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Neurocognitive Characteristics of Individuals with Schizophrenia and Cocaine Dependence: Comparison of Currently Dependent and Remitted Groups

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Abstract

Several investigations of cognitive functioning in indivduals with schizophrenia and co-occurring cocaine use have yielded mixed results when compared to samples with schizophrenia only. However, no studies have specifically compared remitted and current cocaine dependence in schizophrenia. Such an analyis could help clarify the degree and type of cognitive impairment associated with cocaine dependence in schizophrenia. Two samples of individuals with schizophrenia – those with current cocaine dependence (SZ-D; n = 72) and those with cocaine dependence in remission (SZ-R; n = 48) were compared on a brief neuropsychological test battery. Parallel current dependent and remitted samples with affective disorder (AD-D; n = 65 and AD-R; n = 55) were also included in the analyses. Results yielded few neuropsychological differences between remitted and current dependent states across the SZ and AD groups. These findings suggest that cognitive impairment may be relatively static in these populations.

Keywords

Schizophrenia; Cocaine Dependence; Neurocognition; Co-occurring Disorders

Introduction

There is a high prevalence of substance use disorders (SUDs) among individuals with schizophrenia (Regier et al., 1990). SUDs have a profoundly negative impact on course of illness, outcomes and other quality of life indicators (Dixon, 1999; Mueser et al., 1990; Reiger et al., 1990). The negative consequences of SUDs likely compound the existing functional disability associated with schizophrenia. In particular, given that chronic substance use has been associated with neurocognitive deficits in primary substance abuse (Rogers and Robbins, 2001), SUDs may have a significant impact on the already well documented neurocognitive deficits associated with schizophrenia.

The empirical literature on neurocognitive functioning in people with co-occurring schizophrenia and SUD, compared to those with schizophrenia only, reveals a pattern of mixed results. There is some indication that the degree of cognitive impairment may vary depending on the primary substance of abuse (Potvin et al., 2008). Cocaine use is relatively common

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among people with co-occurring schizophrenia and SUDs (Mueser et al., 1990; Shaner et al., 1993; Swartz et al., 2006) and recent data from the CATIE study indicate that individuals who had schizophrenia and a cocaine SUD had poorer overall functioning when compared to those who use other substances, and those with no SUDs (Swartz et al., 2006). However, research has yielded inconsistent results with regard to the specific nature of neurocognitive differences. Some studies suggest a verbal memory impairment (Serper et al., 2000a; Serper et al., 2000b; Sevy et al., 1990) while others suggest better processing speed (Smelson et al., 2002). Several other studies have found no difference on attention and executive functioning measures (Cooper et al., 1999; Copersino et al., 2004; Serper et al., 2000a; Smelson et al., 2003). Only one study included a brief (18 days) follow up to evaluate change in cognitive functioning during a longer period of abstinence and found few differences between time points (Cooper et al., 1999). To date no studies have specifically investigated the neurocognitive characteristics of individuals with schizophrenia in remission for cocaine dependence. Understanding characteristics of a remitted group may help clarify the nature of cognitive impairment associated with cocaine dependence in this population.

As a first step, this study sought to test the hypothesis that individuals with schizophrenia or schizoaffective disorder and current cocaine dependence (SZ-D) would demonstrate greater neurocognitive impairment than those with cocaine dependence in remission (SZ-R). We compared two well characterized samples of individuals, those with SZ-D and SZ-R, on a brief neuropsychological test battery. As a comparison and to further clarify neurocognitive characteristics specific to schizophrenia with SUD, we included parallel samples of individuals with non-psychotic affective disorder and current and remitted cocaine dependence (AD-D and AD-R respectively).

Methods

Participants

Data were taken from a naturalistic longitudinal study examining substance use and motivation to change in people with serious and persistent mental illness (SPMI; see Nidecker, et al., 2008 for a detailed description of the methods). Participants were recruited from outpatient mental health clinics affiliated with a Veterans Administration Medical Center and a division of psychiatry at a public university. Specifically, participants with SPMI and a DSM-IV diagnosis of current cocaine dependence and those who fulfilled criteria for cocaine dependence in early full or sustained full remission (indicating remission for between 1-12+ months) were recruited. Overall, the four study groups were as follows: (1) 72 with schizophrenia/schizoaffective disorder + current cocaine dependence (SZ-D); (2) 48 with schizophrenia/schizoaffective disorder + cocaine dependence in remission (SZ-R), (3) 65 with non-psychotic affective disorder + current cocaine dependence (AD-D); and (4) 55 with non-psychotic affective disorder + cocaine dependence in remission (AD-R). The sample was 62.9% male, 79.2% African-American, with a mean age of 43.17 years (SD = 7.23) and a mean number of years of education of 11.91 (SD = 2.20).

