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Neurocognitive impairment in patients with co-occurring bipolar disorder and alcohol dependence upon discharge from inpatient care

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Abstract

The current study explored the neurocognitive functioning of patients with co-occurring bipolar disorder and alcohol dependence upon discharge from inpatient care. The study compared scores of neuropsychological tests among three groups of bipolar I inpatients without a history of neurological injury or illness: 1) patients meeting DSM-IV diagnostic criteria for alcohol dependence in the past 6 months (n=13), 2) patients diagnosed with alcohol dependence in full remission (n=9), and 3) patients without a history of a substance use disorder (SUD; n=41). Analyses indicated that patients with co-occurring alcohol dependence exhibited more severe impairment on tests of executive functioning (i.e. Stroop Color-Word Interference Test, Wisconsin Card Sorting Test) than patients without SUD. In addition, the group meeting diagnostic criteria for alcohol dependence in the past 6 months exhibited greater decrements in verbal (California Verbal Learning Test – II) and visual (Rey Complex Figure Test) memory. Analysis further indicated that patients in full SUD remission scored lower on measures of fluid intelligence (Wechsler Abbreviates Scale of Intelligence – Performance IQ). Consistent with previous reports, in the current sample, co-occurring alcohol dependence predicted higher rates of disability status. It is possible that cognitive deficits of greater severity in dually diagnosed patients contribute to this unfavorable outcome. Recognizing the extent of cognitive impairment in dually diagnosed patients may facilitate the effort to ameliorate their condition.

Keywords

Cognitive deficits; Neuropsychology; Dual diagnosis; Substance Use Disorders

1. Introduction

Among all major psychiatric disorders, bipolar disorder is associated with the highest prevalence of substance abuse and dependence (Tohen et al., 1998). Patients diagnosed with bipolar and co-occurring substance use disorders (SUD) suffer from a more severe course of illness (Cassidy et al., 2001), poorer long-term recovery (Strakowski et al., 2000), and greater psychosocial disability (Salloum et al., 2000). The prevalence and refractory nature of their condition warrants a continued effort to improve the effectiveness of treatment and illness management.

Innovative interventions may be informed by neuropsychological research. Research on the neuropsychology of bipolar disorder generally indicates the presence of significant cognitive

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impairment persisting into periods of euthymia (Martinez-Aran et al., 2004a), particularly in patients suffering from multiple episodes (Bearden et al., 2001). Similarly, SUDs in general, and alcohol dependence (AD) in particular, are associated with debilitating neuropsychological deficits that do not remit even after enduring periods of abstinence (Paterson, 1998).

Although the neuropsychology of both bipolar disorder and SUDs has been studied extensively, this dual diagnosis condition has largely been ignored. One of the few neuropsychological studies with dually diagnosed patients, who suffer from a range of psychotic disorders, reported unexpected findings, where SUD was associated with better performance on non-verbal cognitive tests and instrumental social role (Carey et al., 2003). However, in a well-controlled study that specifically focused on bipolar disorder and co-occurring AD, Van Gorp et al. (1998) reported additional decrements in executive functioning in dually diagnosed outpatients when compared with controls. It is therefore possible that the neuropsychological deficits associated with both bipolar disorder and AD converge to form impairment of greater severity in patients who suffer from this dual diagnosis. More generally, superimposed on deficits inherent in bipolar disorder, AD may lead to a level of cognitive impairment that interferes with patients' recovery and overall ability to function.

Cognitive deficits in dually diagnosed patients may be most acute during an inpatient admission. The temporal proximity to the peak of both mood disturbance and substance use, coupled with the use of sedating medications over the course of hospitalization, may lead to highly compromised cognitive states at the time of discharge. Underestimating the extent of cognitive impairment in dually diagnosed inpatients can lead to discharge plans that do not fully facilitate recovery.

The current study assessed the cognitive functioning of dually diagnosed patients at the time of discharge from inpatient care. The study compared the scores of neuropsychological measures in bipolar I inpatients with and without alcohol dependence, separating chronic from acute alcohol-related deficits by distinguishing between patients in early and full remission. The hypothesis was that dually diagnosed patients would exhibit more severe cognitive deficits than Bipolar I patients without SUD. Among patients with the dual diagnosis, test performance was expected to co-vary with remission state.

