based estimates of premorbid intelligence may not be appropriate for determining premorbid cognitive function. Thus, Kramen et al. (1996) has recommended including measures such as reading and spelling tests to determine premorbid cognitive functioning since these abilities are resistant to cognitive change. Few studies (e.g., Allen et al., 1999; Sevy et al., 2007) have utilized reading and spelling measures to determine and control for premorbid functioning. These studies found that comorbid patients showed more cognitive deficits than schizophrenia and alcohol disorder patients. In contrast, a

number of studies that did not use alternative measures to confirm premorbid cognitive abilities did not find any cognitive differences between clinical groups (e.g., Addington & Addington, 1997; Cleghorn et al., 1991; Nixon et al., 1996; Pencer & Addington, 2003; Thoma et al., 2007), suggesting that more sensitive measures of premorbid cognitive status should be used to rule out its potential effect as a mediating variable.

Negative Symptomatology. Negative symptoms such as flat affect, avolition, and alogia have been found to be negatively correlated with attention, working memory, and verbal abilities (Basso, Nasrallah, Olson, & Bornstein, 1998; Glasjo et al., 2004). Substance using schizophrenia patients have been noted to have more positive symptoms than non-substance using schizophrenia patients (Addington & Addington, 1997; Sevy et al., 1990), indicating that they may be more cognitively intact than schizophrenia only patients if they experience less negative symptoms that may interfere with their cognitive activity. Negative symptoms in schizophrenia /psychotic disorder groups may interfere with their cognitive performance, thus, diluting the cognitive difference between comorbid and non-substance using psychotic disorder patients. A number of studies that did not examine the relationship between negative symptomatology and cognitive performance yielded no significant or subtle difference between comorbid and psychotic disorder groups (e.g., Allen et al., 1999; Herman, 2004; Nixon et al., 1996; Pencer & Addington, 2003). Studies that did examine and control for negative symptoms yielded mixed results regarding the cognitive status of comorbid patients (Addington & Addington, 1997; Cleghorn et al., 1991; Sevy et al., 1990; Thoma et al., 2007). Overall, given the possible

correlation between negative symptomatology and cognitive functioning, negative symptoms should be examined and controlled.

Cognitive Domains. Another shortcoming of the previous research is the lack of studies that have comprehensively evaluated domains related to cognition in schizophrenia or related psychotic disorder patients. NIMH-MATRICS (Neuchterlein et al., 2004) indicated that studies examining cognition in schizophrenia should consider six cognitive domains: 1) processing speed, 2) attention/vigilance, 3) working memory, 4) verbal learning and memory, 5) visual learning and memory, and 6) reasoning/problem solving. Current literature on comorbid patients has mostly focused on verbal learning and memory and reasoning, with moderate to limited attention on domains of processing speed, attention, working memory, and visual learning and memory, suggesting a need for a more comprehensive evaluation of cognition in order to determine the full cognitive profile of comorbid patients.

Current Study

The purpose of this study is to examine how comorbid psychotic and substance use disorder patients compare with psychotic disorder patients and substance use disorder patients on six cognitive domains that have been identified to be separable cognitive factors in schizophrenia and psychotic disorders (i.e., processing speed, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, and reasoning/ problem solving). This study will contribute to current literature on the cognitive profile of comorbid psychotic and substance use disorder patients by addressing the limitations previously discussed. This study aims to clarify the cognitive status of

comorbid patients by: 1) comparing cognitive performance of comorbid patients, psychotic disorder patients, and substance use disorder patients; 2) controlling for mediating variables (e.g., gender, premorbid cognitive functioning, and negative symptoms) that have been neglected by other studies; and 3) examining cognitive domains (e.g., processing speed, attention, working memory, visual memory and learning) that have been understudied and thereby providing a more comprehensive evaluation of the cognitive profile of comorbid patients. In addition, this study will also compare the cognitive status of psychotic disorder patients and substance use disorder patients to clarify mixed findings regarding the relative cognitive ability of these groups.

Three hypotheses are formulated. For the first hypothesis, which is related to the first aim of the study, it is expected that comorbid patients will perform worse than all other groups on all neuropsychological domains, except for reasoning/problem solving when compared to the psychotic disorder group. This is based on previous findings regarding the poor prognosis of comorbid patients relative to psychotic disorder patients who do not have a substance use disorder. Additionally, comorbid patients are expected to have worse cognitive functioning due to the accumulation of neuroanatomical changes observed in the brains of psychotic disorder patients and substance use patients (Liu et al., 1998; Pettegrew, 1991; Pfeffer-baum et al., 1998; Robinson et al., 2001; Sadock & Sadock, 2003). For the second hypothesis, dually diagnosed patients are expected to perform better than psychotic disorder patients, but worse than substance use patients, on reasoning/ problem solving. This hypothesis is based on previous studies that reported similar results and from the assumption that substance using patients have more intact executive function skills than

non-substance using patients needed to obtain drugs (Herman, 2004; Thoma et al., 2007). It is expected that comorbid patients will perform worse than substance use only patients on executive tasks because of the impaired frontal lobe function related to psychotic disorders. Hypothesis three is related to the second goal of the study. The substance use disorder group is predicted to perform better than the psychotic disorder group based on findings from the substance use disorder literature that cognitive deficits have been less severe than those seen in schizophrenia.

Chapter 2: Methods

Participants

Participants for the current research were drawn from a database of adult patients who had received neuropsychological evaluations in a psychiatric hospital located in Washington, D.C. The hospital specializes in the treatment of outpatient and inpatient mentally ill individuals, as well as, forensic patients with psychiatric diagnoses. Patients were referred for neuropsychological evaluations to assess their cognitive status in order to clarify psychiatric diagnoses or to inform treatment. Participants were selected for the current study if they met DSM-IV-TR (American Psychiatric Association, 2000) criteria for a psychotic disorder and/or a substance use disorder.

Procedure

Neuropsychological Evaluations. Patients in the database were referred by neurologists, psychologists, psychiatrists, or clinical administrators from the hospital for a neuropsychological assessment. Once the referrals were made, trained neuropsychology externs, interns, and post-doctoral fellows conducted all evaluations. The examiners approached all cases with a large neuropsychological battery. First, they reviewed clinical records and interviewed the referral source to gather background information regarding the patient. Next, the examiners conducted an in-person clinical interview with the patient. All patients provided consent that the results of the evaluation would potentially be shared with the court, attorneys, and/or treatment team. Then, all patients were administered a comprehensive neuropsychological battery, which included measures on the severity of

their psychiatric symptoms, estimation of premorbid cognitive function, current cognitive function, and motor function. The measures were administered in person and in the order of the examiners' discretion. All evaluations were conducted after significant admission time (e.g., no one was tested within one week of hospital admission). At times, assessments were prematurely discontinued or shortened due to noncompliance or limited cognitive capacity, upon the approval of a neuropsychology supervisor who is a licensed clinical psychologist. Most assessments were conducted over multiple sessions, and the length of the evaluation typically ranged form 5 hours to 15 hours. Patients were medically stabilized during the evaluation. No one was acutely psychotic; however, some residual psychotic symptoms were sometimes present. Once the evaluation was completed, a comprehensive neuropsychological report followed. The final report provided updated information on demographics, diagnoses, and cognitive status, which were all reviewed by the neuropsychology supervisor and then entered into a database. Archival research involving the database was approved by the IRB of the hospital, giving permission to collect data for normative research.

