Drug Stroop: Mechanisms of response to computerized cognitive behavioral therapy for cocaine dependence in a randomized clinical trial

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Abstract

Background—Poor performance on Drug Stroop tasks, which could indicate attentional bias to drug-related cues, craving, poor cognitive control (including poor response inhibition), has been associated with substance use severity, treatment retention and substance use treatment outcomes. Cognitive Behavioral Therapy (CBT) focuses on training in appraisal and coping strategies, including strategies to minimize the negative impact of triggers and coping with drug-cue-induced craving. One mechanism of action of CBT may be the strengthening of cognitive control processes and reduction of attentional bias to drug-related stimuli.

Methods—Methadone-maintained individuals with cocaine-use disorders, participating in a randomized controlled trial of treatment as usual (TAU) versus TAU plus access to computer-based CBT (CBT4CBT), completed a computerized Drug Stroop task at pre- and post-treatment. Analyses determined whether attentional bias toward drug-related stimuli changed differentially by treatment group or cocaine use outcomes across the treatment period and whether engagement in components of CBT4CBT or TAU treatment related to changes in attentional bias toward drug-related stimuli at post- versus pre-treatment.

Results—Participants achieving a longer duration of cocaine abstinence during treatment (3+ weeks) showed greater reductions in Drug Stroop Effect than those with shorter maximum continuous abstinence. Reductions in Drug Stroop Effect across treatment were associated with

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greater engagement with CBT4CBT-specific treatment components, but not TAU-specific treatment components.

Conclusions—Reduction in attentional bias to drug-related cues and craving and/or improved executive cognitive control and response inhibition may contribute to the mechanism of action of CBT4CBT.

Keywords

cocaine; cognitive behavioral therapy (CBT); Drug Stroop; Emotional Stroop; cognitive control; attentional bias; psychotherapy

1. Introduction

Cognitive Behavioral Therapy (CBT) and computer-based CBT (CBT4CBT) (Carroll et al., 2008; Carroll et al., 2009; Carroll et al., 2014b) are efficacious treatments for cocaine use disorder. CBT4CBT modules focus on strategies to minimize the vulnerability to triggers (e.g., drug-related stimuli), such as avoiding situations likely to involve triggers, recognizing and changing drug-related thoughts, and temporizing behavior. Since CBT contains training in appraisal and coping strategies, one mechanism of action of CBT (and CBT4CBT) may be the strengthening of executive cognitive-control processes and reduction of attentional bias toward drug-related stimuli and reduced craving, which may reduce the vulnerability to drug use.

The Stroop Effect (from the Color-Word Stroop Task) is a measure of executive cognitive control requiring the individual to override the dominant tendency to read the word instead of naming the color of the ink in which the word is printed, for example, the word "red" printed in blue ink with the correct response being "blue" (Stroop, 1935). Drug Stroop tasks compare response times (e.g., indicate the color of the word) in trials with drug-related word versus neutral words. The Drug Stroop effect (i.e., slowed responding to drug, relative to neutral, stimuli) could indicate attention bias to drug-related cues, cue-induced craving, poor cognitive control and poor response inhibition, and has been proposed to be of clinical relevance in substance using populations (Field and Cox, 2008; Field et al., 2014; Smith and Ersche, 2014). The Drug Stroop effect has been demonstrated in substance-using populations and associated with severity of dependence (Ersche et al., 2010). A larger Drug Stroop Effect has been associated with poorer within-treatment cocaine-use outcomes and treatment retention in individuals with cocaine-use disorder (Carpenter et al., 2006). Drug Stroop Effect increased prior to and during periods of reported temptation to use cocaine or heroin (Waters et al., 2012), increased prior to relapse and was associated with higher likelihood of subsequent relapse (Marhe et al., 2013b; Kennedy et al., 2014). Greater drug-cue-induced craving is associated with likelihood of subsequent relapse on longer time-scales (Li et al., 2014). Pre-treatment self-reported craving and Drug Stroop Effect-related neural activity predicted cocaine use in the months following treatment in cocaine users (Marhe et al., 2013a). Drug Stroop Effect with heroin-related stimuli at pre-treatment predicted relapse in months following treatment, even after controlling for pre-treatment craving, and Drug Stroop Effect was reduced following cue-exposure therapy in heroin users (Marissen et al., 2006).