2. Method

2.1 Subjects

A total of 63 inpatients at McLean Hospital who met DSM-IV diagnostic criteria for bipolar I disorder completed the study. Participants were categorized to 3 groups: 1) patients meeting DSM-IV diagnostic criteria for alcohol dependence in the past 6 months (n=13), 2) patients diagnosed with alcohol dependence in full remission, as indicated by at least 12 months of abstinence (n=9), and 3) patients without a history of any SUD (n=41). Patients in the first group did not require medical detoxification during admission, since they were hospitalized primarily due to an acute mood disturbance.

2.2 Inclusion/Exclusion Criteria

A review of medical records and a structured interview excluded patients who received ECT in the past 12 months or presented with a history of neurological illness or injury. To control for the impact of severe mood symptoms, inclusion criteria required a Beck Depression Inventory score < 15 (Dozois et al., 1998), a Beck Hopelessness scale score < 10 (Beck et al., 1974), and a Young Mania Rating Scale score < 15 (Young et al., 1978).

2.3 Diagnosis and Procedure

All participants were recruited for a diagnostic session after signing informed consent for the study. The diagnostic process integrated a review of medical records and verbal communications with the treatment team, which included information from outpatient treaters and family members. In this process, disability status was also determined. Disability status was defined as receiving formal financial support for a recognized psychiatric illness without employment. An independent confirmation of diagnosis and disability status for the purposes of this study was attained by a trained clinician through a clinical interview. This procedure involved the administration of the Structured Clinical Interview for DSM-IV (First et al., 1994) – Part I. After diagnosis was substantiated, the clinician proceeded with administrating the alcohol measures. In a later session, a trained examiner administered the neuropsychological battery and mood measures, typically less than 24 but not more than 48 hours prior to discharge. In the context of the brief window of time available for recruiting participants and conducting the assessments, 38 patients who met inclusion criteria for the study declined participation. The most frequent reason stated for declining involved schedule conflicts with competing agendas the patients opted or were required to pursue prior to discharge.

2.4 Instruments

Substance Use Measures—Participants completed the drug and alcohol sections of the Addiction Severity Index – 5th edition (ASI–5), which assess the duration and severity of substance use problems (McLellan et al., 1992) in the format of a semi- structured interview. To measure actual alcohol consumption (e.g., number of standard alcoholic drinks consumed) and drug use 30 days prior to admission, the assessment adhered to the Timeline Followback method, using a calendar and key date anchors (Sobell and Sobell, 1995). Participants also completed the Alcohol Use Disorder Identification Test (Pal et al., 2004).

The Neuropsychological Battery—IQ estimates were based on the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999). **Attention and Working Memory** were assessed with the Digit Span subtest from the Wechsler Adult Scale of Intelligence – Third Edition (Wechsler, 1997), Trails Making Test parts A and B and the Letter and Symbol Cancellation Task. The score on the latter task reflected speed (i.e. time in seconds) and accuracy (i.e. number of targets correctly identified), as total quality of performance (Lockwood et al., 2001). **Perceptual Organization and Visual Memory** were measured with the Rey Complex Figure test (RCF; Meyers and Meyers, 1995). Measures of **Verbal Memory** included the Logical Memory subtest from Wechsler's Memory Scale-Revised (Wechsler, 1987), and the California Verbal Learning Test II – Short Form (Delis et al., 1999). The battery also included the following measures of **Executive Functioning**: Stroop Color-Word Interference Test (Golden and Freshwater, 2002), Controlled Oral Word Association Test (Tombaugh et al., 1999) - FAS letters format, Animal Naming Task (Tombaugh et al., 1999), Wisconsin Card Sorting Test – 64 Card Version (Heaton et al., 2003).