Current Study. Only data from patients with a psychotic disorder and/or substance use disorder were examined. Participants were sorted into one of the three comparison groups [i.e., comorbid psychotic and substance use disorder (CO), psychotic disorder (PD), substance use disorder (SUD)], based on the DSM-IV-TR diagnostic criteria (American Psychiatric Association, 2000). Diagnoses were obtained from the neuropsychology evaluation and then reviewed and retrospectively confirmed from the clinical record. For

patients who had received multiple neuropsychological evaluations, results of the latest assessment were included in the study.

Measures

Demographics. Participants' demographic information and neuropsychological background (e.g., age, gender, ethnicity, education, psychopathologies, age of onset, childhood disorders, neurological diagnoses) were used to obtain descriptive information about the sample.

Psychiatric Symptomatology. Negative symptomatology was assessed by the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962). The BPRS is an internationally used measure that is recommended in studies of schizophrenia and other psychotic disorders (Bech, 1993). It measures the severity of the psychotic disorder symptoms experienced during the evaluation on 20 items, using a 7-point scale, ranging from 1 (not present) to 7 (very severe). Total scores range from 20 to 140, indicating the severity of overall psychotic state, with higher scores reflecting more severe psychotic symptomatology. The BPRS has been shown to be a reliable and valid measure in psychiatric patients, with good inter-rater reliability (for a review, see Hedlund & Vieweg, 1980). In a study with a schizophrenia sample (Mueser, Curran, & McHugo, 1997), four separate factors were derived from the BPRS: thought disorders, anergia, affect, and disorganization. The four factors are consistent with symptoms of schizophrenia. Particularly, the anergia factor coincides with negative symptoms of schizophrenia.

Premorbid Cognitive Function. The Wide Range Achievement Test- Revision 3: Reading (WRAT-3; Wilkinson, 1993) was used to determine premorbid cognitive ability.

As a test of word recognition, it is frequently used to provide an estimate of premorbid functioning in schizophrenia because of its resistance to cognitive change in schizophrenia and neuropsychologically impaired patients (Dalby & Williams, 1986; Lezak et al., 2004; Nuechterlein et al., 2004). On this test, the examinee was required to read aloud a list of letters and/or words, with a 10 second response time for each letter/word. The total number of correct responses (raw score) was compared with age appropriate norms to achieve a standard score, which is based on a standard scale with a mean of 100 and a standard deviation of 15. The WRAT-3 was normed using a stratified U.S. sample, which was controlled for age, gender, ethnicity, socioeconomic status, and regional residence. Overall, the WRAT-3 has shown good reliability, content validity, and construct validity; and the Reading subtest has coefficient alphas ranging from .88 to .97.

Cognitive Domains. Subtests and index scores from the Wechsler Adult Intelligence Scale- Third Edition (WAIS-III; Wechsler, 1997a) and the Wechsler Memory Scale- Third Edition (WMS-III; Wechsler, 1997b) were used to assess the six cognitive domains: 1) processing speed, 2) attention/vigilance, 3) working memory, 4) verbal learning and memory, 5) visual learning and memory, 6) reasoning/problem solving. All raw scores from the Wechsler tests were converted to standardized scores based on age appropriate norms. Standard scores on the measures were compared to a mean of 100 and a standard deviation of 15, and scaled scores were compared to a mean of 10 and a standard deviation of 3. The Wechsler tests have been standardized to reflect the population of adults, aged 16 to 89 years, living in the U.S. and have been shown to demonstrate good reliability and validity (For a review, The Psychological Corporation, 1997).

Processing Speed. The Processing Speed Index (PSI) from the WAIS-III (Wechsler, 1997a) was used to examine the processing speed domain. This index is represented by a standard score and measures perceptual processing speed and is derived from performance on a subtest that requires the participant to determine as quickly as possible whether one of the presented two symbols is present among an array of five symbols in two minutes and a subtest that requires the participant to quickly and accurately copy as many symbols that correspond to nine numbers using a key in two minutes.

Attention/Vigilance. The Word List I Trial 1 subtest of WMS-III (Wechsler, 1997b) was utilized to assess auditory attention/vigilance, respectively. On this subtest, the individual listens to a list of 12 unrelated words and then recalls as many words as the person can remember. A raw score was obtained from the number of words recalled which was compared with age norms to obtain a scaled score. This subtest was used to evaluate attention/vigilance because attentional capacity is often measured by exposing individuals to information and repeating what is remembered (Lezak, Howieson, & Loring, 2004). Although this procedure requires short-term memory, performance has been found to be more related to attention than short-term memory (Howieson & Lezak, 2002).

Working Memory. Working memory was evaluated by the WAIS-III Letter-Number Sequencing subtest (Wechsler, 1997a). Letter-Number Sequencing is a subtest of verbal working memory that requires the individual sequence mixed groups of letters and numbers of increasing length, with the letters in alphabetical order first and then numbers in numerical order. Performance is calculated from the number of trials the participant is able to complete correctly and converted to a scaled score. This subtest involve the

working memory domain since it requires participants to hold information in mind while conducting mental operations upon it (Lezak et al., 2004).

Verbal Learning/Memory. Word List I and II subtests from the WMS-III (Wechsler, 1997b) were used to measure verbal learning and memory. Word List I involves verbal learning. On this subtest, the individual is exposed to a list of 12 unrelated words and asked to repeat as many words as he or she can remember over four trials. A raw score related to verbal learning ability was derived from the difference between the number of words recalled on trials 1 and 4 (Word List I Learning Slope). Word List II is a subtest of long-term verbal memory. On this subtest, the individual is asked to remember words from Word List I after a 30-minute delay. A raw score is based on the number of words recalled on Word List II. All raw scores from these subtests were converted to scaled scores.

Visual Learning/Memory. Learning and memory in the visual domain were determined by the WMS-III Visual Immediate Index and Visual Delayed Index (Wechsler, 1997b). The Visual Immediate Index, represented by a standard score, is reflective of one's short-term memory for visual information. This index is based on immediate memory for the ability to remember faces and to learn details from complex pictures. The Visual Delayed Index assesses long-term memory for visual information. This index is determined from the ability to recognize faces and recall details from complex pictures after a 30-minute delay.

Reasoning/Problem Solving. Reasoning and problem solving were assessed by Similarities and Matrix Reasoning subtests of the WAIS-III (Wechsler, 1997a). The

Similarities subtest is a measure of verbal abstract reasoning that asks the participant to explain how each member of a pair of words are alike, with 19 pairs in all. Matrix Reasoning is a subtest that involves visual abstract reasoning. On this subtest, the participant is required to complete increasingly difficult, 2-dimensional visuospatial matrices via multiple choice. On both tests, the raw score is derived from the number of correct items and converted to scaled scores.