Here, analyses are presented of a secondary outcome measure (Drug Stroop task) from a randomized controlled trial (RCT) in methadone-maintained individuals with cocaine-use disorder, randomized to receive treatment as usual (TAU) or TAU plus access to CBT4CBT (CBT4CBT+TAU). We assessed whether Drug Stroop Effect changed across treatment differentially by treatment group or cocaine-use outcomes and whether it related to engagement in CBT4CBT or TAU treatment components. Given CBT4CBT's focus on recognizing triggers and coping with craving, we hypothesized a greater reduction in Drug Stroop Effect at post-versus pre-treatment in CBT4CBT+TAU versus TAU groups, and in those with better versus poorer cocaine abstinence outcomes. Furthermore, we hypothesized that greater engagement with CBT4CBT, but not TAU, treatment components will be associated with lower Drug Stroop Effect at post-treatment and greater reduction in Drug Stroop Effect at post- versus pre-treatment.

2. Methods

2.1 Participants

Participants in a RCT evaluating the efficacy of CBT4CBT for cocaine-use disorders (Carroll et al., 2014b) were eligible for the RCT if they were stabilized in methadone maintenance, met criteria for current cocaine dependence (past 30 days) (DSM-IV; American Psychiatric Association, 1994), English-speaking, had a reading-level $\geq$ 6th grade, and no untreated or unstable psychotic disorders. Drug Stroop task data were available on a subset of the individuals participating in the parent RCT. Only those with Drug Stroop data at pre-treatment and post-treatment time points were included in the analyses. Within the RCT sample (N=101), N=22 were missing Drug Stroop data at pre- or post-treatment, leaving a final randomized sample of N=79 with pre- and post-treatment Drug Stroop data. Of the RCT participants who completed treatment (N=69), N=8 were missing Drug Stroop data at pre- or post-treatment, leaving a final completer sample of N=61 with pre- and post-treatment Drug Stroop data. Drug Stroop data were missing due to the task being added after the start of the RCT.

2.2 Treatments

During the 8-week treatment trial, the standard treatment at the outpatient clinic was offered as a platform treatment. 'Treatment as usual' (TAU) consisted of daily methadone-maintenance and weekly counseling sessions. The CBT4CBT+TAU group received access to CBT4CBT over the 8 weeks in addition to TAU. The CBT4CBT program, described in detail elsewhere (Carroll et al., 2008; Carroll et al., 2014b), is a user-friendly computer-based program designed to teach CBT tools in an interactive and engaging environment. The CBT4CBT program consists of seven, 45-minute 'modules' which cover: (1) understanding and changing patterns of drug use, (2) coping with craving, (3) refusing offers of drugs and alcohol, (4) problem-solving skills, (5) challenging thoughts about drug use, (6) improving decision-making skills, and (7) HIV-risk reduction skills. Each module includes a brief check-in and agenda, introduction to skill topic, videos of characters experiencing a common risky situation and demonstrating how to use the targeted skill successfully, interactive exercises, and introduction to the practice assignment (i.e., homework). For CBT4CBT, privacy and confidentiality were protected by using a dedicated computer with a login and

password system, located in a private room at the clinic. No protected health information (PHI) is collected by the program. Computerized urn randomization balanced TAU and CBT4CBT+TAU groups on gender, race/ethnicity, education level, and cocaine use at baseline (# days of use in past month).

2.3 Assessments

Research assistants assessed participants at baseline, twice-weekly during treatment and at the 8-week treatment termination point. Detailed day-by-day self-reports of drug and alcohol use were collected with the Timeline Followback method (Robinson et al., 2014) for the 28-day period prior to randomization and throughout treatment. Measures of longest duration of abstinence during treatment were based on these self-report measures. Urine toxicology screens for cocaine, marijuana, benzodiazepines, opiates, methamphetamine were collected at each research visit. Other assessments are described in detail in the main study report (Carroll et al., 2014b). Assessments were completed at the clinic, after participants had received their methadone dose. Cognitive assessments (e.g., Drug Stroop task) were completed last, after all other assessment components were done.

