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# Cognitive deficits in marijuana users: effects on motivational enhancement therapy plus cognitive behavioral therapy treatment outcome

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## Abstract

Clinical variables that affect treatment outcome for marijuana dependent individuals are not yet well understood, including the effects of cognitive functioning. To address this, level of cognitive functioning and treatment outcome were investigated. Twenty marijuana-dependent outpatients were administered a neuropsychological battery at treatment entry. All patients received 12 weekly individual sessions of combined motivational enhancement therapy and cognitive behavioral therapy. The Wilcoxon Exact Test was used to compare cognitive functioning test scores between completers and dropouts, and the Fisher Exact Test was used to compare proportion of negative urines between those with higher and lower scores on the cognitive tests. Marijuana abstinence was unrelated to cognitive functioning. However, dropouts scored significantly lower than completers on measures of abstract reasoning and processing accuracy, providing initial evidence that cognitive functioning plays a role in treatment retention of adult marijuana dependent patients. If supported by further studies, the findings may help inform the development of interventions tailored for cognitively impaired marijuana dependent patients.

### Keywords

Marijuana; Cognitive functioning; Treatment; Motivational Enhancement Therapy; Cognitive Behavioral Therapy

## 1. Introduction

Approximately 14.6 million Americans use cannabis (Substance Abuse and Mental Health Services Administration (SAMHSA), 2005); 36% of current users have DSM-IV marijuana

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disorders (Compton et al., 2004). Thus, effective interventions are needed. Promising therapies adapted for marijuana patients include cognitive behavioral therapy (CBT), motivational enhancement therapy (MET), and contingency management, which all assume adequate cognitive functioning. Thus, patients with less cognitive ability may be vulnerable to dropout or poor outcome. Subjective reports of deficits in memory, attention or concentration are common among marijuana users, e.g., (Stephens et al. 2002; Gruber et al., 2003), and neuropsychological testing in chronic marijuana abusers shows impaired memory, attention (Solowij et al., 1995; 2002), abstraction, decision-making and executive functioning (Fletcher et al., 1996; Lamers et al., 2006; Pope and Yurgelun-Todd, 1996; Whitlow et al., 2004).

Effects of cognitive functioning on treatment outcome have been studied among cocaine dependent patients (Aharonovich et al., 2006) but not marijuana dependent patients. We studied cognitive functioning at treatment entry and outcome among marijuana dependent patients. The behavioral treatment included weekly sessions combining MET and CBT. Based on previous work (Aharonovich et al., 2003; 2006), we predicted that lower scores on neuropsychological measures, specifically attention and memory, would predict poorer treatment outcome.

## 2. Methods

### 2.1 Participants

Participants were 20 consecutively enrolled marijuana dependent outpatients in a parent study (a placebo-controlled randomized trial) consisting of 12 weeks of MET+CBT combined with medication (nefazodone n=7, buproprion n=9) or placebo (n=3). Eligible participants were those aged 18–50 meeting DSM-IV criteria for cannabis dependence. Participants were excluded if they 1) met DSM-IV criteria for current psychiatric disorders requiring intervention (assessed by the SCID) or substance dependence other than cannabis; 2) current use of prescription psychoactive medication 3) history of seizure disorder or head injury with loss of consciousness >1 hour, or 4) prior diagnosis of learning disability. The study was described to patients as assessment of marijuana effects on cognitive functioning. All patients approached agreed to participate and gave written consent as approved by the New York State Psychiatric Institute IRB.

### 2.2 Neuropsychological Measures

All patients were assessed with the computerized MicroCog (MC) Assessment of Cognitive Functioning (Powell et al., 1993). This 45–60 minute battery is normed and standardized for adults, with population mean scores for each component of 100 (SD=15). Patients also took the Wisconsin Card Sort Test (WCST), Computer Version–2 Research Edition (Heaton, 1999). This 15–20 minute non-verbal test assesses executive functioning, including strategic planning, cognitive flexibility, and use of environmental feedback to shift cognitive sets. We report on perseverative error and response scores as they indicate cognitive flexibility and are widely used. The WCST raw scores were transformed to standard scores (mean=100, SD=15).

### 2.3 Outcome Measures

**Retention—**Completion was defined as attending ≥75% of the 12 MI+CBT sessions, compatible with standard CBT length (Carroll, 1998) but allowing for the typical mixed compliance in substance abuse treatment.

**Level of abstinence—**This was indicated by the proportion of urines negative for marijuana out of total possible urines. Drug use levels were analyzed with the THC Fluorescence Polarization Immunoassay (FPIA). The cutoff for positive was ≥ 50 ng/mL. Missed urines were considered positive.

### 2.4 Procedures

During treatment, participants attended weekly 60-minute individual MET+CBT sessions and gave observed urine specimens twice a week. Urine samples were analyzed for THC and seven other drugs. No participant was positive for any drug except THC when tested. To preclude acute intoxication at testing, patients reported their last marijuana use and submitted observed urine specimens and a breath alcohol test. Participants reporting any new illicit drug or alcohol use <7 h. before testing were rescheduled to avoid acute intoxication effects. The neuropsychological battery was administered immediately after the first therapy session during the placebo lead-in week. Patients were paid $20 for completing the battery.