Chapter 3: Results

Demographic Characteristics of Study Participants

Data from 170 participants were examined for the current study (CO: n = 81, PD: n = 30, SUD: n = 59). Table 1 presents details of participants' clinical diagnoses. Among participants with psychotic disorders, most were diagnosed with schizophrenia, schizoaffective disorder, and psychotic disorder NOS. Most of the participants with substance use disorders used alcohol, cannabis, and cocaine. These patterns of psychosis and substance use were also present in comorbid patients. Furthermore, 38.0% of substance users in the comorbid group used only one substance, 29.6% used two substances, 28.3% used three substances, and 4.2% used four or more substances. In the substance use only group, 52.6% used one substance, 28.1% used two substances, 12.3% used three substances, and 7.0% used four or more substances.

Table 2 presents more detailed demographic characteristics of all participants. The majority of participants were male (82.4%) and African American (86.3%). The participants had a mean age of 47.60 and mean years of education of 10.48. The mean years of illness was 24.69. The average estimated premorbid cognitive ability, as measured by the WRAT Reading test (Wilkinson, 1993), was in the borderline impaired range at the 4^{th} percentile. Most participants' current level of cognitive function is categorized as demented (28.6%), borderline impaired/mentally retarded (26.8%), or as cognitive disorder NOS (20.8%). Regarding psychiatric diagnoses other than psychotic and substance use disorders, 26.7% have a mood disorder and 6.3% have an anxiety disorder. Neurological

conditions were present in 67.5% of the sample. Participants took atypical (53.5%) and conventional (28.8%) antipsychotic medications, as well as other psychiatric medications (57.1%); only 14.1% of participants were not on any medication. Additionally, the mean severity of psychiatric symptoms on the BPRS (Overall & Gorham, 1962) was mild, and the BPRS also indicated mild negative symptomatology.

Comorbid vs. Psychotic Disorder vs. Substance Use Disorder: Covariates

One-way analysis of variance (ANOVA) and chi-square tests were used to compare demographic information between the three clinical groups. As shown in Table 2, participants in the groups were not significantly different on most demographic variables. However, the clinical groups significantly differed on the following variables: 1) gender, 2) presence of a mood disorder, 3) presence of an anxiety disorder, 4) use of atypical antipsychotic medication, 5) use of conventional antipsychotic medication, and 6) no use of any medication. An independent samples T-test was conducted to determine whether the demographic variables of gender, presence of a mood disorder, presence of an anxiety disorder, use of atypical antipsychotic medication, use of conventional antipsychotic medication, and no use of any medication were related to the cognitive measures (See Table 3 and 4). For instance, results of the t-test indicate that gender was not significantly related to any cognitive abilities (i.e., male and female participants' performance did not differ on any of the cognitive measures). However, the presence of mood disorder was significantly related to better working memory (Letter-Number Sequencing) and visual reasoning /problem solving (Matrix Reasoning). The presence of anxiety disorder was significantly related to increased processing speed (Processing Speed Index) and better

working memory (Letter-Number Sequencing) and verbal and visual reasoning/problem solving (Similarities; Matrix Reasoning). The use of atypical antipsychotic medication was associated with improved performance on the Processing Speed Index. The use of conventional antipsychotic medication was associated with higher working memory scores (Letter-Number Sequencing). Lastly, not using any medication was significantly related to faster processing speed (Processing Speed Index). As a result, these potential confounders, with the exception of gender, will be controlled as covariates in subsequent analyses during the comparison of the clinical groups.

Relationship between Cognitive Measures

Pearson's correlations were calculated to determine whether the cognitive measures examined similar mental abilities. As illustrated in Table 5, most measures were not highly correlated with each other ($r < .60$), indicating that the tests evaluated different cognitive abilities. However, the high correlation between the WMS-III Visual Immediate and Visual Delayed indexes ($r = .72$) suggested limited differentiation between short-term and long-term visual memory. As a result, the average of the combined Visual Immediate and Visual Delayed index scores, which have the same mean and standard deviation (i.e., $M = 100$, $SD = 15$), were calculated to achieve a combined measure of visual learning and memory.

Statistical Analyses for Hypothesis Testing

Statistical Package for Social Science, Version 15 was used to conduct analyses for hypothesis testing. Planned comparison analyses via Helmert contrast with univariate analysis of variance (ANOVA) and analysis of covariance (ANCOVA) were used to

compare: 1) the CO group against combined PD and SUD groups, and 2) the PD group versus the SUD group for a priori hypotheses 1 and 3. Planned comparison analyses via Simple contrast was used for a priori hypothesis 2, involving comparisons between the CO and SUD groups, as well as CO and PD groups. ANOVA was used to evaluate cognitive domains of attention (Word List I Trial 1), verbal learning and memory (Word List I Learning Slope, Word List II), and visual learning and memory (average score of Visual Immediate and Visual Delayed Indices). ANCOVA was utilized to examine cognitive domains of processing speed, working memory, and problem solving/abstract reasoning, all which have been found to be influenced by covariates. For processing speed (Processing Speed Index), covariates included the presence of anxiety disorder, use of atypical antipsychotics, and no use of medication which were entered into the analysis of variance as covariates. The covariates of presence of mood disorder, presence of anxiety disorder, and use of conventional antipsychotics were added into the analysis as covariates for the domain of working memory, which is measured by the Letter Number Sequencing subtest. Lastly, the problem solving/abstract reasoning domain included the covariate presence of anxiety disorder for the Similarities subtest and the covariates presence of mood disorder and anxiety disorder for the Matrix Reasoning subtest in the analysis of variance. When results were not significant or in the expected direction, analyses were performed with or without covariates to further examine differences and similarities between the clinical groups on the cognitive measures.

Hypothesis 1: It is expected that CO patients will perform worse than both PD and SUD patients on the following neuropsychological domains: processing speed,

attention/vigilance, working memory, verbal learning and memory, visual learning and memory.

Planned comparison analyses via Helmert contrast with one-way ANOVA and ANCOVA showed that that CO patients did not perform significantly worse than either the PD or SUD patients on these cognitive domains (see Table 6). No significant differences were present among the three groups on any of the measures examining processing speed, $F(2, 117) = .73$, $p = .49$; attention/vigilance, $F(2, 91) = .98$, $p = .38$; working memory, $F(2, 108) = 1.03$, $p = .36$; verbal learning and memory, $F(2, 78) = 1.33$, $p = .26$; and visual learning and memory $F(2, 97) = .89$, $p = .41$. Additionally as shown in Table 7, covariates did not influence the comparison between the CO group and other clinical groups on these domains.

Hypothesis 2: Comorbid patients are hypothesized to perform better than psychotic disorder patients, but worse than substance use disorder patients, on reasoning/problem solving domain (executive function tasks).