2.5 Statistical Analysis

Analysis of group differences in demographic and clinical data applied Pearson's chi-square test and ANOVA for categorical and continuous variables, respectfully. In the analysis of neuropsychological data, the cognitive tests were categorized as measures of attention, visual memory, verbal memory and executive functioning. A Multivariate Analysis of Variance, using age, mood (i.e. BDI-II and YMRS) and IQ scores as covariates (MANCOVA), was applied to each category. Due to the heterscedastic nature of the data,

post-hoc pairwise comparisons adhered to the Dunnett T3 procedure, which provides adequate control over type I error under these conditions.

3. Results

3.1 Clinical and Demographic Variables

The ASI and diagnostic measures indicated the presence of polysubstance abuse in the sample. In the group diagnosed with alcohol dependence in the past 6 months, 2 participants met diagnostic criteria for marijuana abuse, 1 was diagnosed with past cocaine abuse and 3 were diagnosed with past abuse of both substances. In the fully remitted group, 3 participants met diagnostic criteria for both past marijuana and cocaine abuse (i.e. over 12 months of abstinence), and 1 participant met criteria for past opioid dependence (i.e., over 5 years of abstinence). Notable reported medical conditions in both groups diagnosed with alcohol dependence included cirrhosis of the liver (n=3), thyroid dysfunction (n=2), high blood pressure (n=6), high cholesterol (n=6), joint disease (n=2) and diabetes (n=2). In the group without SUD, there were 3 patients with high blood pressure, 4 with high cholesterol and 2 with diabetes. All of these conditions received medical treatment prior to admission and did not manifest with acute symptoms over the course of hospitalization.

Analysis of the clinical variables indicated group difference in disability status, where both groups with the dual diagnosis (present and past) reported higher disability rates (84.6%, 88.9%, respectively) than the group without SUD (51.2%; chi square=7.67, df=2, $P<0.02$). No group differences emerged in age of onset for bipolar disorder, rates of psychosis upon admission, duration of hospital stay (ranging from 6 to 18 days in the entire sample) and number of psychiatric medications taken on the day of testing. Preliminary analysis also failed to detect group differences in diagnostic subtype (in the entire sample, manic=41, depressed=11, mixed=11) upon admission. Of particular interest, analysis did not detect a mean difference of previous number of hospitalizations ($F=0.95$, $P<0.39$), possibly due to high variance. However, an examination of the medians did reflect at least twice as many admissions for the dual diagnosis groups (6 and 8 admissions in the groups with current and past AD, respectively, versus 3 admissions in the group without SUD). Comparisons of mood measures taken before testing provided no evidence for group differences in depressive or manic symptoms.

With respect to demographic variables, the sample consisted of 35 men and 28 women. Fifty-one participants reported Caucasian descent and 12 identified an affiliation with an ethnic minority group. Thirty-two were single, 16 married and 15 divorced. Analysis revealed no group differences in gender, marital status, or years of education. Group comparisons of age (ANOVA; $F=3.10$, $P<0.05$), however, indicated that the dual diagnosis group in full remission was older than the group presenting with current alcohol dependence (Dunnett T3 post-hoc procedure; Mean Difference (ME) = 11.8 years, Standard Error (SE) = 5.33, $P<0.05$). For means and standard deviations of demographic and clinical measures for each of the groups, refer to Table 1 in the supplementary materials available on the web through www.elsevier.com.

3.2 Alcohol Measures

Consistent with the design of the study, a multivariate analysis of variance (MANOVA) revealed significant group differences across measures of alcohol consumption (Wilk's Lambada; $F_{(6, 55)}=123.66$, $P<0.0001$). All subsequent between-group comparisons indicated highly significant group differences for each measure. As expected, Dunnett T3 post-hoc pairwise comparisons indicated that drinking behavior in the month prior to admission was most heightened in the group with current alcohol dependence and least present in the full

remission group. These results, summarized in Table 2 in the supplementary materials, indicated a problem drinking pattern in the group with current alcohol dependence, mild to moderate social drinking in the group without SUD, and mostly abstinence in the group in full remission.

3.3 Cognitive Measures

Attention and Working Memory—A MANCOVA procedure revealed no group differences on measures of attention and working memory (Wilk's Lambada; $F_{(14,100)}$=0.54, P<0.9). Likewise, no differences emerged on any of these measures in the consequent ANCOVA analysis.