2.3.1 Drug Stroop task—A computerized 'Drug Stroop' task (Reeves et al., 1991; Reeves et al., 2002) was completed at pre- and post-treatment (week 8). The task consisted of a practice and a task condition. During the practice, a series of letters were displayed on the screen in different colored font. Participants were asked to press quickly and accurately on buttons corresponding with different colored fonts, to teach color-button pairings. During the task, which required the participants to override the dominant tendency to word read, participants were shown words on the screen, written in different colored fonts and asked to press as quickly accurately as possible on buttons corresponding with the different colored font (button-color combinations were consistent with the practice condition). Words were either cocaine-related 'drug' (e.g., cocaine) or 'neutral' (e.g., chair) words.

2.4 Statistical analyses

Data presented are from a subset of parent RCT participants who were randomized to a treatment condition and performed the Drug Stroop task at pre-treatment and post-treatment (randomized N=79; treatment completer N=61). Treatment groups were compared with chi-square and ANOVAs to assess for baseline differences, as well as primary clinical outcomes, as defined in the parent RCT (Carroll et al., 2014b). Repeated measures ANOVAs were run and included trial type (drug-related versus neutral words) and time-point (pre- versus post-treatment) as within-subject factors to assess whether attentional bias toward drug-related stimuli changes across treatment, and whether this occurs differentially across treatment group or cocaine abstinence outcomes. Treatment group (CBT4CBT+TAU, TAU) or longest duration of cocaine-abstinence during treatment (greater or less than 3 weeks) were included as between-subject factors in separate ANOVAs. The 3-week cut-off for abstinence was based on prior work supporting this measure as a meaningful cocaine outcome (Carroll et al., 2014a). These analyses focused on the completer sample (N=61) because sufficient treatment exposure and duration of treatment retention (results for the randomized sample reported in Supplemental Table 1) was needed to examine treatment mechanisms. The primary outcome measure for the Drug Stroop task was mean response time (RT) for correct

responses by trial-type (drug, neutral trials). Trials with response times <100ms were excluded (n=4 trials excluded) from the calculation of participants' mean correct response times, since <100ms is considered insufficient time to visually process and respond to the stimulus. A secondary outcome measure was percent correct responses by trial-type. Generalized eta squared (η^2_G) effect sizes were calculated for the ANOVA analyses (Bakeman, 2005). Kendall's rank correlation (i.e., Kendall's tau (T)) assessed the relationship between the Drug Stroop 'Effect' (average correct response time for drug trials-average correct response time for all neutral trials) at pre-treatment, post-treatment, and change (post-pre-treatment), and indicators of treatment engagement that were TAU-related (present in both groups: number of group sessions, methadone dose), CBT4CBT-related (present in CBT4CBT condition only: number of CBT4CBT sessions, number of CBT4CBT homework assignments done); and overall days in treatment protocol. Correlations were carried out within each treatment group separately within the randomized sample (N=79), since continuous measures of exposure were used, making the restriction to treatment completers unnecessary. Correlations reported as significant survived Bonferroni corrections for multiple comparisons within each treatment group (e.g., 15 correlations within CBT4CBT+TAU; $p_{corrected}$=0.05/15=0.0033).

3. Results

3.1 Baseline demographics

There were no significant differences in demographics, baseline substance use, treatment engagement or treatment outcomes between treatment groups in completer (N=61) or randomized (N=79) samples, except baseline cigarette-smoking (CBT4CBT+TAU>TAU; randomized sample) (Table 1).

3.2 Changes in Drug Stroop task performance by treatment group and abstinence status

Changes in Drug Stroop task performance results are presented in full in Table 2.

In the analysis comparing treatment groups, within the completer sample, a trend (p<0.1) time-point-by-trial-type-by-group interaction, and significant time-point-by-group and trial-type-by-time-point interactions reflected greater reduction in RT to the drug-related (versus neutral) trials at post- versus pre-treatment in the CBT4CBT+TAU versus TAU group. This pattern indicates more reduction in Drug Stroop Effect in the CBT4CBT+TAU versus TAU group. In addition, there were significant effects on mean correct RT for time-point (pre>post-treatment; with no significant change in percent accuracy) reflecting faster RT at post- relative to pre-treatment, and trial-type (drug>neutral) indicating the expected Drug Stroop Effect (slower responding to drug versus neutral stimuli).