Similarities and Matrix Reasoning subtests represent verbal and visual reasoning/problem solving abilities, respectively. According to Table 8, simple contrast with ANCOVA showed that CO patients did not achieve a significantly better score than the PD patients on Similarities ($p = .11$). On the contrary, the CO group performed significantly better than the SUD patients on Similarities ($p = .02$). As predicted, CO patients achieved a higher score than PD patients ($p = .02$, one-tailed) on Matrix Reasoning. Again, CO patients unexpectedly performed better than SUD patients on this test ($p = .004$).

Hypothesis 3: Substance use disorder patients will perform better than the psychotic disorder patients on all domains because substance use disorder literature indicates that cognitive deficits have been less severe than those seen in schizophrenia.

SUD patients only performed significantly better than PD patients on WMS Word List II (p = .04, one-tailed; see Table 6). When covariates (i.e., anxiety disorder, atypical medication, and no medication) were not included in the analysis, SUD patients performed significantly better than PD patients on the processing speed domain, t(72) = -1.83, p = .04, one-tailed (see Table 7). When only anxiety was added as a covariate in the ANOVA, the SUD group continued to exhibit better processing speed than the PD group t(58) = -1.62, p = .05, one-tailed. However, when the comparison between the two groups was controlled for the covariate use of atypical medication t(72) = -1.22, p = .11, one-tailed, and the covariate no use of medication, t(72) = -1.42, p = .08, one-tailed, the difference in processing speed was no longer significant, suggesting that that the processing speed domain may be sensitive to the effect of medication. Interestingly, PD patients did not achieve significantly lower scores than SUD patients on any other measures (see Tables 6 and 7).

Chapter 5: Discussion

The goal of this study is to examine how CO patients compare with PD and SUD patients on six cognitive domains (i.e., processing speed, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, and reasoning/problem solving) that have been identified to be separate cognitive factors in schizophrenia and psychotic disorders. In addition to examining the cognitive status of CO patients relative to PD and SUD patients, the study also evaluated the cognitive status of PD patients and SUD patients to clarify mixed findings regarding the relative cognitive abilities of these two groups. This was an archival study of patients from a psychiatric hospital that specializes in the treatment of outpatient and inpatient mentally ill adults and forensic patients with psychiatric diagnoses. The study sample was mainly composed of low-functioning, African American males with less than 12 years of education. Overall, the cognitive function of CO, PD, and SUD patients appear to be similar on most of the cognitive domains evaluated, except for the domain of reasoning/problem solving. Between PD and SUD groups, the SUD patients appear to have better visual memory than PD patients.

Processing Speed, Attention, Working Memory, Verbal and Visual Learning and Memory

The first research question focused on evaluating cognitive domains (i.e., processing speed, attention, working memory, and visual learning and memory) that have been understudied in previous literature, as well as the domain of verbal learning and memory. No significant differences were found between the CO patients and other patients on any of these domains, suggesting that CO, PD, and SUD patients have comparable

cognitive abilities in these domains. Explanation for similar cognitive abilities in CO and PD patients may lie in brain morphology. For instance, Scheller-Gilkey, Lewine, and Brown (1999) found that substance use in schizophrenia patients does not necessarily result in more brain abnormalities. However, studies have not compared the brains of CO patients to that of SUD patients. The effect of substance in psychotic disorder may be more apparent starting in the fifth decade of life (Allen et al., 1999). The average age of this study sample is 48, suggesting that there may not have been enough time for the deficits to manifest in CO patients.

The small sample size of this study may not have provided sufficient power to detect a difference between the CO group and other clinical groups. Not separating the negative impact of particular substances may have decreased power as well. Most studies (e.g., Addington & Addington, 1997; Cleghorn et al., 1991; Herman, 2004; Pencer & Addington, 2003), including the present study, only examined the effect of substance use as a whole, without differentiating the impact of specific drugs. Failure to evaluate the neurocognitive impact of different substances may limit the ascertainment of an accurate picture of how substance use can affect cognition in CO patients. For instance, in line with expectations, cocaine has been demonstrated to have a negative impact on verbal learning and memory and processing speed in schizophrenia patients (Serper et al., 2000; Sevy et al., 1990). However, the effects of alcohol or cannabis use in psychotic disorder patients are considered to be subtle (Allen et al., 1999; Hannay et al., 2004; Verdejo-Garcia et al., 2004), suggesting that the type of substances used has contribution to the cognition of psychotic disorder patients. The inclusion of the two most frequently used drugs (alcohol

and cannabis) that may have little or no impact on cognition can limit the detectability of substances that have more impact, such as cocaine.

Some studies have found significant differences between the cognitive ability of CO patients and PD patients without examining the specific types of substances used. Contrary to expectation, dual diagnosis patients may exhibit significantly better performance on processing speed, attention, working memory, verbal learning and memory, and visual learning and memory domains. Comorbid schizophrenia patients with various substance use disorders can perform better than schizophrenia patients without substance use disorders on tasks that require both processing speed and working memory (Thoma & Daum, 2008). In a sample of mixed schizophrenia and bipolar patients with substance use diagnoses, Carey, Carey, & Simons (2003) found that CO patients performed better on visual memory tasks than patients without a history of substance use. In a study that examined the effects of cocaine on cognitive functioning in schizophrenics, comorbid patients appeared more attentive than schizophrenia patients (Sevy et al., 1990). Similarly, better performances in attention, visual and verbal learning and memory have been found in substance using psychotic disorder patients than in non-substance using psychotic disorder patients (Mcleery, Addington, & Addington, 2006). However, it is not certain whether the differences detected in these studies are related to the effect of substance use or to the impact of having a comorbid disorder, since these studies did not include a substance use group for comparison.

This study's insignificant finding was not entirely unexpected given that previous studies have shown similar results. For instance, a lack of cognitive differences on

measures of processing speed, attention, working memory, verbal and visual memory and learning have been noted in schizophrneia patients who used a variety of drugs and schizophrenia patients who did not use any drugs (Addington & Addington, 1997; Cleghorn et al., 1991; Herman, 2004). In patients with various psychotic disorders, Pencer & Addington (2003) also reported no significant differences in performance on processing speed, attention, and verbal and visual learning and memory tests between those with and without substance use diagnoses.

Reasoning/Problem Solving

For the cognitive domain of reasoning/problem solving, it was first hypothesized that CO patients would achieve higher scores than PD patients on reasoning/problem solving tasks. This hypothesis was partially supported in that CO patients performed significantly better than PD patients on a visual abstract reasoning task. However, CO patients' achievement on a verbal abstract reasoning task was similar to that of PD patients, suggesting better visual reasoning and problem solving for substance using psychotic disorder patients. Although previous research did not specifically examine differences between verbal and visual reasoning domains, studies have demonstrated a pattern of superior performance in substance using psychotic disorder patients on visual reasoning tasks. For instance, Mcleary et al. (2006) found that first episode psychotic disorder patients in an early psychosis specialty program who met criteria for substance abuse or dependence disorder performed significantly better than first episode psychotic disorder patients who did not have a substance use disorder diagnosis on the Wisconsin Card Sort Test (WCST; Malmo, 1974), a visual abstract reasoning and problem solving test, both at

baseline and one year after first episode psychosis. Similarly, forensic schizophrenia patients with substance use disorders have been found to obtain better performance on the WCST than non-substance using schizophrenia patients (Letter to Editors, 2003).