Memory—Analysis detected significant differences in visual memory (Wilks' Lambada; F(8,106)=1.96, F<0.05), as measured by the Rey Complex Figure test. As Table 2 reveals, the Dunnett T3 post-hoc comparisons indicated significantly more compromised performance in the group with current alcohol dependence relative to the group without SUD in the immediate recall and recognition of the figure's parts. The analysis of delayed recall was marginally significant (P<0.058). Table 1 reveals mean and median test scores among patients with current alcohol dependence to be between 2 and 3 standard deviations below the mean of the normed sample, suggesting the presence of moderate to severe impairment in visual memory in this group.

The MANCOVA procedure for measures of verbal memory was not significant (Wilk's Lambada; $F_{(14,100)}$= 1.12, P<0.34); however, Dunnett T3 comparisons indicated a significantly lower performance on the CVLT-II measures of immediate and delayed free recall in the group with current alcohol dependence relative to the group without SUD (P<01.025 and P<0.031, respectively). The mean and median scores for these measures ranged between 1.8 and 2.5 standard deviations below the normed sample (see Table 1). The scaled scores of these measures conform to the standard normal distribution with a mean of 0, and a standard deviation of 1.

Executive Functioning—Analysis also indicated significant group differences in measures of executive functioning. The MANCOVA procedure was highly significant (Wilk's Lambada; $F_{(14,100)}$= 2.77, P<0.002). As Table 2 indicates, in the group comparisons of specific measures, highly significant results emerged for the Stroop and Wisconsin Card Sorting Test. The Dunnett T3 comparisons revealed a significantly more compromised performance on these measures for both the group with current alcohol dependence and the group in full remission, relative the group without SUD. Table 1 reveals that mean and median scores on these measures fell in the borderline to moderately impaired range.

IQ—An ANCOVA procedure for IQ measures revealed significant group differences in Performance IQ (F=3.8, P<0.03), which measures fluid intelligence (Horn & Cattell, 1966) - the ability to problem solve in new situations or draw inferences about relationships of various concepts, independent of acquired knowledge. Dunnett T3 comparisons indicated a significantly lower performance in the group in full remission relative to the group with current alcohol dependence (mean difference =10.88, SE=4.70, P<0.01), as well as relative to the group without SUD (mean difference=11.49, SE=3.99, P<0.006).

4. Discussion

Consistent with previous findings, the results of this study indicated neurocognitive impairment of greater severity in the dually diagnosed groups on measures of executive functioning and memory tests that are particularly sensitive to the adverse impact of

executive dysfunction (i.e. RCF and CVLT-II). While not surprising, it is noteworthy that the group in full remission from alcohol dependence also exhibited more compromised performance on measures of fluid intelligence. As the group in full remission was older than the group diagnosed with AD in the past 6 months, this result raises the hypothesis of an accelerated age-related decline of fluid intelligence in dually diagnosed patients. A solid support for this hypothesis, however, will require a longitudinal design.

The type of deficits found in this study is consistent with previous reports, which emphasized deficits in the domains of memory and executive functioning in bipolar disorder patients without SUD (Altshuler et al., 2004; Martinez-Aran et al., 2004b). It is therefore possible that co-occurring alcohol dependence adds a degree of severity to a pattern of cognitive impairment that is found in bipolar disorder. The results of the current study suggest that the additional decrements may be clinically significant. Most of the means and medians of the test scores showing greater impairment in dually diagnosed patients fell within the clinically impaired range – approaching or exceeding 2 standard deviations below the mean of normative samples. These findings suggest that the treatment and overall level of functioning of patients with bipolar disorder and co-occurring alcohol dependence may be impeded by cognitive impairment.