In the analysis comparing abstinence outcomes, within the completer sample, there was a time-point-by-trial-type-by-abstinence interaction showed greater reduction Drug Stroop Effect in the group that achieved longer (3+ weeks) abstinence during treatment, relative to the group with shorter abstinence duration. Furthermore, a time-point-by-trial-type-interaction and a main effect on mean correct RT of time-point (pre-treatment>post-

treatment) indicated less slowing to drug-related stimuli at post- versus pre-treatment (Figure 1).

Within the completer sample, there were no significant main or interactive effects on the secondary outcome of proportion correct responses when analyzed by treatment group or abstinence outcome.

3.3 Associations between Drug Stroop task performance and treatment engagement

Correlation results are reported in full in Table 3. Correlations between treatment engagement indicators and Drug Stroop Effect performance assessed whether this measure at pre-treatment, post-treatment or change (post-pre-treatment) was associated with treatment engagement and retention. Larger 'Drug Stroop Effect' scores reflect greater response time slowing to drug-related stimuli versus neutral stimuli (mean correct RT for drug - neutral trials). Change in Drug Stroop Effect scores at post- vs. pre-treatment were negatively correlated with CBT4CBT treatment engagement indicators (number of CBT4CBT Sessions, CBT4CBT Homework Assignments Done, and Days in Treatment Protocol (CBT4CBT+TAU group; Figure 2a–c). These associations were not observed at pre- or post-treatment for CBT4CBT+TAU-related treatment components and were not observed or for TAU-related treatment components in either the CBT4CBT+TAU group or the TAU group at any time-point. Therefore, more engagement with CBT4CBT, but not TAU, treatment components were associated with a greater reduction in Drug Stroop Effect at post- relative to pre-treatment.

4. Discussion

First, reduction in Drug Stroop Effect (cocaine-related cues) at post- relative to pre-treatment was affected by treatment assignment: participants assigned to CBT4CBT+TAU showed a trend towards greater reduction in Drug Stroop Effect across treatment relative to those receiving TAU. Second, individuals who achieved three or more weeks of continuous cocaine abstinence during treatment showed significantly greater reduction in Drug Stroop Effect relative to those who did not. Third, greater engagement with CBT4CBT-specific treatment components (e.g., CBT4CBT sessions, homework, days in treatment protocol within the CBT4CBT+TAU group) was associated with greater reduction in Drug Stroop Effect across treatment, despite no association with pre-treatment Drug Stroop Effect. Conversely, engagement with TAU-specific components of treatment (e.g., TAU sessions, methadone dose, days in treatment protocol within the TAU only group) did not correlate with Drug Stroop Effect at any time-point or change in Drug Stroop Effect.

Attentional bias toward drug-related cues, which could enhance the Stroop effect and interfere with executive cognitive control, is thought to relate to drug use and treatment outcomes in part due to its association with cue-induced craving as well as possible general effects on cognitive resources (e.g., (Field and Cox, 2008)). Drug Stroop Effect for cocaine related cues is associated with severity of cocaine craving (Copersino et al., 2004). Cocaine users display poorer response inhibition in response to cocaine-related cues relative to neutral cues (Pike et al., 2013). Poorer cognitive-control in response to cocaine-related cues has been found in cocaine users, compared to healthy non-substance users (Dias et al., 2015)

and is associated with more cocaine-cue-induced craving (DiGirolamo et al., 2015). Poor attentional control under increased cognitive load further worsened in the presence of cocaine-related stimuli in cocaine users (Hester and Garavan, 2009). Therefore, our findings of an association between better Drug Stroop task performance and longer abstinence and may reflect improved cognitive control in presence of drug cues, which may either arise from or result in improved ability to resist use. Greater reduction in Drug Stroop Effect in those with longer abstinence supports the clinical relevance of this measure.