However, current study results contradict studies that found no significant differences between performances on reasoning tests of psychotic disorder patients with and without substance use disorder. Herman (2004) found no significant differences between substance and non-substance using schizophrenia patients on Matrix Reasoning and Similarities. However, dual diagnosis patients did perform better on other tests of executive functioning that involved both verbal and visual domains in the study. Additionally, Wobrock, Sittinger, Behrendt, D'Amelio, Falkai, & Caspari (2007), Cleghorn et al. (1991), and Addington and Addington (1997) all reported similar performances on visual abstract reasoning tests (i.e., WSCT) between CO and PD patients. The lack of significant differences in the reasoning/executive function domain between dually diagnosed patients and patients without any substance use diagnoses in previous studies may be related to the lack of a priori, directional hypotheses, which could result in insufficient power to detect differences between the two clinical groups. The directional hypothesis of current study was designed to increase power to address the limitation of small sample size.

The ability of CO and SUD patients on the reasoning/problem solving domain was also compared. It was expected that the CO patients would perform worse than SUD. On the contrary, results indicate that CO patients performed significantly better than SUD patients on both verbal and visual abstract reasoning tests. Few studies have compared the

cognitive performances of substance using and comorbid substance using psychotic disorder patients. Nixon et al. (1996) did not find any significant difference between alcoholic patients and comorbid schizophrenia and alcoholic patients on the Trail Making Test B (TMT B), an executive function test of response inhibition and cognitive flexibility. Thoma et al. (1997) obtained similar results when comparing between alcoholic patients and schizophrenia patients who used a variety of substances using the TMT B. These findings contradict the results of current study and may be related to differences in the measure used. Good performance on the TMT B requires processing speed, which is generally impaired in substance use and psychotic disorders. Slow processing may have limited the ability to detect differences between CO and SUD patients in previous studies. On the other hand, Matrix Reasoning and Similarities subtests are un-timed tests, providing for the removal of processing speed and thereby increasing variation in performances between groups. Even when the same test is used to examine reasoning/problem solving involved in the executive function domain, Allen et al. (1999) did not find any significant differences between alcoholic patients and alcoholic schizophrenia patients on Similarities (Matrix Reasoning was not available for comparison). However, the study did find that alcoholic patients performed significantly better than comorbid patients on other reasoning/ executive functioning tests; but the authors noted that the additive effect of alcohol use on cognitive functioning is subtle. Discrepant findings may be related to differences in study sample, since the current study examined patients with a range of psychotic and substance use disorders, whereas, the Allen et al. study only examined the effects of alcohol on schizophrenia.

Overall, results of the second research hypothesis add to the growing literature that substance use disorders may not necessarily further deteriorate the executive functioning of psychotic disorder patients. Substance use may actually increase dopaminergic activity in the brain, which can enhance frontal lobe executive functioning. Executive deficits that are prevalent in schizophrenia are often related to a decrease in the level of dopamine in the brain; thus, increased dopaminergic activity from substance use may alleviate negative cognitive sequalae of psychosis, such as executive dysfunction, to the point that this may override any structural damage and cognitive impairment induced by drug use (Thoma & Daum, 2008; Thoma, Wiebel, & Daum, 2007). In some instances, it may be that there is even an improvement in abilities, especially in the reasoning/problem solving domain, as demonstrated by this study. Or, this may be possible when one considers that comorbid patients may have more intact executive functioning skills for the purposes of obtaining drugs and managing psychotic symptoms. In this context, dually diagnosed patients appear to require more reasoning and problem solving skills for the management of their symptoms than non-comorbid patients (letter to editor, 2003), which is consistent with current study's finding that CO patients have better verbal and visual abstract reasoning/ problem solving than both PD and SUD patients combined. Even if the combination of psychosis and substance use proves to be detrimental to the neuroanatomy of comorbid patients, the finding that CO patients are not more impaired than PD and SUD patients suggests the possibility that either the brains of comorbid patients are higher functioning to begin with or may recruit other brain areas to compensate or enhance executive functioning (Thoma & Daum, 2008).

PD Patients vs. SUD Patients

The last hypothesis predicted that the SUD group has better cognitive abilities than PD group to clarify mixed findings regarding the relative cognitive ability of these groups. The comparison between PD and SUD groups is also useful to evaluate the lack of significant difference between CO patients and other clinical patients on measures of processing speed, attention, working memory, verbal and visual learning and memory (hypothesis 1). For instance, nonsignificant differences between the CO group and other groups may be related to significant differences between PD and SUD groups. For example, the SUD group achieved significantly higher scores than PD patients on a verbal memory test (WMS-III Word List II), which may have limited the differences in performance when the CO group is compared against both PD and SUD groups in the first hypothesis.

Few studies have compared the cognitive abilities of PD and SUD patients. The finding that SUD patients performed better than PD patients on verbal memory is consistent with results of Allen et al. (1999), which found that alcoholic patients performed better than schizophrenia patients without substance use disorder on a verbal auditory perception task. Verbal auditory perception is essential for obtaining verbal information needed for learning and memory. Better performance in SUD patients may be explained by the greater brain volume deficit and structural brain abnormalities noted in psychotic disorder patients than in alcoholic patients (cited in Allen et al., 1999). However, current study's finding in verbal memory contradicts Nixon et al's (1996) finding that non-substance using schizophrenia patients show verbal learning and memory pattern similar to

that of cocaine addicted patients. This could be related to differences in the type of substance used, that cocaine can cause deficits similar to that of psychotic disorder. Marked deficits in verbal learning and memory have been noted in patients who use cocaine during both acute and prolonged cessation (Beatty, 1995; van Gorp, 1999). Significant differences between SUD and PD patients on cognitive domains of processing speed, working memory, attention, visual learning and memory, and reasoning/problem solving were not detected in this study. This is consistent with the few studies available for comparing between SUD and PD patients (Allen et al., 1999; Serper et al., 2000; Nixon et al., 1996). Imaging studies have found a decrease in frontal cortical brain volume in participants who are addicted to heroin, cocaine, and alcohol relative to normal controls (Liu et al., 1998; Jennigan et al., 1991; Pfefferbaum et al., 1997). This decrease in cortical brain volume may be similar to that found in psychotic disorder patients since reduced frontal grey matter volume is observed in brains of patients who experienced psychosis (Pantellis et al., 2003). However, there is a trend that the SUD group performed better than the PD group on all cognitive domains. The small sample size of the comparison groups, especially that of PD group, may have limited the power to detect differences between PD and SUD groups. Overall, current findings are demonstrative of mixed results in previous studies regarding the relative abilities of SUD and PD patients. More research is needed to compare the cognitive functioning of SUD patients and PD patients in order to inform studies on the cognitive performance of CO patients.

