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Neuropsychological Changes in Patients With Substance Use Disorder After Completion of a One Month Intensive Outpatient Treatment Program

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Abstract

Background and Objectives: Data suggest individuals with substance use disorders (SUD) exhibit high rates of executive functioning (EF) impairment, and that EF level can predict treatment retention. The primary aim of the present study was to investigate if patients who completed a 1 month intensive outpatient program (IOP) for SUD demonstrated recovered EF.

Methods: Baseline and follow-up neurocognitive functioning was assessed by the Cambridge Neuropsychological Test Automated Battery (CANTAB) and the self-reported Behavior Rating Inventory of Executive Functioning (BRIEF-A) questionnaire.

Results: The final sample included 15 patients who completed the one month IOP and for whom data were available (53% male, aged 36 years ± 13.4). Despite exhibiting general improvements in EF and significant improvements in organization, subjects continued to manifest significant executive dysfunction as evaluated by self-report and computerized assessment.

Conclusions and Scientific Significance: Patients with SUD often manifest high levels of executive dysfunction upon entry into SUD treatment that, while improving minimally, appears to persist despite intensive outpatient treatment at 1 month. These persistent EF deficits may affect patient engagement and participation in treatment, thus necessitating SUD programs to assess and accommodate EF issues throughout treatment.

INTRODUCTION

Up to 29% of adults in the US manifest an alcohol use disorder[1] while 10% manifest an illicit drug use disorder.[2] Substance use disorders (SUD) are associated with morbidity and

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mortality[3] and frequently co-occur with mental health impairments, medical conditions, and cognitive deficits.[4–6]

Impairments to neurocognitive functioning, and more specifically the domain of Executive Functioning (EF), are highly prevalent in those with SUD. EF is broadly defined as a set of cognitive skills involved in the regulation of attention, inhibition, concentration, emotional control, organization, and self-regulation,[7] and data indicate that 30 to 80% of SUD patients experience EF impairment[8] in one or more areas, including sustained attention, working memory, visuospatial ability, and decision making.[9] Our own group recently showed that treatment-seeking patients with SUD who prematurely dropped out of an intensive outpatient program (IOP) had more severe EF impairment than those who completed the IOP.[10] Considering that many evidence-based SUD treatment programs have a cognitive-behavioral basis and rely on self-directed learning, compromised EF may be an impediment to fully benefitting from treatment.

Although research has shown that many SUD patients enter treatment with impaired EF,[11] it remains to be determined if these impairments are ameliorated during SUD treatment. Follow-up studies have shown that after three months of abstinence, cocaine dependent patients with impaired neuropsychological functioning experience mild cognitive recovery, specifically in the domains of cognitive flexibility and planning/organization,[12] and polysubstance dependent patients self-report greater improvements in global EF after one year of sobriety than those who relapsed.[13] Neuroimaging studies support these findings and demonstrate that patients with current cocaine dependence exhibit hypoactivity in regions of the response inhibition circuit, and that this lower brain activity is no longer present in formerly cocaine dependent individuals after 13 weeks of abstinence.[14] Similarly, Scott et al.[15] reported that six months of buprenorphine treatment was associated with improvements in global neuropsychological functioning in patients with opiate use disorder.

However, other follow-up studies have noted a lack of improvement in EF following SUD treatment. For instance, Prosser et al.[16] reported that patients enrolled in methadone maintenance did not experience greater EF recovery than those not receiving treatment. Another study similarly found that six months of psychosocial therapy was not associated with improvements in EF for substance dependent adolescents.[17]

Remarkably, there has been very little research on changes in EF in standard treatment settings such as an IOP—a common SUD treatment. Understanding the degree to which impaired EF associated with SUD improves with treatment is critical from a clinical standpoint given the need to match the neurocognitive abilities of the patient with the neurocognitive load of treatment.

To this end, we sought to examine if patients enrolled in an IOP would evidence improvements in EF after treatment completion. We hypothesized that there would be significant improvements in clinical and neuropsychological functioning after completion of the four-week program. However, based on the literature, we also hypothesized that despite completing the IOP, patients would continue to exhibit clinically relevant EF impairment.

METHODS

Participants

The current study is a follow-up to our initial examination of EF and psychiatric impairment as predictors of treatment retention in treatment-seeking patients enrolled in an IOP.[10] In the present study, we sought to extend these findings by examining changes in EF over the month-long IOP.