Using data from a well-characterized RCT sample is a strength. A limitation of the study is that it is possible that methadone could impact cognitive task performance. All cognitive testing occurred after methadone daily dosing (so subjects should not have been in acute withdrawal) and following all other assessments. However, the time between dosing and cognitive testing could have varied somewhat across individuals, which could, theoretically, have had an impact on task performance. All subjects were stabilized on their methadone doses for at least two months prior to beginning the study and were maintained on this stable dose, which provided the benefit of minimizing methadone-related variability across test days. Furthermore, any possible variability in cognitive performance arising from this slight variation in timing between dosing and testing would mirror what would happen in clinical practice as patients meet with clinicians or participate in groups following methadone dosing. While test-retest reliability of Drug Stroop tasks may be higher than other tasks designed to measure attentional bias (e.g., visual probe), a subset of studies have found it to have acceptable test-retest reliability (Cronbach's $\alpha > 0.7$), while others have not (for review; (Ataya et al., 2012)). Test-retest reliability of the task may be lower in individuals with lower dependence on the substance used in the cues (e.g., in cigarette smokers responding to smoking cues; Spiegelhalder et al., 2011). This limitation was partially mitigated by all participants in this study meeting criteria for cocaine dependence. While the classic color-word Stroop task and emotional Stroop tasks showed high reliability when response times are directly analyzed, difference scores showed lower test-retest reliability in healthy young adults (Strauss et al., 2005). Diminished test-retest reliability could reduce power to detect treatment related effects. Nevertheless, this is the first clinical trial to indicate differential reduction in attentional bias to drug-related cues by treatment condition, in this case standard methadone maintenance versus computer-based CBT. If replicated, this suggests reduction in attentional bias may be one mechanism of action of CBT4CBT, consistent with the treatment's focus on recognizing triggers and coping with craving.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- Computer based cognitive behavioral therapy (CBT4CBT) versus treatment as usual Randomized Controlled Trial (RCT)

- Participants were methadone-maintained, seeking treatment for cocaine-use disorders

- Reduced (i.e., improved) Drug Stroop effect observed at post- versus pre-treatment

- Greater reductions in Drug Stroop effect correlated with more CBT4CBT engagement