Limitations

This study has several limitations. First, the small sample sizes of the groups may have limited the number of between group differences detected. However, a priori hypotheses were developed to increase power as a way to address this limitation. Next, the generalizability of the current study is limited given that results were derived from a sample of low-functioning, mostly inpatient African American males with severe psychiatric disorders. This restricts the external validity of our findings to a very specific population. Another weakness of the study is related to measures of substance use. Assessment of substance use was based on patient report, interviews, and record reviews, without corroboration from objective measures. Duration and quantity of substance use were not measured, as these variables may influence the severity of cognitive impairment. Furthermore, over half of the study participants have at least one neurological diagnosis. The neurocognitive sequalae of different neurological conditions varies and may have obscured cognitive differences between groups; however, the distribution of the number of patients with at least one neurological diagnosis is similar across groups. Lastly, the study only examined statistically significant differences in cognitive performance between groups. The practical significance of cognitive differences between groups was not assessed in this study. Variation between scores of clinical groups was within one standard deviation, even though differences between the groups have been shown to be statistically significant. It was assumed that statistical significance may also be reflective of clinical significance.

Implications: Research

Despite these limitations, this study underscores the importance of examining cognitive dysfunction of comorbid psychotic and substance use disorder patients. Current findings have important research implications and directions for future studies. Given that comorbid psychotic and substance use disorders can occur in individuals of different age, ethnicity, gender, socioeconomic status, and inpatient/outpatient status with different types of psychotic and substance use disorders, future studies should examine whether current results can be replicated to demographically different samples. Next, corroborating imaging studies are needed to confirm and explain the seemingly better executive functioning of comorbid patients. Structural MRI may help to elucidate anatomical differences, perhaps related to brain atrophy, between comorbid and non-comorbid patients. Additionally, functional MRI may help to explore functional differences or differences in compensatory mechanisms in the brains of comorbid and non-comorbid patients. Furthermore, this study emphasizes the need for a standard battery for comparing comorbid and non-comorbid psychotic disorder and substance use disorder patients across studies. Different cognitive measures make it difficult to evaluate and compare results from different studies. Subtle differences also may exist between measures that are designed to evaluate the same cognitive domain. For instance, the WCST and the Category Test (Halstead, 1947) are two commonly used measures to evaluate frontal lobe functioning. However, these two tests are not clinically interchangeable given that the WCST is also a measure of mental flexibility in addition to visual abstract reasoning, whereas, the Category Test is considered to be a more sensitive measure of visual abstraction and concept formation (Pendleton & Heaton, 1982). Variations in psychometric properties of similar measures can lead to

differences in interpretation of research findings. Therefore, harmonization standards in test batteries can aid in the integration of knowledge and accelerate research progress. Lastly, future studies should clarify statistical and clinical differences. Evaluation of functional and quality of life measures is imperative to establish differences in clinical outcome, as a way to examine the practicality of the variations noted in cognitive functioning.

Implications: Theoretical

Several theoretical frameworks have been developed to understand the comorbidity of psychotic and substance use disorder. The expectation that comorbid patients have more cognitive impairment than non-substance using psychotic disorder patients is based on the exacerbation model, which assumes that comorbid patients show a similar cognitive profile to that of non-substance using psychotic disorder patients but with more severe deficits. The exacerbation model does not address the possibility that substance use disorder may cause cognitive deficits that are different from those of psychosis. The sensitivity model postulates that dually diagnosed patients experience cognitive deficits from both psychosis and substance use. The interactive model took the sensitivity model a step further, suggesting that the interaction of the two disorders can create a unique set of cognitive problems. Lastly, the enhancement model addresses cognitive improvement, rather than deficits, that psychotic disorder patients may gain from substance use (i.e., self-medication hypothesis). Results of this study support the enhancement model since dually diagnosed patients appear to have similar or better cognitive functioning than PD patients and SUD patients. Despite the lack of relative cognitive deficits, comorbid patients have been noted

to have more psychosocial problems, lower treatment compliance, more suicide attempts, and more deterioration in functioning over time (Choulgian et al., 1995; Saddock & Saddock, 2003; Thoma et al., 2007; Westermeyer, 2006). This discrepancy between poor functional outcome and more intact cognitive abilities may be related to the timing of the neuropsychological evaluation. Neuropsychological evaluations on the cognitive functioning of comorbid patients have been performed when the patients' psychiatric and physical conditions are stable in order to obtain an accurate evaluation of these patients' true abilities. This stable condition is not likely to be representative of comorbid patients' functioning outside of medical research setting, since low treatment compliance has been noted in dually diagnosed patients. Dual diagnoses patients' lives may be more chaotic, and they experience more negative psychosocial, psychiatric, and physical outcomes than non-comorbid patients (cited in carey et al., 2003).

Implications: Clinical

If alleviating psychotic symptoms and cessation of substance use reveal better cognitive function in comorbid patients, then effective intervention is essential for rehabilitating these patients. Current study also has implications related to the treatment of dual diagnoses psychotic and substance use disorder patients. However, it must be noted that clinical implications should be interpreted with caution since statistically significant differences between the groups do not equate clinical significance. However, current results illustrate cognitive deficits that need to be addressed for rehabilitation. For instance, comorbid patients may benefit from being in their own treatment group so that they can receive interventions to manage their psychotic symptoms, as well as their substance use

disorder. This group is unique in the sense that it requires synthesis of treatment principles from multiple interventions. For example, strategies involving cognitive behavioral (CBT) therapy for ameliorating delusions and hallucinations and strategies involving stages of behavioral change or motivational interviewing for substance use disorder are effective interventions for comorbid patients (Barrowclough et al., 2001; Osher & Kofoed, 1989). Given this group's more superior reasoning/problem solving ability, they may gain from examining thoughts and feelings that are related to their psychotic symptoms and substance use. If separating comorbid and non-comorbid patients for treatment is not possible in group therapy settings, then patients should have similar cognitive abilities in order to maximize treatment benefits (Osher & Kofoed, 1989).

PD patients tend to have poorer cognitive abilities than CO and SUD patients by significance testing or trend. Instead of focusing on the interaction between thoughts, feelings, and behavior, their lower cognitive abilities may benefit from slower pace of intervention and symptom reduction and behavioral change. Highly structured and low intensity programs are essential for the rehabilitation of patients with cognitive deficits (Osher & Kofoed, 1989).

Results of the study also illustrate that SUD patients can function at a level similar to that of PD patients even when they have been abstinent from substance use, suggesting the need to tailor intervention to their level of cognition for comprehension. This is a surprising finding, given that SUD patients typically perform one standard deviation below normals, whereas, psychotic disorder patients typically perform more than one standard deviation below normals (Gold & Harvey, 1993; Nixon, 1995). Among SUD patients,

cognitive impairments are often misinterpreted as a lack of motivation to change by clinicians (Bates, 2005). For instance, deficits in verbal skills are related to limited expressive language functioning, memory impairments can lead to expression of impatience, and executive deficits can interfere with one's ability to understand other's perspective (Verdego-Garcia et al., 2004). These impairments can make patients appear less engaged in the treatment. Thus, clinicians need to be cognizant of potential cognitive deficits of substance use patients.