Participants from this initial study who completed the month long IOP were included in the present study (See ref.[10] for details). To be part of the initial study, patients seeking treatment in a specialty addiction treatment clinic associated with a large general hospital had to be referred to the IOP. Potential participants had to be aged 18–65 years and have a clinical diagnosis(es) of full Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) substance abuse or dependence (excluding nicotine and caffeine) or DSM-5 SUD. Potential participants were excluded if they had a history or current diagnosis of: intellectual disability (IQ less than 70), history of or current neurological disorder, moderate/severe traumatic brain injury, loss of consciousness>30 minutes, schizophrenic spectrum disorder, a history of psychosis within the past two months, or if the participant posed a significant risk of harm to self or others. The IOP was one month in duration, with three two-hour groups on three days of the week. No ethnic or racial groups were excluded. Participants provided written informed consent and the institution's review board approved the study. A federal release of confidentiality was obtained.

Assessments

All study staff underwent extensive training by the PI (PhD) and co-investigator (MD) of the study. The PI administered the Timeline Followback. Repeated measures to assess neurocognitive functioning included self-report questionnaires and study staff administered tests. Study staff conducted chart review to obtain mental health and substance use history.

Background History—Demographics, history and current substance use, urine/oral fluid toxicology results, and psychiatric, medical and treatment history were gathered from patients' evaluations at the clinic and during their tenure in the IOP as part of the standard intake process.

Repeated Measures—The following assessment measures were completed within a week of the patient starting the IOP (baseline) and within one week of completion of the IOP (follow-up).

Interview

Timeline Follow-back (TLFB): Timeline Follow-back (TLFB)[18] assesses past 30-day substance use in a calendar format. This interview documents an individual's drinking and other drug use frequency and quantity. The TLFB has excellent reliability (ranging from r=.86 to .97) and validity.[19]

Questionnaires

Behavior Rating Inventory of Executive Functioning (BRIEF-A): Behavior Rating Inventory of Executive Functioning (BRIEF-A)[20] is a self-report measure assessing a range of EFs including inhibition, set shifting, emotional control, initiating tasks, working memory, planning/organizing, and self-monitor. *T*-Scores are used to standardize outcomes with a clinical cut off score≥65 indicating impairment. This measure has excellent internal consistency (α ranging from .93 to .94 for the three major indices) and one-month test-retest reliabilities (ranging from r=.93 to .94 for the three major indices).[21]

Adult ADHD Self-Report Scale (ASRS-v1.1): Adult ADHD Self-Report Scale (ASRS-v1.1)[22] is an 18-item self-report screening questionnaire assessing DSM-IV symptoms of adult ADHD. The ASRS has reliable internal consistency ranging from .63 to .72 and test-retest reliability (Pearson correlations) ranging from .58 to .77.[23]

Beck Depression Inventory—Second Edition (BDI-II): Beck Depression Inventory—Second Edition (BDI-II)[24] is a 21 item self-report measure assessing DSM-IV symptoms of depression. This measure has high internal consistency (.86), and reliability (.93). Concurrent validity demonstrated a correlation of .65 and .67 in comparing results of the BDI with psychiatric ratings of participants.[25] Total scores from 0 to 13 suggest minimal, 14–19 mild, 20–28 moderate, and 29+ severe depressive symptoms.

Beck Anxiety Inventory (BAI): Beck Anxiety Inventory (BAI)[26] is a self-report measure assessing symptoms of anxiety. The scale has high internal consistency (.92)[27] and item-total correlations ranging from .30 to .71 (median=.60).[26] Total scores are calculated with ranges from 0 to 13 suggesting minimal, 14–19 mild, 20–28 moderate, and 29 + severe anxiety symptoms.

Leeds Dependence Questionnaire (LDQ): Leeds Dependence Questionnaire (LDQ)[28] is a 10-item self-report questionnaire assessing symptoms and behaviors associated with alcohol or drug dependence. Internal consistency is very high (.93). Concurrent and convergent validity of dependence criteria, substance use frequency, and general symptom severity, respectively, were also acceptable.[29] Total scores falling in the 1–10 range suggest low to moderate dependence, 11–20 moderate to high dependence, and 21–30 high dependence.

