



Cognitive Enhancement Therapy in substance misusing schizophrenia: Results of an 18-month feasibility trial



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ABSTRACT

Substance use is a frequent problem in schizophrenia, and although many substance misusing patients with the disorder also experience considerable cognitive impairments, such individuals have been routinely excluded from clinical trials of cognitive remediation that could support their functional and addiction recoveries. This study conducted a small-scale feasibility trial of Cognitive Enhancement Therapy (CET) in substance misusing schizophrenia patients to assess the feasibility and efficacy of implementing comprehensive neurocognitive and social-cognitive remediation in this population. A total of 31 schizophrenia outpatients meeting addiction severity criteria for alcohol and/or cannabis use were randomized to 18 months of CET or usual care. Feasibility findings indicated high degrees of satisfaction with CET, but also presented significant challenges in the recruitment and retention of substance misusing patients, with high levels of attrition (50%) over the study period, primarily due to positive symptom exacerbation. Intent-to-treat efficacy analyses showed large and significant improvements in neurocognition ($d = .86$), social cognition ($d = 1.13$), and social adjustment ($d = .92$) favoring CET. Further, individuals treated with CET were more likely to reduce alcohol use (67% in CET vs. 25% in usual care) during treatment ($p = .021$). These results suggest that once engaged and stabilized, CET is a feasible and potentially effective treatment for cognitive impairments in patients with schizophrenia who misuse alcohol and/or cannabis. Substance misusing patients who are able to engage in treatment may be able to benefit from cognitive remediation, and the treatment of cognitive impairments may help improve substance use outcomes among this underserved population.

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1. Introduction

Schizophrenia is characterized by marked impairments in social cognition (Green et al., 2012; Horan et al., 2012) and non-social cognition (Heinrichs and Zakzanis, 1998) that significantly limit functional recovery from the disorder (Green et al., 2000; Fett et al., 2011). Cognitive remediation has emerged as an effective intervention for addressing cognitive deficits in schizophrenia, with recent meta-analyses indicating small to medium-size effects on cognition and functional outcome, particularly for strategic approaches that are integrated into broader psychosocial treatment programs (McGurk et al., 2007; Wykes et al., 2011; Keshavan et al., 2014). Cognitive Enhancement Therapy (CET; Hogarty and Greenwald, 2006) is one approach to the remediation of cognitive impairments in schizophrenia that we have previously shown can produce significant improvements in neurocognitive and

social-cognitive function in both chronic (Hogarty et al., 2004) and early course (Eack et al., 2009) patients with schizophrenia, with generalizable and durable benefits to social and vocational functioning (Hogarty et al., 2006; Eack et al., 2010a, 2011). When applied as an early intervention approach, CET has also been shown to protect against gray matter loss in service of cognitive enhancement in the disorder (Eack et al., 2010b).

While evidence is steadily growing to support the efficacy of CET and other cognitive remediation interventions in treating cognitive deficits in schizophrenia, such evidence has been largely limited to patients who do not experience comorbid substance use problems. As many as 65% of patients with schizophrenia misuse substances (Volkow, 2009), and most trials of cognitive remediation have excluded substance misusing patients (see McGurk et al., 2005 for a notable exception). Such individuals are frequently unstable (Schmidt et al., 2011) and have challenges with medication adherence (Perkins et al., 2008), making them less ideal candidates for clinical trials of new interventions. There has also been controversy over the degree to which cognitive deficits are present in patients with substance use problems (Yücel

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et al., 2012), although larger studies using carefully assessed samples indicate impairments similar to those individuals not misusing substances (Wobrock et al., 2013; Bahorik et al., 2014). Given the general lack of efficacy of antipsychotic treatment on cognitive impairment in schizophrenia (Keefe et al., 2007), some patients may turn to substances to cope with residual cognitive deficits and associated social dysfunction (Blanchard et al., 2000; Gregg et al., 2007). At the same time, executive and problem-solving impairments may limit the decision-making abilities needed to prevent or recover from substance misuse problems in the disorder (Chambers et al., 2001).

If substance misusing schizophrenia patients can be successfully engaged in cognitive remediation interventions that are sensitive to addiction problems, this may help support the recovery of these individuals. Unfortunately, little is known about cognitive remediation in this population. This study sought to examine the feasibility of applying an adapted version of CET to patients with schizophrenia and comorbid alcohol and/or cannabis misuse problems, the two most commonly misused substances in the disorder (Volkow, 2009), and evaluate its initial efficacy compared to usual care in a small-scale randomized-controlled trial.

2. Method

2.1. Participants

Participants included 31 substance misusing patients with schizophrenia ($n = 17$) or schizoaffective disorder ($n = 14$) enrolled in an 18-month randomized feasibility trial (NCT01292577) of Cognitive Enhancement Therapy (CET) or treatment as usual (TAU).

Patients were enrolled if they (1) were between the age of 18 and 60 years, (2) were diagnosed with schizophrenia or schizoaffective disorder according to the Structured Clinical Interview for DSM-IV (SCID; First et al., 2002), (3) met criteria for moderate or higher (≥ 4) addiction severity for cannabis or alcohol on the Addiction Severity Index (McLellan et al., 1980), (4) were stabilized on antipsychotic medications, (5) had an IQ ≥ 80 , (6) were able to read and speak fluent English, (7) were not abusing or dependent on cocaine or opioids, (8) did not have another persistent medical condition producing significant cognitive impairment, (9) were not receiving any substance abuse pharmacotherapies (e.g., naltrexone), (10) did not experience persistent homicidality or suicidality, and (11) displayed significant cognitive and social disability on the Cognitive Styles and Social Cognition Eligibility Interview (Hogarty et al., 2004). Eligibility criteria focused on including participants misusing the two most common substances of abuse in schizophrenia, reducing heterogeneity by excluding cocaine and opioid users, and avoiding concomitant substance abuse pharmacotherapies that could impact outcomes.