Table 1

Clinical Characteristics of Comorbid (CO), Psychotic Disorder (PD), and Substance Use Disorder (SUD) Patients

	CO (n = 81)	PD (n = 30)	SUD (n = 59)
Psychotic disorders (%)			
Schizophrenia	60.5	60.0	
Schizoaffective disorder	17.3	20.0	
Delusional disorder	2.5	6.7	
Substance induced	2.5	0.0	
Psychotic disorder NOS	17.3	13.3	
Substance use disorders (%)			
Alcohol	78.7		75.4
Cannabis	54.8		32.1
Cocaine	42.9		32.8
Opiod	11.4		14.0
Phencyclidine	14.3		16.1
Other	2.9		5.4

Table 2

Demographic Characteristics of the Entire Sample and Clinical Groups

	Sample	CO (n = 81)	PD (n = 30)	SUD (n = 59)	CO vs. PD vs. SUD	
					F	*df*
Age (n = 169)					2.53	2
M	47.60	46.89	52.27	46.20		
(SD)	(12.76)	(10.72)	(10.69)	(15.62)		
Years of education (n = 166)					1.99	2
M	10.48	10.08	11.33	10.59		
(SD)	(2.99)	(2.93)	(2.80)	(3.11)		
Years of illness (n = 85)					0.74	2
M	24.69	24.43	27.70	22.57		
(SD)	(13.89)	(12.27)	(17.04)	(13.87)		
WRAT reading (n = 146)					1.43	2
M	74.47	71.82	78.96	76.14		
(SD)	(19.95)	(19.91)	(19.69)	(19.7)		

BPRS						
(n = 71)					0.62	2
M	39.62	39.89	42.26	37.18		
(SD)	(14.17)	(13.64)	(13.48)	(15.63)		
Negative						
Symptomatology						
(N = 75)					2.13	2
M	8.59	9.03	9.88	7.06		
(SD)	(4.70)	(4.73)	(4.91)	(4.25)		
					x^2	*df*
Gender						
(%; n = 170)					7.30*	2
Male	82.4	90.1	70.0	78.0		
Female	17.6	9.9	30.0	22.0		
Ethnicity						
(%; n = 168)					5.93	2
African	86.3	91.3	73.3	86.2		
American						
Other	13.7	8.8	26.7	13.8		
Level of cognition						
(%; n = 168)					8.65	8

Normal	6.0	7.5	0.0	6.9		
Borderline/ Mentally retarded	26.8	30.0	30.0	20.7		
Dementia	28.6	21.3	36.7	34.5		
Cognitive disorder NOS	20.8	18.8	20.0	24.1		
Other	17.9	22.5	13.3	13.8		
Mood disorder (%; n = 146)	26.7	8.5	5.0	58.2	44.73**	2
Anxiety disorder (%; n = 144)	6.3	1.4	4.8	14.0	8.17*	2
Neurological diagnosis (%; n = 157)	67.5	61.6	65.4	75.9	3.04	2
Medication (%; n = 170)						
Atypical antipsychotics	53.5	60.5	76.7	32.2	18.82**	2
Conventional antipsychotics	28.8	32.1	50.0	13.6	13.68**	2

Other psychiatric medications	57.1	63.3	63.3	45.8	4.81	2
Non-psychiatric medications	46.5	38.3	50.0	55.9	4.46	2
No medications	14.1	11.1	3.3	23.7	7.98*	2

*$p < .05$. **$p < .01$

Table 3

Potential Influence of Gender, Mood Disorder, and Anxiety Disorder on Cognitive Measures

Measures	Gender		Mood disorder		Anxiety disorder	
	Male	Female	No	Yes	No	Yes
Processing Speed Index						
M	70.36	73.70	69.99	74.03	70.21	80.56
(SD)	(8.91)	(11.46)	(8.60)	(11.84)	(9.31)	(9.14)
Letter-Number Sequencing						
M	5.32	5.14	4.94	6.32	5.13	8.13
(SD)	(3.03)	(3.29)	(3.01)	(3.14)	(3.07)	(2.85)
Word List I , Trial 1						
M	5.62	4.50	5.22	6.74	5.32	7.00
(SD)	(3.57)	(2.97)	(3.49)	(3.96)	(3.50)	(2.83)
Word List I, Learning Slope						
M	7.83	8.59	8.05	8.00	8.03	7.50
(SD)	(2.98)	(2.90)	(2.88)	(2.85)	(2.91)	(1.64)

Word List II						
M	7.32	7.29	7.16	8.59	7.31	7.50
(SD)	(2.78)	(1.90)	(2.55)	(2.85)	(2.59)	(2.74)
Visual Immediate						
Index						
M	73.27	74.62	73.62	75.52	73.66	81.50
(SD)	(11.96)	(16.80)	(11.65)	(15.80)	(12.08)	(21.69)
Visual Delayed						
Index						
M	72.92	71.92	72.18	77.54	72.97	83.00
(SD)	(15.05)	(15.94)	(14.22)	(17.40)	(14.80)	(18.12)
Similarities						
M	6.36	5.15	5.97	7.09	6.03	9.67
(SD)	(3.13)	(2.77)	(2.97)	(3.55)	(3.05)	(2.74)
Matrix Reasoning						
M	6.89	6.70	6.59	7.97	6.85	9.22
(SD)	(2.88)	(3.55)	(2.68)	(3.10)	(2.82)	(1.92)
	t	df	t	df	t	df
Processing Speed	-1.67	143	-1.84	122	-3.21*	121
Index						

Letter-Number Sequencing	.28	140	-2.18*	119	-2.68*	118
Word List I, Trial 1	1.17	92	-1.60	77	-1.14	76
Word List I, Learning Slope	-.96	95	.06	80	.44	79
Word List II	.04	84	-1.96	70	-.17	69
Visual Immediate Index	-.36	97	-.61	84	-1.44	84
Visual Delayed Index	.22	95	-1.46	82	-1.58	82
Similarities	1.85	148	-1.78	128	-3.48*	127
Matrix Reasoning	.30	146	-2.39*	125	-2.48*	125

*p <.05.