Neurocognitive Battery

Cambridge Neuropsychological Test Automated Battery (CANTAB): Cambridge Neuropsychological Test Automated Battery (CANTAB)[30] is a computerized test system assessing a range of EF abilities including cognitive flexibility and planning, decision-making and response control, attention, visual memory, and semantic/verbal memory. The CANTAB allows for repeated administration of measures as it contains counter-balanced and/or alternative tests to eliminate practice effects. The CANTAB has been used in previous studies assessing cognitive functioning in substance-using patients.[31,32] Test-retest reliability ranges from .59 to .89 depending on the subtest.[33] The Motor Screening and Big/Little Circle subtests were first used to ascertain whether participants had the necessary cognitive abilities to complete subsequent measures and become familiar with the touch screen

system. If participants were unable to complete this screen, they were not able to remain enrolled in the study. The CANTAB included 6 subtests:

1. Spatial Working Memory (SWM) tests the participant's ability to retain spatial information and to manipulate remembered items in working memory.
2. Stockings of Cambridge (SOC) is a spatial planning test, which provides a measure of frontal lobe function.
3. Intra-Extra Dimensional Set Shifting (IED) assesses shifting in the context of problem solving.
4. Rapid Visual Information Processing (RVP) assesses vigilance.
5. Reaction Time (RTI) assesses speed of processing and reacting to stimuli.
6. Cambridge Gambling Task (CGT) assesses risk taking and decision-making abilities while controlling for impulsivity.

Statistical Analysis

Prior to analyses, all variables were examined for normality, linearity, univariate and multivariate outliers, and multicollinearity. Correlations between all variables were then examined using Pearson correlation coefficients. Paired samples mean *t*-tests were used to compare study variables of interest at baseline and upon completion of the IOP. Analyses were done using SPSS 20.0. Raw scores for the CANTAB were used to calculate changes between baseline and follow-up tests. Raw score norms were provided by Cambridge Cognition, developers of the CANTAB. Norms are collapsed by gender and age, with norm comparison group ages ranging from 16 to 49 years (except for CGT which ranges from 16 to 69 years). Impairment was defined by comparing observed scores to norm scores falling at or below the 15th percentile and/or greater than one standard deviation difference from norm score (this method for detemining impairment using CANTAB norm data has been used in prior published work, see ref.[34]). All data are presented as±standard deviation unless otherwise stated, and effect size (ES) was calculated using Cohen's *d*. All tests were two-tailed and statistical significance was determined at α=.05.

RESULTS

Screening

As previously reported,[10] the majority of patients informed about the study by the IOP intake coordinator agreed to be screened (N = 113/160; 66%). Of this subgroup, 49% (N 55) completed the screening process. Reasons for not completing the screening process included: no longer interested, unable to contact, and did not follow-up in treatment at the program. Among those screened, 82% (N = 45) were eligible to participate, and 78% (N = 35) enrolled in the study. Our sample (N = 30) included 20 "completers" (mean age: 39.5 ± 13.1 years) who finished the IOP, and 10 "dropouts" (32.0 ± 11.1 years). Although 20 patients completed the IOP,[10] only 15 provided data at the second follow-up assessment period, as 5 were lost to follow-up. Thus, a priori for the present analyses, our

final sample included 15 patients, ranging in age from 22 to 64, on whom we had pre- and post-neurocognitive measures (see Table 1 for sample description).

A high severity of substance use was reported at baseline during the initial intake interview: 100% were found to have current drug or alcohol (or combined) dependence, 27% a history of overdose and 53% indicated alcohol as their primary substance of use and 33% opiates. Similarly, high rates of mental health comorbidities and functional impairment were found during chart review: 87% were currently diagnosed with a psychiatric disorder (67% mood disorder and 47% anxiety disorder), 40% reported some form of child abuse/neglect, 40% had a history of a suicide attempt, and only 13% were currently employed. Additionally, the highest degree of education obtained by participants were self-reported as follows: graduate (7%), college (26%), completed some college (47%), high school diploma only (0%), GED (13%), neither high school diploma nor GED (7%).

Mental Health and SUD Outcomes

We first examined the impact of the IOP on SUD outcomes (see Table 2). Regarding change in measures of substance use, while in the direction of improvement, there were no significant changes in level of dependence or days of substance use in the past 30 days as measured by the LDQ and TLFB. We then analyzed mental health indices in our IOP completers. There were significant improvements in measures of self-reported depressive symptoms (p=.015, ES=.59, moderate); however, change in anxiety and ADHD symptoms did not reach statistical significance.