- More reduction in Drug Stroop effect with longer within-treatment cocaine abstinence
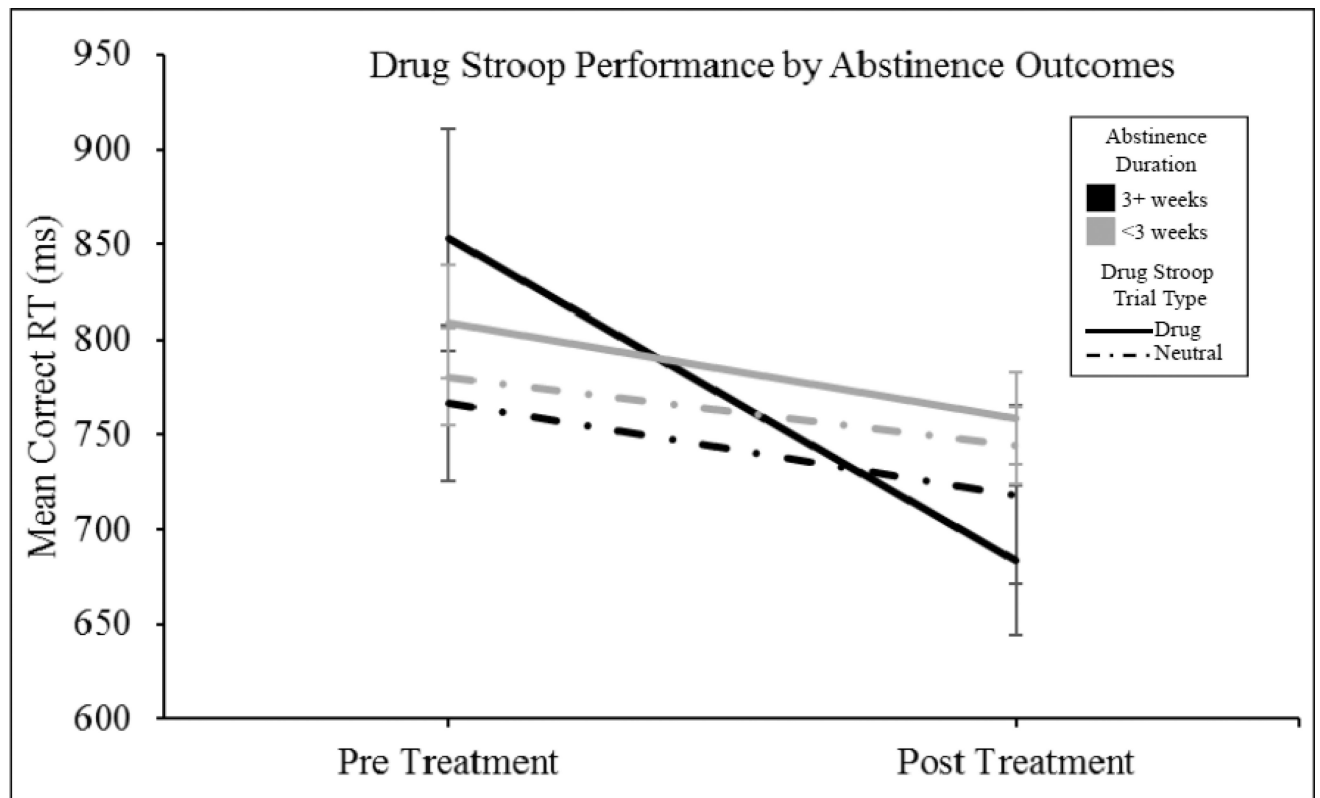
Figure 1. Changes in Drug Stroop Performance across Treatment Period by Abstinence Outcome
Within the completer sample (N=61), a significant time point (pre-, post-treatment) by trial type (drug, neutral) by longest duration of abstinence during treatment (3+ weeks; <3 weeks) reflected greater improvement in Drug Stroop performance (reduced slowing to drug-related stimuli relative to neutral stimuli) in the group that achieved longer (3+ weeks) abstinence during treatment, relative to the group with shorter abstinence duration. Color indicates abstinence outcome (black=3+ weeks continuous abstinence during treatment; gray=<3 weeks continuous abstinence during treatment). Line type indicates Drug Stroop trial type (solid=Drug trials; dotted=Neutral trials). RT= response time (in milliseconds).
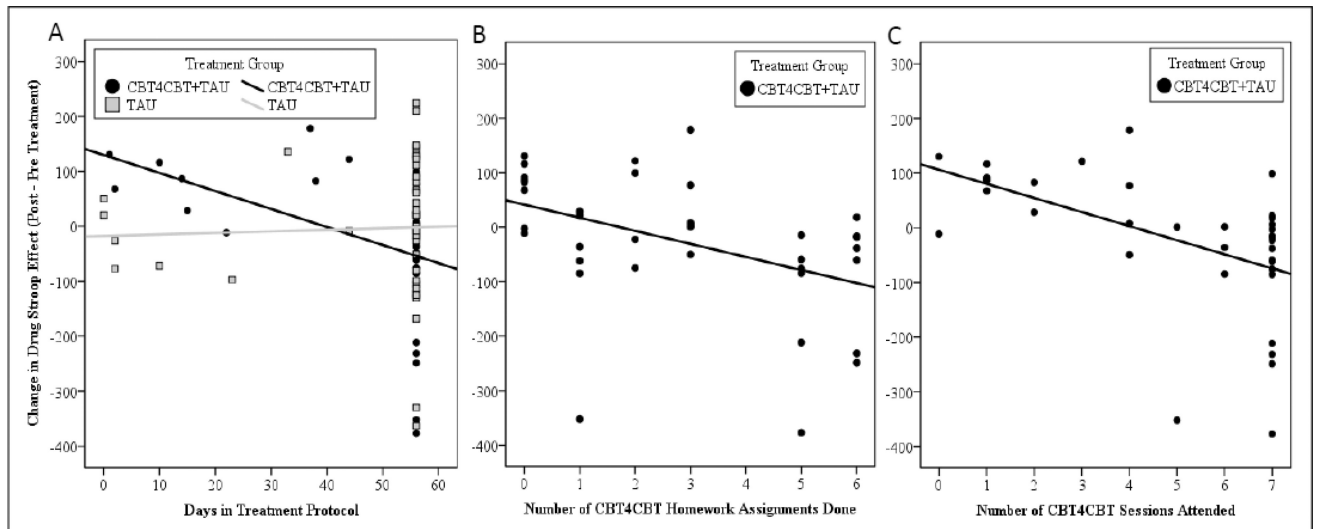
Figure 2. Associations between change in Drug Stroop Effect at post- relative to pre-treatment and indicators of CBT4CBT treatment engagement

Drug Stroop Effect indicates slower responding to drug (cocaine) cues relative to neutral cues (mean correct RT for drug trials – mean correct RT for neutral trials). Therefore, a negative change score, showing lower Drug Stroop Effect at post-treatment relative to pre-treatment, reflects an improvement on this task. Greater reduction in Drug Stroop Effect was associated with (A) more 'days in the treatment protocol' within the CBT4CBT+TAU group but not in the TAU only group; (B) more CBT4CBT homework assignments completed in the CBT4CBT+TAU group; and (C) more CBT4CBT sessions attended in the CBT4CBT group. For full correlation matrix, including non-significant associations between TAU treatment components and Drug Stroop measures, see Table 3.