Table 4

Potential Influence of Atypical Antipsychotic Medication, Conventional Antipsychotic Medication, and No Use of Medication on Cognitive Measures

Measures	Atypical antipsychotics		Conventional antipsychotics		No medication	
	Yes	No	Yes	No	Yes	No
Processing Speed Index						
M	72.64	69.34	71.8	68.98	70.26	74.78
(SD)	(10.37)	(8.27)	(9.48)	(9.34)	(9.19)	(10.33)
Letter-Number Sequencing						
M	5.39	5.18	5.62	4.43	5.31	5.13
(SD)	(3.15)	(3.01)	(3.05)	(3.00)	(3.14)	(2.79)
Word List I, Trial 1						
M	5.34	5.47	5.23	5.96	5.51	4.50
(SD)	(3.77)	(3.34)	(3.26)	(4.07)	(3.54)	(2.93)

Word List I,						
Learning Slope						
M	8.11	7.87	8.30	7.04	8.00	7.50
(SD)	(2.72)	(3.12)	(2.94)	(2.89)	(2.98)	(2.98)
Word List II						
M	7.45	7.25	7.49	6.76	7.38	6.57
(SD)	(2.86)	(2.52)	(2.68)	(2.41)	(2.59)	(3.05)
Visual Immediate						
Index						
M	75.85	71.18	73.64	72.77	73.32	74.00
(SD)	(13.15)	(11.75)	(12.84)	(12.03)	(13.06)	(10.64)
Visual Delayed						
Index						
M	74.47	71.20	73.31	71.09	72.35	74.82
(SD)	(15.78)	(14.39)	(15.08)	(15.33)	(14.77)	(16.86)
Similarities						
M	6.04	6.24	6.21	5.98	6.04	6.67
(SD)	(3.05)	(3.16)	(3.07)	(3.20)	(3.14)	(2.87)
Matrix Reasoning						
M	7.01	6.71	6.98	6.57	6.89	6.70
(SD)	(3.10)	(2.91)	(3.14)	(2.65)	(2.96)	(3.28)

	t	*df*	*t*	*df*	*t*	*df*
Processing Speed Index	2.12*	143	1.63	143	-2.12*	143
Letter-Number Sequencing	.41	140	2.11*	140	.27	140
Word List I, Trial 1	-.18	92	-.89	92	.78	92
Word List I, Learning Slope	.39	95	1.87	95	.45	95
Word List II	.34	84	1.11	84	.78	84
Visual Immediate Index	1.87	97	.28	97	-.21	97
Visual Delayed Index	1.07	95	.62	95	-.61	95
Similarities	-.39	148	.41	148	-.91	148
Matrix Reasoning	.62	146	.76	146	.28	146

*$p < .05$.

Table 5

Relationship Between Cognitive Measures

	1	2	3	4	5	6	7	8	9
1	1.00								
2	.58**	1.00							
3	.37**	.42**	1.00						
4	.32**	.28*	-.01	1.00					
5	.30**	.20	.52**	.54**	1.00				
6	.41**	.30**	.41**	.41**	.40**	1.00			
7	.42**	.35**	.34**	.49**	.53**	.72**	1.00		
8	.62**	.57**	.47**	.28**	.37**	.40**	.53**	1.00	.
9	.52**	.47**	.23*	.33**	.26*	.46**	.58**	.56**	1.00

Note. 1 = Processing Speed Index; 2 = Letter Number Sequencing; 3 = Word List I, Trial I; 4 = Word List I, Learning Slope; 5 = Word List II; 6 = Visual Immediate Index; 7 = Visual Delayed Index; 8 = Similarities; 9 = Matrix Reasoning.

*$p < .05$. **$p < .01$.

Table 6

Planned Comparison Analyses via Helmert Contrast with ANOVA and ANCOVA to Compare Clinical Groups on Cognitive Domains

Measures	CO	PD	SUD	CO vs. PD + SUD		PD vs. SUD	
				t	*df*	*t*	*df*
Processing speed domain							
Processing Speed Index	n = 63	n = 17	n = 43	1.19	121	-.49	58
M	70.75	67.35	72.72				
(SD)	(9.48)	(8.47)	(10.11)				
Working memory domain							
Letter-Number Sequencing	n = 61	n = 16	n = 37	1.00	112	.85	51
M	5.20	5.38	5.46				
(SD)	(3.25)	(2.99)	(3.08)				
Attention domain							
Word List I, Trial 1	n = 44	n = 19	n = 31	.48	92	-1.38	48
M	5.52	4.47	5.87				
(SD)	(3.66)	(2.48)	(3.75)				

Verbal learning and memory domain							
Word List I,	n = 39	n = 19	n = 28	1.18	84	-1.00	45
Learning Slope							
M	8.44	7.21	8.11				
(SD)	(3.08)	(3.46)	(2.60)				
Word List II	n = 39	n = 19	n = 28	.13	84	-1.77[a]	45
M	7.28	6.53	7.89				
(SD)	(2.60)	(2.20)	(2.86)				
Visual learning and memory domain							
Visual Immediate	n = 55	n = 13	n = 32	1.14	98	-1.04	43
& Delayed							
M	71.31	65.54	70.31				
(SD)	(14.23)	(11.64)	(14.46)				
Problem solving/ abstract reasoning domain							
Similarities	n = 67	n = 19	n = 43	2.44*	127	.27	60
M	6.72	5.63	5.83				
(SD)	(3.02)	(2.87)	(3.44)				
Matrix	n = 62	n = 17	n = 42	2.59*	119	-.19	57
Reasoning							
M	7.44	6.00	6.86				
(SD)	(3.04)	(2.53)	(2.59)				

[a] PD group's performance is significantly less than the SUD group at *p <.05, one tailed.

Table 7

Planned Comparison Analyses via Helmert Contrast with ANOVA to Compare Clinical Groups on Cognitive Domains, without Controlling for Covariates

Measures	CO	PD	SUD	CO vs. PD + SUD		PD vs. SUD	
				t	*df*	*t*	*df*
Processing speed domain							
Processing Speed Index	n = 71	n = 24	n = 50	.05	143	-1.83*	72
M	70.63	68.42	72.70				
(SD)	(9.33)	(8.29)	(10.07)				
Working memory domain							
Letter-Number Sequencing	n = 71	n = 26	n = 45	-.27	140	.01	69
M	5.21	5.35	5.36				
(SD)	(3.12)	(2.84)	(3.07)				
Problem solving/ abstract reasoning domain							
Similarities	n =73	n = 26	n = 47	1.68*	144	.12	71
M	6.58	5.73	5.64				
(SD)	(3.00)	(2.99)	(3.37)				

Matrix	n = 73	n = 26	n = 47	1.88*	144	-1.00	71
Reasoning							
M	7.18	5.92	6.62				
(SD)	(3.08)	(2.65)	(2.58)				

*p < .05, one-tailed.

Table 8

Comparison Analyses via Simple Contrast to Compare: 1) CO group and PD group, 2) CO group and SUD group, on Problem Solving/Abstract Reasoning Domain

Measures	*CO*	*PD*	*SUD*	*CO vs. PD*		*CO vs. SUD*	
				t	df	t	df
Similarities	n = 67	n = 19	n = 43	*-1.61*	*84*	*-2.44**	*108*
M	6.72	5.63	5.83				
(SD)	(3.02)	(2.87)	(3.44)				
Matrix Reasoning	n = 62	n = 17	n = 42	*-2.02**	*77*	*-2.91***	*102*
M	7.44	6.00	6.86				
(SD)	(3.04)	(2.53)	(2.59)				

*p < *.05.* **p < *.01.*

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