We then evaluated cognitive changes as measured by self-report BRIEF and computer administered CANTAB. We utilized T-Score changes on the BRIEF, and raw score changes using CANTAB measures given that the CANTAB standardizes output using Z-Scores.[10]

As seen in Fig. 1, BRIEF scores indicated that patients continued to evidence high levels of impairment at follow-up, with all measures falling just below the clinical threshold for impairment. Although there was improvement in all subscales on the BRIEF over the 4 weeks, only the Organization subscale was associated with a statistically significant change (p = .04, ES .68; moderate). Similarly, regarding CANTAB measures, no specific test of neurocognitive functioning achieved a statistically significant change (all p's>.05; see Table 3) between baseline and follow-up. Regarding degree of impairment associated with CANTAB scores, we compared baseline and follow-up raw scores to established CANTAB norms. Only baseline RVP and follow-up IED scores fell below the 15th percentile and ± 1 SD compared to established norms. However, all scores fell very close to the 15th percentile suggesting the sample evidences below average scores compared to healthy controls (see Table 3 for norm data including 15th percentile rank cut score).[35]

DISCUSSION

The findings from the present study indicate that despite meager improvements to EF, as measured by self-report and computer-administered tasks, patients continue to manifest clinically significant impairments upon completion of a four-week IOP. Notably, these neuropsychological deficits persisted despite low levels of use or abstinence from

substances at testing periods and during the IOP. These data suggest the need to recognize patients presenting for standard outpatient intensive treatment as evidencing significant EF impairment that may affect their ability to fully benefit from standard treatment interventions.

Our data showing nominal improvements in EF are supported by several other studies demonstrating that SUD patients remain impaired cognitively even after completing treatment. Utilizing the BRIEF-A, one study found that despite exhibiting improvements in EF after one week, one month, and three months of abstinence, the inhibition, self-monitoring, working memory, planning/organization, and task monitoring of cocaine dependent individuals remained significantly impaired relative to healthy controls.[12] Another study examining neuropsychological change in 169 patients with SUD over a 6-week period found little improvement in EF, processing speed, and verbal skills; and only modest improvement in memory.[36] The present finding that SUD patients remain impaired after treatment and abstinence are also supported by studies examining EF in former heroin users both enrolled and not enrolled in methadone maintenance.[16]

Differing from the present findings, some research suggests that abstinence and standard forms of treatment can lead to clinically impactful recovery of EF. In a prospective cohort study of 115 polysubstance dependent patients, those who successfully completed one year of abstinence demonstrated greater improvements in EF (as measured by the BRIEF-A) than those who relapsed and healthy controls.[13] It is important to note that despite manifesting greater *improvements* in EF than healthy controls, SUD patients' *overall* EF remained lower than that of the controls, as was also found in the present study.

For those with SUD, the cognitive learning and EF required to organize one's treatment, know when and where to show up, recall medication instructions (frequency and dosage), follow typical cognitive behavioral therapy (CBT) skills training—a common component of standard treatment for SUD—and recall skills taught between sessions to apply to stressors outside of group, likely make full participation in and benefit from such treatments challenging. As shown in our data and the aggregate literature, patients continue to evidence significant weakness in attention, memory, and flexible thinking, all of which can be defined as executive skills necessary to follow standard treatment demands. Patients with SUD frequently struggle with inconsistent treatment attendance, poor medication adherence, and lack of skills practice between sessions. Some patients' difficulties may be multifactorial, including addiction and mental health issues, as well as "slowly recovering" EF over and above substance use. Indeed, our data indicate that patients continued to manifest EF impairment despite improvement in depressive symptoms and continued minimal substance use.

One way to address the disparity between the demands of treatment and the cognitive abilities of patients with SUD could be to, firstly, assess EF of patients entering treatment and attempt to tailor/adapt treatment to match the patient's abilities. This has been common practice when using CBT for children with developing EF,[37] but less data exists evaluating such an approach for patients with SUD and EF impairments. In the few studies employing cognitive remediation therapy, a form of therapy that utilizes cognitive exercises to repair

impaired functioning, patients receiving cognitive rehabilitation in addition to standard SUD treatment exhibited improvements in overall cognitive functioning[38] Notably, these interventions are virtually non-existent in standard programs for patients with SUD.

Despite meager change in EF in the present study, it is curious that the Organization of Materials (OOM) subscale evidenced significant improvement over the four-week period. The OOM subscale taps into higher order learning skills and is comprised of questions such as “I am disorganized,” “I lose things,” I have trouble finding things,” and “I leave my room/house a mess.” We also found statistically significant improvements in level of depression symptom burden, but no significant changes were noted in self-reported anxiety or ADHD. Substance use severity remained stable and low. It may be that organizational skills are the first area of EF in which benefits start to emerge, a topic that deserves replication.