Table 1

Baseline demographic, psychiatric, and substance-use characteristics by treatment group

	COMPLETER SAMPLE				RANDOMIZED SAMPLE			
	Total Completers (n=61)	CBT4CBT+TAU (n=29)	TAU (n=32)	Statistics by Treatment Group	Total Randomized (n=79)	CBT4CBT+TAU (n=38)	TAU (n=41)	Statistics by Treatment Group
Demographics				$F(p)$ or $X^2(p)$				$F(p)$ or $X^2(p)$
Sex, N (%) Female	34 (55.7)	16 (55.2)	18 (56.3)	0.01 (0.93)	46 (58.2)	23 (60.5)	23 (56.1)	0.16 (0.69)
Age	43.1 (9.2)	44.3 (8.6)	42.0 (9.8)	0.93 (0.34)	42.2 (9.6)	43.0 (9.3)	41.5 (9.9)	0.46 (0.50)
High School Graduate or Higher, N (%)	44 (72.1)	21 (72.4)	23 (71.9)	0.002 (0.96)	55 (69.6)	25 (65.8)	30 (73.2)	0.51 (0.48)
Race, N (%)				1.5 (0.68)				1.81 (0.61)
Caucasian	35 (57.4)	16 (55.2)	19 (59.4)		50 (63.3)	24 (63.2)	26 (63.4)	
African-American	20 (32.8)	11 (37.9)	9 (28.1)		22 (27.8)	12 (31.6)	10 (24.4)	
Hispanic	5 (8.2)	2 (6.9)	3 (9.4)		6 (7.6)	2 (5.3)	4 (9.8)	
Multiracial/Other	1 (1.6)	0 (0.0)	1 (3.1)		1 (1.3)	0 (0)	1 (2.4)	
Estimated IQ (SILS)	88.2 (12.6)	88.7 (12.0)	87.8 (12.8)	0.08 (0.77)	87.5 (13.1)	88.4 (13.1)	86.6 (13.3)	0.35 (0.56)
Number of months incarcerated, lifetime	41.2 (64.8)	34.8 (55.3)	47.0 (72.8)	0.53 (0.47)	36.9 (60.5)	32.7 (49.3)	40.9 (69.8)	0.35 (0.56)
On probation or parole, N (%)	8 (13.1)	2 (6.9)	6 (18.8)	1.9 (0.17)	12 (15.2)	5 (13.2)	7 (17.1)	0.24 (0.63)
Current Substance Use Measures								
Route of Cocaine Administration, N (%)				0.69 (0.71)				0.35 (0.84)
Smoke	50 (82.0)	25 (86.2)	25 (78.1)		67 (84.8)	33 (86.8)	34 (82.9)	
Snort	8 (13.1)	3 (10.3)	5 (15.6)		9 (11.4)	4 (10.5)	5 (12.2)	
Intravenous	3 (4.9)	1 (3.4)	2 (6.3)		3 (3.8)	1 (2.6)	2 (4.9)	
Methadone Dose	82.1 (27.1)	83.8 (28.7)	80.6 (25.9)	0.21 (0.65)	83.1 (26.8)	84.1 (28.2)	82.2 (25.8)	0.10 (0.76)
Age first used Cocaine	19.6 (5.0)	20.2 (5.5)	19.0 (4.5)	0.98 (0.33)	19.7 (4.9)	19.9 (5.3)	19.5 (4.6)	0.10 (0.75)
Other Lifetime Psychiatric Diagnoses, N(%)								
Alcohol-Use Disorder	49 (80.3)	25 (86.2)	24 (75.0)	1.21 (0.27)	61 (78.2)	30 (81.1)	31 (75.6)	0.34 (0.56)
Sedative-Use Disorder	20 (33.3)	10 (34.5)	10 (32.3)	0.03 (0.86)	26 (33.3)	12 (31.6)	14 (35.0)	0.10 (0.75)
Cannabis-Use Disorder	42 (71.2)	22 (75.9)	20 (66.7)	0.61 (0.44)	56 (73.7)	29 (76.3)	27 (71.1)	0.27 (0.60)
Hallucinogen-Use Disorder	9 (14.8)	4 (13.8)	5 (15.6)	0.04 (0.84)	14 (17.7)	7 (18.4)	7 (17.1)	0.03 (0.88)