Table 1 presents the characteristics of enrolled participants, who were mostly male, ethnically diverse, and ill for many years. All but 2 individuals met full SCID criteria for at least one substance abuse or dependence diagnosis, and all individuals met ASI criteria for moderate or greater addiction severity. Moderate ASI severity criteria can be achieved through frequent use and/or significant need for substance use treatment. The majority (68%) of enrolled participants were actively using either alcohol or cannabis at study enrollment, with the remaining individuals meeting ASI criteria based on treatment need. No significant differences were observed between treatment groups in the number of patients actively using substances at enrollment, $\chi^2(1, N = 31) = .26$, $p = .614$, and no significant differences emerged between treatment groups with regard to any demographic, clinical, substance use, or cognitive characteristics prior to treatment (see Table 1). Service use data collected at 18 months on exposure to community substance use treatments in the last 6 months indicated that only 3 patients (2 in CET/PT and 1 in TAU) participated in dual diagnosis, Alcoholics Anonymous, or Narcotics Anonymous treatment programs, with no significant differences between treatment groups ($p = 1.000$).

Table 1

Characteristics of substance misusing schizophrenia patients enrolled in an 18-month feasibility trial of Cognitive Enhancement Therapy (CET) or treatment as usual (TAU).

| Characteristic | TAU (N = 9) N (%) | CET (N = 22) N (%) | p^a |
|--|----------------------|-----------------------|-------|
| Age—mean (SD) | 34.67 (12.99) | 39.68 (13.64) | .354 |
| Male | 7 (78%) | 15 (68%) | .689 |
| White | 3 (33%) | 13 (59%) | .252 |
| Attended college | 7 (78%) | 14 (64%) | .677 |
| Employed | 1 (11%) | 5 (23%) | .642 |
| Primary diagnosis | | | 1.000 |
| Schizophrenia | 5 (56%) | 12 (55%) | |
| Schizoaffective disorder | 4 (44%) | 10 (45%) | |
| Substance abuse or dependence diagnosis | 8 (89%) | 21 (95%) | .503 |
| Alcohol abuse | 3 (33%) | 4 (18%) | .384 |
| Alcohol dependence | 3 (33%) | 14 (64%) | .233 |
| Cannabis abuse | 1 (11%) | 0 (0%) | .290 |
| Cannabis dependence | 7 (78%) | 16 (73%) | 1.000 |
| <i>Daily substance use among active users, mean (SD)</i> | | | |
| Alcohol usage occasions per day | 1.67 (1.11) | 1.15 (.84) | .355 |
| Cannabis usage occasions per day | 3.88 (.47) | 4.30 (1.69) | .681 |
| <i>Addiction Severity Index score, mean (SD)</i> | | | |
| Alcohol | 4.22 (2.05) | 4.00 (2.60) | .821 |
| Drugs | 4.78 (1.79) | 4.41 (2.34) | .676 |
| Schizophrenia illness duration, mean (SD) | 11.78 (11.26) | 15.18 (11.40) | .455 |
| IQ, mean (SD) | 99.33 (10.45) | 99.32 (12.18) | .997 |
| BPRS total, mean (SD) | 42.67 (12.32) | 43.27 (9.30) | .882 |
| Antipsychotic dose (cpz equivalent), mean (SD) | 450.00 (306.19) | 400.30 (329.00) | .700 |
| Receiving second generation antipsychotic | 9 (100%) | 18 (82%) | .295 |
| Medication adherent | 9 (100%) | 19 (86%) | .537 |

Note. BPRS = Brief Psychiatric Rating Scale, cpz = chlorpromazine.

^a Results of independent sample *t*-test or Fisher's exact test, two-tailed.

2.2. Measures

A comprehensive battery of cognitive and behavioral assessments was collected to examine the impact of CET on neurocognition, social cognition, dysfunctional cognitive style, social adjustment, symptomatology, and substance use. Neurocognition was assessed using the NIMH MATRICS Consensus Cognitive Battery (Green et al., 2004). Social cognition was assessed using the Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT: Mayer et al., 2003), the Penn Emotion Recognition Test-40 (Kohler et al., 2003), and the Hinting Task (Corcoran et al., 1995). Dysfunctional cognitive style was assessed using the Cognitive Style and Social Cognition Eligibility Interview and the Cognitive Styles Inventory (Hogarty et al., 2004). Social adjustment was assessed using the Social Adjustment Scale-II (Schooler et al., 1979), Major Role Adjustment Inventory (Hogarty et al., 1974b), and the Global Assessment Scale (Endicott et al., 1976). Symptomatology was assessed using the Brief Psychiatric Rating Scale (Overall and Gorham, 1962), Wing Negative Symptom Scale (Wing, 1961), Raskin Depression Scale (Raskin et al., 1969), and Covi Anxiety Scale (Lipman, 1982). Finally, previous 30-day substance use was assessed using the Timeline Follow-Back interview (Sobell and Sobell, 1992), which has been shown to be a reliable and valid measure of substance use in psychosis (Hjorthøj et al., 2012).

2.3. Treatments

2.3.1. Medication

All participants were maintained on antipsychotic medication indicated for the treatment of schizophrenia or schizoaffective disorder by their treating psychiatrist. The majority of patients (87%) were maintained on second-generation antipsychotic medication. There were no significant differences between treatment groups with regard to

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