Several explanations may account for the additional cognitive deficits found in dually diagnosed patients. First, research evidence suggests that long-term alcohol abuse may have direct neurotoxic effects on the brain and cognition (Adams et al., 1993; Parsons, 1993). Alternatively, cognitive impairment in dually diagnosed patients may be related to the severity of bipolar disorder. Mood episodes of greater severity and duration have been independently associated with both poor cognitive functioning (Kessing, 1998; Zubieta et al., 2001) and the co-occurrence of SUD (Winokur et al., 1995). Dually diagnosed patients may therefore suffer from a more severe form of bipolar disorder. Conversely, a growing volume of evidence points to an inherent neurocognitive dysfunction in bipolar disorder that is independent of mood states (Ferrier et al., 1999; Thompson et al., 2005). It is therefore worthwhile to consider the possibility that cognitive impairment existing prior to the onset of bipolar disorder contributes to mood instability and substance dependence.

Consistent with the results of the current study, previous investigations reported that dually diagnosed patients suffer greater psychosocial disability (Altshuler et al., 2004; Keck et al., 1998). This unfavorable outcome may emanate, at least in part, from poor cognitive functioning. Even in euthymic bipolar disorder patients without SUD, neurological abnormalities indicative of frontal lobe and executive dysfunction predict social disability (Goswami et al., 2006). More specifically, deficits in planning and problem-solving can seriously compromise the ability of patients to cope with everyday life and negotiate demands of work and family (Ferrier et al., 1999; Laes and Sponheim, 2006). Psychosocial functioning, in fact, was found to correlate more with neuropsychological measures than with other clinical variables of bipolar disorder (Martinez-Aran et al., 2004b). This suggests that cognitive functioning may play an important mediating role between illness process and functional outcome (Martinez-Aran et al., 2002). It is therefore plausible that bipolar disorder patients with co-occurring AD suffer greater social disability particularly due to more severe cognitive impairment. Thus far, this notion received little, if any, attention in the treatment of dually diagnosed patients.

Several limitations of the current study must be acknowledged. The sample size of the groups with the dual diagnosis was relatively small, so results require replication with a larger sample. Since most participants were admitted due to a manic episode, residual manic symptoms present at the time of discharge may have increased the severity of executive dysfunction in the entire sample. In addition, it is likely that medications affected

performance on testing; however, medication type and doses varies widely in the context of a naturalistic clinical setting, so their impact could not be assessed. Similarly, some differences in health conditions among the groups may have increased between group variance in test performance. The current study is also limited in determining important cause and effect relationships among cognitive impairment, illness severity and level of psychosocial disability.

Despite these limitations, the current study supports the notion that bipolar disorder patients with co-occurring AD may suffer more severe cognitive deficits than patients without SUD. These results may help to understand the nature of the struggle dually diagnosed patients face during recovery and discover additional avenues to improve treatment and illness management after discharge from inpatient care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Means, Medians, Range and Standard Deviations of Scaled Scores of Cognitive Measures