### 2.5 Statistical analysis

We tested normality assumptions and homogeneity of variance (Levene's test) on each neuropsychological test score. Several Microcog subtest scores were significantly skewed (z-scores 0.002 to −2.631), as were Completed Categories and Failure to Maintain Set from the WCST (z-scores −3.50 and 2.92, respectively). In addition, two subtests had unequal variances between completers and dropouts (WCST Failure to Maintain Set, p=.008; Microcog Spatial Processing, p=.08). Therefore, the Wilcoxon Exact Test was used to compare cognitive functioning in completers and dropouts on the summary scores of attention, abstract reasoning, memory, spatial ability, MC composite scores, and WCST scores. WCST scores were missing for two patients. All scores were adjusted for age and education.

To address the relationship of cognitive functioning to abstinence (proportion of negative urines) during treatment, the General Cognitive Proficiency (GCP) score was dichotomized to represent high and low levels of functioning, using the sample median (90.5) as the cut-off. The GCP score was chosen because it combines accuracy and speed, with more weight to accuracy, consistent with methods used previously (Aharonovich et al., 2006). Fisher's Exact Test was used to test differences in proportions between patients defined by categorical variables (completers/dropouts; high/low cognitive functioning). All tests were two-tailed.

## 3. Results

### 3.1 Sample characteristics

Completers (n=7) and dropouts (n=13) did not differ significantly on mean age (completers=30.0, SD 5.0, dropouts= 31.2, SD 9.6); education (completers=14.6 years, SD 2.8; dropouts=13.4 years, SD 2.3) or mean years using marijuana (completers=12.1, SD 7.3; dropouts=13.1, SD 7.8). They also did not differ on ethnicity (43% of completers, 31% of dropouts were white); full-time employment (57% of completers, 46% of dropouts); being married (14% of completers, 15% of dropouts); using alcohol (29% of completers, 15% of dropouts) or using cocaine (0% of completers, 15% of dropouts). All patients used marijuana daily in the prior 30 days. No observed urine at the time of testing was positive for drugs other than marijuana. The sample had one left-handed completer and one left-handed dropout. Treatment groups (medication vs. placebo) did not differ on retention (completers vs. dropouts; Fisher Exact p=0.10) or marijuana abstinence (Kruskal-Wallis non-parametric test: chi-square=0.64, df=2, p=0.74).

### 3.2 Observed urine results at treatment entry

Overall mean THC levels prior to testing were 617.5 ng/mL (SD 603.3). Completers and dropouts did not differ on mean THC levels at the time the battery was administered (635.1; SD 943.1 and 607.9; SD 362.3, respectively; Wilcoxon Test, p=0.35). THC levels did not correlate with cognitive functioning indicated by the cognitive proficiency score ($r^2$ (20) =0.018; p=0.57).

### 3.3 Cognitive functioning and treatment retention

Microcog scores among completers ranged from the population mean to about.5 SD above the mean (99.9–107.1). Microcog scores among dropouts ranged from nearly one standard deviation below the population mean to near the population mean (87.7–99.5). Dropouts had significantly lower scores on abstract reasoning, spatial processing and accuracy (Table 1), with similar trends ($p<.10$) for general cognitive performance and general cognitive proficiency. For example, completers scored about .5 SD above the population mean on abstract reasoning, while dropouts scored approximately .5 SD below the population mean. In contrast, WCST scores of perseverative errors and responses were near the mean and similar among completers and dropouts.

### 3.4 Cognitive functioning and abstention

The mean proportion of negative urines did not differ between the high and low cognition groups (.18 and .17, z-statistic 0.47; p=.64). We explored whether the groups differed in likelihood of a negative urine test at their last test in the study. There were 5 such patients in the study, 4 in the low cognition group and 1 in the high cognition group, a difference not statistically significant (Chi-square=2.4, df=1, Fisher's Exact Test p=0.30). We further explored mean consecutive weeks of negative urine tests in the high and low cognition groups (3.6 and 2.0, respectively), which did not differ significantly (Wilcoxon rank sum test: z-statistic=0.48, p=0.63).

## 4. Discussion

This study investigated cognitive functioning at treatment entry and its relation to retention and drug use outcome in MET+CBT treatment in marijuana dependent patients. Higher cognitive ability in the domains of mental reasoning, spatial ability and overall accuracy significantly distinguished completers from dropouts. The association between lower cognition levels at treatment entry and treatment dropout is consistent with studies in cocaine-dependent patients (Aharonovich et al., 2003; 2006) and poly-substance abusers (Fals-Stewart et al., 1994; Teichner et al., 2002).