Measures

Diagnostic assessment—The Structured Clinical Interview for DSM-IV (SCID-IV; First et al., 1994) was used at baseline to establish a diagnosis of non-psychotic affective disorder or schizophrenia/schizoaffective disorder as well as cocaine dependence (current or in remission). Remission was defined based on the DSM-IV criteria and remitted groups included both early full remission (no dependence or abuse criteria have been met for at least 1 month but less than 12 months) and sustained full remission criteria (no dependence or abuse criteria have been met for 12 months or more). SCID interviews were completed by doctoral or masters level clinicians. Diagnoses were achieved utilizing all available information for the patient

(patient-report, medical records, treatment providers). The inter-rater reliability (kappa) for the SCID-P diagnoses (psychiatric and substance abuse/dependence) was greater than 0.80. Urinalysis was employed to increase the validity of the self-report of substance use for cocaine, heroin, and/or cannabis using the Syva RapidTest (formerly called Accusign). Diagnostic assessment data also included Global Assessment of Functioning (GAF) and history of psychiatric illness.

Substance use and severity—To further describe substance use, the Addiction Severity Index (ASI; McLellan et al., 1992), a semi-structured clinical interview, was used to assess drug use frequency and severity. We used specific ASI items as indicators of chronicity and recent use for alcohol and cocaine. For chronicity we computed years of use by subtracting years abstinent from total years since initiating substance use. For recent use we used the ASI items assessing days of use in the past 30 days for cocaine and alcohol.

Neuropsychological Assessment—A brief neuropsychological battery was administered to assess domains of cognition which have been reliably reported to be impaired in schizophrenia including memory and executive functioning. Where available we report standard scores to compare our sample to test norms. The Wide Range Achievement Test (WRAT-3rd edition; Wilkinson, 1993) was employed to estimate general intellectual functioning. The total score from the immediate memory condition of the Logical Memory task (LM-IMM) from the Wechsler Memory Scale-III (Wechsler, 1997) was used to assess memory. Working memory was assessed with the scaled score of total trials correct from a letter number sequencing task (LNS; Gold et al., 1997). To assess executive function we administered the Wisconsin Card Sorting Test (WCST; Heaton et al., 1993), a widely used task that taps flexible problem solving. The present study used percent perseverative errors (PPE), a WCST score commonly reported in the schizophrenia literature. The battery also used total words generated from a verbal fluency task (categories; CVFT) that required participants to generate as many items as possible within a minute for a given category.

Procedures

All study procedures were approved by the University of Maryland Institutional Review Board and VA Research and Development office. Briefly, medical records of new intakes at our recruitment sites were reviewed once per week to determine preliminary eligibility, including diagnosis of SMI. All potential participants completed a standardized informed consent process with trained recruiters and were advised at the time that a Federal Certificate of Confidentiality would protect the information they provided. Patients completed the diagnostic interview first to confirm eligibility, and then completed the substance use/severity instruments and neuropsychological assessment battery within a week.

Results

Table 1 lists clinical, substance abuse, and neuropsychological variables by group. The sample was relatively chronic with regard to length of psychiatric illness, and the pattern of neuropsychological impairment is largely consistent with previous research (e.g., Goldberg et al., 1993). Based on test norms, all four groups demonstrate some degree of cognitive impairment, with impairments in the SZ groups being more pronounced.

To test for differences in neurocogntive functioning between groups a 4 (diagnostic group) × 5 (neuropsychological scores) Multivariate Analysis of Variance (MANOVA) was conducted. Post hoc Tukey's Honestly Significantly Different (HSD) tests were used to further specify differences between groups. MANOVA results indicated a significant difference between diagnostic groups in neurocognitive functioning [Wilks $\lambda = 0.75$; F (15,566.32) = 4.18; $p <$.