Limitations

There are several limitations of note. First, the sample size was relatively small, therefore limiting the generalizability of the findings and sensitivity to detect change. Second, the follow-up period was 4 weeks which may be too short of a period to detect significant changes; however, many treatment programs are one month in duration, highlighting that many patients still experience EF impairment even at the end of an IOP. Although the impact of substance use on cognitive function cannot be ruled out as accounting for our findings, the majority of the sample (57%) was sober for the week prior to baseline testing and treatment initiation, and a low rate of substance use was reported on the TLFB (mean # past 30 days use 7.8) at baseline and follow-up (mean # past 30 days use 1.4). It is thus unlikely that active substance use fully mediated these results. Finally, there was a high level of psychological distress in the sample, with many patients evidencing elevated scores on anxiety and depression measures. It may be that symptom burden accounted for aspects of EF weakness; however, there was a significant reduction in depression scores between baseline and follow-up but no significant change on most EF measures. Anxiety symptom burden remained in the mild range from baseline to follow-up, with a slight decrease over time. It is therefore unlikely that these findings were fully accounted for by psychiatric burden.

Despite these limitations, our data indicate that patients enrolling in a standard IOP manifest significant and persistent cognitive deficits across many domains of EF after one month of treatment. Although generally improving over the period of study, patients continue to struggle with executive dysfunction and may not be able to maximally benefit from intensive cognitive/behavioral interventions which require high demands on cognitive learning and EF skills. Moreover, patients with inconsistent attendance or tardiness are frequently conceptualized as not being “ready” or “motivated” for treatment, but may in fact be struggling with clinically significant EF impairments making the logistics of treatment difficult to navigate. Treatment programs should consider assessing EF issues at treatment inception, and adjust interventions and clinic workflow to provide more individualized treatment interventions.

Declaration of Interest

James McKowen, PhD, Benjamin M. Isenberg, BA, Nicholas W. Carrellas, BA, and Courtney Zulauf, MA: The authors report no conflicts of interest. Ronna Fried, EdD: Dr. Ronna Fried is currently receiving research support from Lundbeck. In 2015, Dr. Fried received honoraria from the MGH Psychiatry Academy for tuition-funded CME course. During previous years, she received research support from the National Institutes of Health and Shire. E. Nalan Ward, MD: Dr. Nalan Ward serves a medical consultant at the Massachusetts Department of Health Bureau of Susbtance Abuse Services (BSAS). Dr. Timothy Wilens is or has been a consultant for Alcobra, Neurovance/Otsuka, and Ironshore. Dr. Timothy Wilens receives grant funding from NIH (NIDA). Dr. Timothy Wilens has published the book: Straight Talk About Psychiatric Medications for Kids (Guilford Press); and co/edited books ADHD in Adults and Children (Cambridge University Press), Massachusetts General Hospital Comprehensive Clinical Psychiatry (Elsevier) and Massachusetts General Hospital Psychopharmacology and Neurotherapeutics (Elsevier. Dr. Wilens is co/owner of a copyrighted diagnostic questionnaire (Before School Functioning Questionnaire). Dr. Wilens has a licensing agreement with Ironshore (BSFQ Questionnaire). Dr. Wilens is Chief, Division of Child and Adolescent Psychiatry and (Co) Director of the Center for Addiction Medicine at Massachusetts General Hospital. He serves as a clinical consultant to the US National Football League (ERM Associates), U.S. Minor/Major League Baseball; Phoenix/Gavin House and Bay Cove Human Services.