WCST scores were near normal in completers and dropouts. In laboratory settings, the WCST is useful in differentiating between marijuana smokers and controls (Lane et al., 2007) or between heavier and lighter marijuana smokers after abstinence (e.g., Bolla et al., 2002). However, the WCST at treatment entry was not informative in predicting treatment outcome, consistent with other reports on substance abusers (e.g., Morgenstern and Bates, 1999). We discussed the discrepant findings in these different studies previously (Aharonovich et al., 2006).

Marijuana dependent dropouts in this study performed at a lower level on abstract reasoning than completers. This finding did not support our hypothesis that dropouts would differ from completers on memory and attention, and was inconsistent with results from cocaine dependent treatment dropouts (Aharonovich et al., 2006). This suggests substance-specific differences in cognitive impairments, although larger studies are needed to confirm this.

Baseline cognitive functioning (GCP score) was unrelated to marijuana abstinence during treatment. To explore if this result would differ with abstract reasoning (the cognitive score that most strongly differentiated between the groups) in place of GCP, we re-ran all tests using abstract reasoning dichotomized at the median to define the high and low cognitive groups for analyses of marijuana abstinence. Results were unchanged. Earlier studies show that CBT effects on drug use may be delayed, emerging during long-term follow-up (Carroll et al., 1994; Rawson et al., 2002). Future work with longer follow-up will allow further exploration

of the impact of cognitive functioning in conjunction with other outcome predictors (e.g., motivation, external pressure) on marijuana use during and after treatment.

Study limitations are noted. The study was not designed to investigate differences in acute vs. residual effects of cannabis, or pre-morbid impairment vs. impairment secondary to marijuana dependence. As residual effects may last several days (Pope et al., 2001), a more rigorous procedure to determine cannabis use at the time of testing (Solowij et al., 2002) could assist in future studies. However, from a treatment development viewpoint, given the high dropout early in outpatient treatment, the source of cognitive impairment may be less important than the need to tailor the initial sessions to accommodate deficits of cognitively impaired patients. Also, the N limited analyses, and post-treatment follow-up data were unavailable. Thus, replication and extension of this research is important. Finally, our method of assessing marijuana use (results of urine tests) was not sensitive to short periods of abstinence followed by additional use, since up to 20 days of abstinence may be required before users' urine tests reach a "clean" level. Therefore, our results reflect sustained periods of abstinence (a stringent requirement), which did not differ between the high and low cognition groups. Future research could incorporate other methods of measuring abstinence if information on shorter or more intermittent periods of abstinence is of interest.

Study strengths include excellent participation rate and careful evaluation of inclusion and exclusion criteria, decreasing potential confounding. Patients were dependent only on marijuana. The screening, treatment and neuropsychological assessment were similar to those used in a larger study of cocaine dependent patients (Aharonovich et al., 2006); consistency of the results suggests validity of the present findings despite the sample size.

This empirical study of the impact of cognitive impairments on treatment of marijuana dependence can bring the issue to the attention of clinicians and researchers in a variety of settings, stimulating further research. Furthermore, given that cognitive effects of cannabis dependence are likely to have some degree of cognitive impairments (Solowij et al., 2002), highlighting the importance of our study. The findings suggest that mild cognitive impairments at treatment entry reduce treatment retention of marijuana dependent patients. Clinicians may consider shorter and more frequent therapy sessions, memory aids and repetition in delivering the behavioral intervention. If supported by further studies, this will suggest modifying behavioral interventions to address the difficulties of cognitively impaired marijuana users to improve their treatment outcome.

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**Table 1**

Completers vs. dropouts: Differences in cognitive functioning on the Neuropsychological Assessment

| | Completers | Dropouts | |
|---|---|---|---|
| **Microcog Cognitive Domains**** | **n=7 Mean (SD)** | **n=13 Mean (SD)** | **P (2-tailed)*** |
| Attention | 103.4 (16.1) | 99.5 (11.0) | 0.60 |
| Abstract Reasoning | 107.1 (12.5) | 93.2 (07.0) | 0.005 |
| Memory | 104.7 (13.2) | 96.4 (12.2) | 0.32 |
| Spatial Processing | 99.9 (13.4) | 90.8 (05.4) | 0.02 |
| **Microcog Composite Scores**** | | | |
| Processing Speed | 100.7 (20.2) | 95.0 (15.6) | 0.32 |
| Processing Accuracy | 101.9 (13.8) | 89.2 (08.7) | 0.05 |
| General Cognitive Performance | 101.6 (15.5) | 90.0 (08.9) | 0.09 |
| General Cognitive Proficiency | 101.0 (19.0) | 87.7 (08.9) | 0.06 |
| **Wisconsin Card Sort Test***** | (n=7) | (n=11) | |
| Perseverative Errors | 91.7 (16.6) | 100.2 (18. 6) | 0.33 |
| Perseverative Responses | 93.8 (17.6) | 96.6 (17.7) | 0.75 |

* Wilcoxon Exact Test

** Population mean score for the Microcog=100, SD=15

*** Raw scores of the WCST perseverative errors and perseverative responses were transformed to standard scores (SS) with a mean of 100 and a standard deviation of 15. Higher scores reflect less perseverative errors and responses.