	BP with current AD				BP with AD in full remission				BP without SUD			
Measures	**Mean**	**Median**	**SD**	**Range**	**Mean**	**Median**	**SD**	**Range**	**Mean**	**Median**	**SD**	**Range**
Digit span	8.6	8.0	3.1	4–15	7.66	8.0	2.0	5–11	8.6	8.0	2.7	4.0–15
Trails A	36.3	38.0	11.2	20–52	33.3*	20.0***	16.6	20–59	39.0	42.0	12.7	20–60
Trails B	34.4*	20.0***	15.4	20–57	34.5*	34.0*	10.8	20–51	35.6*	34.0*	14.4	20–67
CT1	40.7	40.0	15.1	20–64	30.6*	33.0*	11.2	20–47	40.5	42.0	14.0	20–67
CT2	42.9	42.0	13.2	20–61	39.1	37.0	17.6	20–66	42.1	46.0	12.9	20–69
CT3	41.3	43.0	12.6	20–63	37.0	30.0**	16.7	20–62	42.6	45.0	11.9	20–74
CT4	38.9	40.0	10.2	20–57	35.2*	40.0	9.8	20–45	40.7	43.0	13.5	20–70
LM-I	43.4	44.0	10.5	24–61	46.4	47.0	13.9	22–65	45.5	46.0	9.95	25–68
LM-D	38.5	40.0	7.8	25–50	45.5	46.0	10.6	28–59	45.2	45.0	10.5	25–74
CVLT-A	38.5	33.0*	14.8	19–60	46.3	48.0	10.0	25–60	42.2	43.0	11.5	12–62
CVLT-I	−1.8*	−2.0**	1.0	−3.0–0	−1.0	−1.0	1.3	−3–0	−0.7	−0.5	1.5	−3.–2
CVLT-D	−2.0**	−2.5**	0.8	−3.0–3	−1.0	−1.0	1.2	−3–1	−1.2	−1.0	1.2	−4.–1
CVLT-R	−1.5*	−1.5*	1.4	−4–0	−0.6	0.0	1.3	−2.5–1	−1.1	−0.5	5.5	−4–0.5
Rey-C	26.6**	27.5**	8.6	3–36	32.1*	33.0*	3.3	26–36	30.4*	32.0*	4.6	21–36
Rey-I	25.0**	20.0***	8.5	20–49	36.3	41.0	15.4	20–57	33.8*	31.0*	12.2	20–62
Rey-D	22.7**	20.0***	7.7	20–48	29.0**	20.0***	13.2	20–54	29.5**	24.0**	11.1	20–53
Rey-R	31.0*	30.0**	10.6	20–46	37.1	40.0	12.2	18–59	42.6	46.0	12.1	20–63
FAS	52.3	55.0	16.1	20–70	47.7	50.0	7.5	35–55	56.4	55.0	11.1	20–70
Animals	39.9	38.0	10.5	26–60	45.9	46.0	9.6	29–70	42.6	44.0	6.1	33–55
Stroop-CW	33.2*	30.0*	8.8	20–51	34.3*	37.0	6.59	27–47	44.7	45.0	10.1	25–65
Stroop-I	38.6	38.0	7.8	25–53	39.7	40.0	5.05	32–49	51.9	51.0	8.5	38–79
WCST-C	0.92	1.0	1.03	0–3	0.77	1.0	0.66	0–2	2.39	2.0	1.48	0–5
WCST-NPE	30.8*	33.0*	8.79	20–46	25.8**	27.0**	5.71	20–37	39.0	40.0	11.2	20–61
WCST-PRE	35.3*	35.0*	9.58	20–50	36.3	35.0*	10.6	20–53	41.1	41.0	8.64	20–59
VIQ	102	100	10.52	89–126	97.3	106	18.6	70–116	105	106	13.0	74–130

	BP with current AD				BP with AD in full remission				BP without SUD			
Measures	**Mean**	**Median**	**SD**	**Range**	**Mean**	**Median**	**SD**	**Range**	**Mean**	**Median**	**SD**	**Range**
PIQ	100	102	6.74	88–110	89.1	93.0	7.7	75–100	100	102	12.2	71–126
FSIQ	101	101	8.3	89–118	92.1	97.0	13.9	72–107	104	105	13.3	71–128

Note: AD=Alcohol Dependence, CT= Cancellation Test (1=unstructured symbol, 2=structured symbol, 3=unstructured letter, 4=structured letter), LM= Logical Memory (I=immediate recall, D=delayed recall), CVLT-II=California Verbal Learning Test- second edition (A=Acquisition phase, trials 1 through 4, I=immediate free recall, D=delayed recall, R=recognition, FAS=COWAT, Stroop (CW=Color-Word, I=interference).

* <1.5 standard deviations (SD) of normative sample mean,

** <2.0 SD,

*** <3.0 SD.

Note: AD=Alcohol Dependence, WCST=Wisconsin Card Sortin Test (C=number of categories completed, NPE=none perseverative errors, PRE=perseverative errors). VIQ=Verbal IQ, PIQ=Performance IQ, FSIQ=Full scale IQ.