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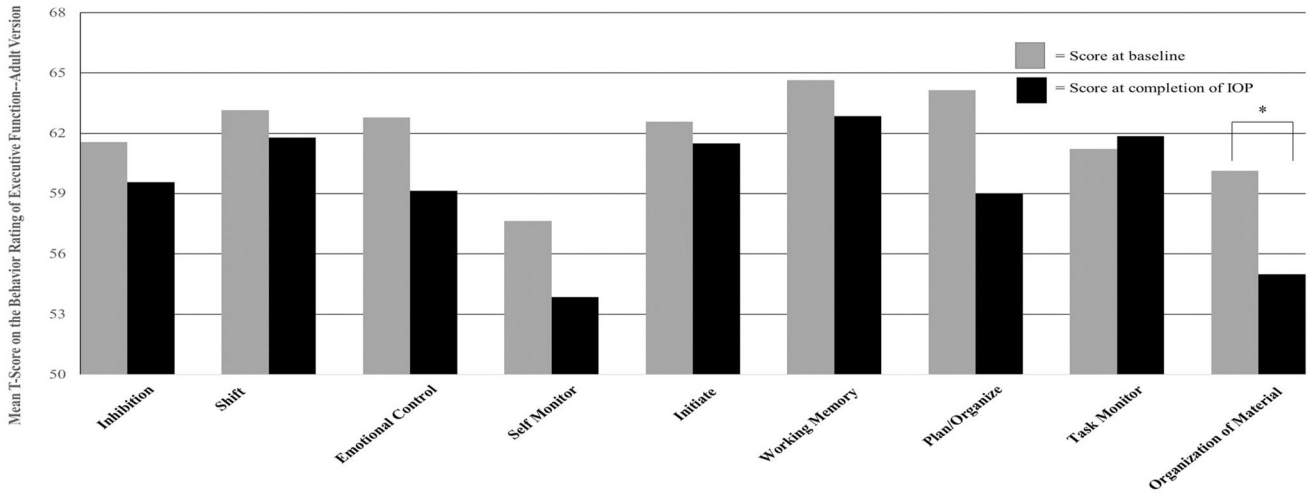

FIGURE 1.

Comparison of mean raw scores on the Behavior Rating Inventory of Executive Functioning-Adult version at baseline to scores upon completion of IOP. *$p \leq .05$;**$p \leq .01$;***$p \leq .001$.

TABLE 1.

Demographics and clinical characteristics of patients who completed an intensive outpatient program

	Follow-up (*N* = 15)
Demographics	**Mean ± SD or *N* (%)**
Age (years)	36 ± 13.4
Sex (% male)	8 (53)
Ethnicity (Caucasian)	14 (93)
Current substance use disorder (s)	
Alcohol	11 (73)
Marijuana	4 (26)
Opiate use	4 (26)
Cocaine	3 (20)
Amphetamine	4 (26)
Other drugs	4 (26)

TABLE 2.

Mental health indices of patients who completed an intensive outpatient program (IOP) at baseline and upon completion of an IOP at one month follow-up

Measure	Baseline (*N* = 15)	Follow-Up (*N* = 15)	Change (*N* = 15)
Beck Depression Inventory (BDI) total score	21.5	16.6	−4.9 *
Beck Anxiety Inventory (BAI) total score	15.5	13.5	−2.00
Adult ADHD Self-Report Scale (ASRS) total score	34.5	30.0	−4.5
Leeds Dependence Questionnaire (LDQ) total score	7.47	4.00	−3.47
Timeline Followback (TLFB) days of substance use	3.92	.69	−3.23 *

* $p \leq .05$.

** $p \leq .01$.

*** $p \leq .001$.

TABLE 3.

T-test results comparing baseline and follow-up neuropsychological outcomes in patients with SUD after completing a four-week intensive outpatient program

	Norm	Baseline (*N* = 15)	Follow-Up (*N* = 15)	Change[a] (*N* = 15)
Measure	**Mean ± SD ≤15th% Impairment cut score**	**Mean ± SD**	**Mean ± SD**	**Mean**
Spatial Working Memory (SWM-Between Errors)	17.95 ± 15.42 >33	25.2 ± 24.5	32.7 ± 24.6	−7.50
Stockings of Cambridge (SOC-Minimum Moves)	9.25 ± 1.89 <7.33	8.53 ± 2.33	9.24 ± 2.48	−.71
Rapid Visual Processing (RVP-A)	.92 ± .04 <.87	.83 ± .24	.91 ± .05	−.08
Intra-Extra Dimensional Set Shift (IED-Total Adjusted Errors)	19.29 ± 22.21 >25	23.1 ± 14.9	57.6 ± 65.5	−34.5
Reaction Time (RTI-Total Adjusted Errors)	318.16 ± 54.48 >358	334 ± 70.7	345 ± 94.9	−11.0
Reaction Time (RTI-Five-Choice RT)	348.28 ± 52.70 >395	347 ± 66.9	354 ± 56.2	−7.0
Cambridge Gambling Task (CGT-Delay Aversion)	16.93 ± 16.89 <.27	.50 ± .20	.56 ± .14	−.06

[a]Cambridge Neuropsychological Test Automated Battery (CANTAB) mean raw scores at entry into an IOP minus mean raw scores upon completion of IOP.