01]. Table 2 shows the Least Square Means for neuropsychological scores for diagnostic groups and results of Tukey's HSD post-hoc tests. With regard to general intellectual functioning, there were no significant differences between groups on the WRAT reading subtest. In terms of immediate and working memory, both SZ-D and SZ-R groups were significantly more impaired than the AD-D and AD-R groups. There were no significant differences between SZ-R and SZ-D groups nor between AD-R and AD-D groups on either measure of memory. Results for the CVFT showed generally the same pattern, with the exception of the SZ-R group, which was not significantly different from the AD-D group. In contrast, on the WCST-PPE, the SZ-D group was significantly more impaired than the other 3 groups, which were not significantly different from each other. This was the only variable on which there was a significant difference between dependent and remitted groups (either SZ or AD).

Based on recent findings that age and alcohol use impacted cognitive functioning in co-occurring schizophrenia and SUD samples (Potvin et al., 2008) we included these as covariates in a follow-up Multivariate Analysis of Covariance (MANCOVA). Using ASI data, we also controlled for chronicity and recency of cocaine use. Results indicated that inclusion of these variables did not impact the pattern of results (Wilks $\lambda = 0.74$; F (15,544.23) = 4.22; $p < .01$) and the pattern of Tukey's HSD post-hoc comparisons remained unchanged.

Discussion

Contrary to our initial hypothesis, there were minimal cognitive differences between individuals with schizophrenia and current cocaine dependence and those who were in remission. These groups performed similarly on measures of intellectual functioning and immediate and working memory. The schizophrenia-dependent group performed more poorly than the remitted group only on a single measure of executive functioning. The results remained the same even after controlling for age, chronicity, and recency of alcohol and cocaine use. Notably, the pattern of results was also largely consistent with a parallel analysis in an affective disorder sample.

The lack of differences in neurocognitive functioning between schizophrenia-dependent and schizophrenia-remitted samples has several interpretations. First, it is possible that the pre-existing cognitive impairment in schizophrenia is so pronounced that it is minimally impacted by cocaine use. Our data are consistent with a recent metanalysis (Potvin et al., 2008) and several individual studies (e.g., Cooper et al., 1999; Smelson et al., 2003) that have found few cognitive differences between schizophrenia samples with and without a co-occurring SUD. Given the pattern of results in the affective disorder groups, cognitive functioning in patients with affective disorder may also be minimally impacted by cocaine use. Specifically, affective disorders have been shown to have a similar pattern of cognitive impairment although less severe than schizophrenia (Goldberg et al., 1993; Schrelten et al., 2007). To a large extent, our data are consistent with these findings and suggest that psychiatric diagnosis is a greater determinant of level of cognitive functioning than current dependence or remission status.

A second interpretation is that the combination of schizophrenia and cocaine dependence results in changes in cognitive functioning that do not substantially improve in remission. That is, individuals with schizophrenia may accrue significant deficits from cocaine dependence that are not reversible once drug use stops. The similar findings seen in the affective disorders group suggests that this is not limited to schizophrenia but is seen in other forms of dual disorders. Several findings from the literature support this interpretation. First, there is little evidence of cognitive improvement after brief periods of abstinence from cocaine in schizophrenia (Cooper et al., 1999). Second, in primary SUD samples (those without co-occurring psychiatric diagnoses) there are only slight and inconsistent improvements in cognitive functioning following longer term cocaine abstinence (Di Sclafani, et al., 2002;

Horner, 1999). Third, other research in SPMI outpatients has found no cognitive differences between current and former substance abusers (Carey et al., 2003). Finally, our sample had an extensive history of cocaine use (on average, 11 years or more). Thus, it is plausible that over such an extended period of chronic use there is little opportunity for cognitive improvement once remission is attained. Indeed previous research in a dual disorder sample found that duration of lifetime cocaine use was associated with cognitive impairment whereas recent cocaine use was not (Carpenter & Hittner, 1997). It is unclear as to whether cognitive recovery would be present following remission in samples with a shorter duration of lifetime cocaine use.

Research in the area of co-occurring schizophrenia and SUDs has frequently been hampered by methodological limitations including small sample sizes, reliance on chart diagnoses, and a lack of biological verification of substance use status. The present study overcame several of these limitations: it included a large sample with SCID-verified psychiatric diagnoses and SUDs that were corroborated by drug urinalysis. It also included an extensive assessment of substance use history that allowed for the evaluation of factors previously associated with cognitive impairment in SUD. The inclusion of the affective disorder sample demonstrated that minimal cognitive differences between dependent and remitted drug status are consistent across these two chronic psychiatric disorders.