Table 2

Group Comparison of Scaled Scores of Memory and Executive Functioning Measures

	ANCOVA		Post Hoc Dunnett T3 Pairwise Comparisons								
			BP with current AD vs. BP with AD in full remission			BP with current AD vs. BP without SUD			BP with AD in full remission vs. BP without SUD		
Measures	**R^2**	**F**	**MD**	**SE**	**CI-95%**	**MD**	**SE**	**CI-95%**	**MD**	**SE**	**CI-95%**
Verbal Memory											
LM-I	0.04	1.4	−2.9	4.6	−17.7−11.7	−2.0	3.4	−10.7−6.5	0.9	3.9	−12.9—14.7
LM-D	0.10	2.1	−7.0	4.4	−18.2−4.2	−6.7	3.2	−13.6−0.1	0.2	3.7	−0.4—10.9
LM-R	0.02	1.3	−1.8	1.4	−5.9−2.3	−2.2	1.0	−5.5−0.1	−0.4	1.2	−3.7−2.9
CVLT-A	0.00	0.78	−7.8	5.2	−21.5−5.9	−3.7	3.8	−15.5−8.1	4.1	4.5	−6.2−14.4
CVLT-I	0.00	1.06	−0.8	0.6	−2.2−0.7	−1.0	0.4	−2.0-(−0.1)*	−0.3	0.5	−1.6−1.1
CVLT-D	0.09	2.1	−0.9	0.5	−2.2−0.4	−0.8	0.3	−1.6–(0.0)*	0.0	0.4	−1.2—1.4
CVLT-R	0.01	1.1	−0.9	0.6	−2.4−0.6	−0.4	0.5	−1.6−0.7	0.5	0.5	−0.9—1.8
Visual Memory											
Rey-C	0.11	2..3*	−5.5	2.4	−12.5−1.4	−3.8	1.8	−10.5−2.9	1.7	2.0	−1.7−5.3
Rey-I	0.03	1.3	−11.2	5.2	−27.0−4.5	−8.8	3.9	−16.4-(−1.1)*	2.5	4.4	−13.0—17.9
Rey-D	0.08	1.9	−6.2	4.7	−19.7−7.2	−6.8	3.5	−13.7−0.18	−0.5	1.0	−13.8−12.6
Rey-R	0.14	2.7*	−6.0	5.1	−19.3−7.2	−11.2	3.8	−20.5-(−2.5)***	−5.5	4.3	−17.8−6.8
Executive Functioning											
FAS	0.10	2.2*	4.5	5.2	−8.9—17.9	−4.1	3.8	−16.8−8.5	−8.7	4.4	−16.7-(−0.6)*
Animals	0.14	2.7*	−2.7	4.0	−12.0−6.5	−6.0	3.0	−14.5−2.5	−3.9	3.8	−.9.9−3.4
Stroop-CW	0.26	4.7***	−1.1	4.0	−9.6−7.4	−11.3	3.0	−18.9-(−4.0)***	−10.4	3.7	−17.5-(−3.3)***
Stroop-I	0.40	8.0***	−1.1	3.5	−8.2−5.9	−13.2	2.5	−19.8-(−6.7)***	−12.1	2.9	−17.7-(−6.5)***
WCST-C	0.21	3.7***	0.1	0.6	−0.8−1.0	−1.5	0.4	−2.4-(−0.5)***	−1.6	0.5	−2.4-(−0.8)***
WCST-N	0.18	3.3***	4.9	4.4	−3.0—12.9	−8.2	3.2	−15.8-(−0.5)*	−13.1	3.7	−19.7-(−6.5)***
WSCT-P	0.01	1.2	−0.9	3.9	−12.6−10.8	−5.7	2.9	−13.5−2.0	4.8	3.4	−15.5−5.9

Note: AD=Alcohol Dependence, MD.=Mean Difference, CI= Confidence Interval, SE=Standard Error, LM= Logical Memory (I=immediate recall, D=delayed recall), CVLT-II=California Verbal Learning Test- second edition (A=Acquisition phase, trials 1 through 4, I=immediate free recall, D=delayed recall, R=recognition, FAS=COWAT, Stroop (CW=Color-Word, I=interference), WCST=Wisconsin Card Sortin Test (C=number of categories completed, N=none perseverative errors, P=perseverative errors.

* P<0.05,
** P<0.01
*** P<0.001.