While these strengths are noteworthy, there are also limitations to the study. The assessment battery used in the present study was brief. It is possible that a broader assessment battery may have detected additional areas of impairment in the cocaine dependent groups. The study design did not allow for evaluation of within subjects neurocognitive change as a result of remission from cocaine dependence, or a comparison of cognitive functioning in these groups with individuals with schizophrenia and no history of cocaine dependence. In addition, for the remitted groups, data on length of remission or remission status (early vs. sustained) were not available. Such data could help determine whether cognitive impairment improves over longer periods of remission. These issues should be addressed in future research to further clarify the relationship between cognitive impairment and cocaine dependence.

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Figure 2.

Table 1

Clinical, substance abuse, and neuropsychological variables by group

Variable	AD-D Mean (SD)	AD-R Mean (SD)	SZ-D Mean (SD)	SZ-R Mean (SD)
Length of psychiatric illness in years	14.05 (10.0)	14.85 (11.5)	19.16 (9.5)	22.37 (11.3)
# of lifetime psychiatric hospitalizations	4.25 (4.6)	3.24 (4.6)	8.06 (7.4)	7.96 (11.9)
Current GAF	44.11 (7.8)	47.67 (6.4)	38.01 (6.0)	40.42 (7.6)
Lifetime cocaine use in years	11.73 (6.8)	12.72 (8.8)	11.58 (7.9)	11.79 (7.7)
Lifetime alcohol use in years	19.80 (9.6)	20.98 (9.7)	18.82 (10.6)	20.10 (10.5)
Cocaine days of use in past 30	5.42 (7.1)	0	6.64 (8.1)	0
Alcohol days of use in past 30	5.54 (8.9)	0.26 (1.1)	5.20 (7.8)	1.33 (4.1)
WRAT (standard score) [1]	87.71 (17.4)	83.70 (19.1)	78.76 (19.2)	84.87 (18.3)
LNS (scaled score) [2]	8.86 (2.6)	8.75 (2.0)	6.67 (2.7)	7.35 (2.9)
LM-IMM (scaled score) [2]	8.50 (2.8)	8.32 (3.3)	5.82 (3.2)	6.32 (2.8)

[1] Standard score mean = 100; standard deviation = 15.

[2] Scaled score mean = 10; standard deviation = 3.

AD-D = Affective Disorder-Dependent; AD-R = Affective Disorder-Remitted; SZ-D = Schizophrenia-Dependent; SZ-R = Schizophrenia-Remitted; GAF = Global Assessment of Functioning; LNS = Letter Number Sequencing; LM-IMM = Logical Memory − immediate memory; WRAT = Wide Range Achievement Test.

Table 2

Least Square Means and Standard Errors from Multivariate Analysis of Variance for Diagnostic Group Differences in Neuropsychological Measures

Measure	AD-D	AD-R	SZ-D	SZ-R
LNS	$8.79(0.34)_{a}$	$8.83(0.38)_{a}$	$6.62(0.33)_{b}$	$7.47(0.39)_{b}$
LM-IMM	$33.98(1.41)_{a}$	$33.85(1.57)_{a}$	$24.08(1.35)_{b}$	$26.78(1.60)_{b}$
CVFT	$44.10(1.25)_{ab}$	$47.89(1.39)_{a}$	$38.95(1.20)_{c}$	$40.96(1.42)_{bc}$
WCSTPPE[1]	$22.71(2.01)_{b}$	$22.45(2.23)_{b}$	$34.05(1.93)_{a}$	$24.64(2.28)_{b}$
WRAT	$87.74(2.42)_{a}$	$85.04(2.69)_{a}$	$79.75(2.32)_{a}$	$85.98(2.74)_{a}$

Note. Means with the same subscript are not statistically significantly different.

[1]Higher scores indicate greater impairment.

LNS = Letter Number Sequencing standard score; LM-IMM = Logical Memory − immediate memory; CVFT = categories verbal fluency test; WCSTPPE = Wisconsin Card Sorting Task percent perseverative errors; WRAT = Wide Range Achievement Test standard score. AD-D = Affective Disorder-Dependent; AD-R = Affective Disorder-Remitted; SZ-D = Schizophrenia-Dependent; SZ-R = Schizophrenia-Remitted.