	COMPLETER SAMPLE				RANDOMIZED SAMPLE			
	Total Completers (n=61)	CBT4CBT+TAU (n=29)	TAU (n=32)	Statistics by Treatment Group	Total Randomized (n=79)	CBT4CBT+TAU (n=38)	TAU (n=41)	Statistics by Treatment Group
Major Depression	20 (32.8)	10 (34.5)	10 (31.3)	0.07 (0.79)	24 (30.4)	13 (34.2)	11 (26.8)	0.51 (0.48)
Anxiety Disorder	17 (27.9)	10 (34.5)	7 (21.9)	1.20 (0.27)	23 (29.1)	13 (34.2)	10 (24.4)	0.92 (0.34)
Panic Disorder	8 (13.1)	6 (20.7)	2 (6.3)	2.78 (0.10)	12 (15.2)	8 (21.1)	4 (9.8)	1.95 (0.16)
Antisocial-Personality Disorder	5 (8.2)	3 (10.3)	2 (6.3)	0.34 (0.56)	7 (8.9)	5 (13.2)	2 (4.9)	1.67 (0.20)
Post-Traumatic Stress Disorder	10 (16.7)	6 (20.7)	4 (12.9)	0.65 (0.42)	12 (15.4)	6 (15.8)	6 (15.0)	0.01 (0.92)
Days of Use in Month Prior to Treatment[1]								
Cocaine	14.2 (9.0)	14.6 (8.7)	13.9 (9.4)	0.10 (0.76)	14.8 (9.3)	16.2 (9.5)	13.5 (9.1)	1.6 (0.20)
Heroin	1.8 (5.3)	1.4 (5.2)	2.1 (5.5	0.22 (0.64)	1.7 (5.2)	1.2 (4.6)	2.2 (5.7)	0.67 (0.42)
Alcohol	0.4 (0.5)	0.4 (0.5)	0.3 (0.5)	0.66 (0.42)	0.4 (0.5)	0.4 (0.5)	0.3 (0.5)	0.92 (0.34)
Cannabis	3.0 (6.9)	2.6 (6.6)	3.4 (7.3)	0.18 (0.68)	2.7 (6.5)	2.1 (5.8)	3.2 (7.1)	0.63 (0.43)
Cigarettes	26.4 (6.1)	27.4 (3.0)	25.5 (7.8)	1.54 (0.22)	25.7 (7.3)	27.6 (2.6)	23.9 (9.5)	**5.23 (0.03)**
Lifetime Years of Regular Use								
Cocaine	11.6 (8.5)	12.0 (6.5)	11.3 (10.1)	0.13 (0.72)	11.7 (8.4)	12.4 (6.7)	11.0 (9.7)	0.55 (0.46)
Opiate	10.2 (8.3)	9.8 (7.0)	10.6 (9.4)	0.14 (0.71)	10.8 (8.7)	10.5 (7.6)	11.0 (9.7)	0.08 (0.78)
Alcohol	8.0 (8.8)	7.6 (8.6)	8.4 (9.0)	0.13 (0.72)	8.2 (9.5)	8.9 (10.4)	7.5 (8.7)	0.40 (0.53)
Cannabis	8.3 (9.3)	6.7 (7.5)	9.8 (10.6)	1.74 (0.19)	8.0 (9.5)	6.9 (8.1)	9.0 (10.6)	0.91 (0.34)
Treatment Engagement								
Days in Treatment (out of 56)	56.0 (0.0)	56.0 (0.0)	56.0 (0.0)	0.00 (1.00)	47.7 (17.6)	47.6 (17.1)	47.9 (18.2)	0.01 (0.94)
Number of CBT4CBT Sessions Attended	n/a	6.2 (1.4)	n/a	n/a	n/a	5.1 (2.5)	n/a	n/a
Number of CBT4CBT Homework Assignments Done	n/a	3.5 (2.1)	n/a	n/a	n/a	2.8 (2.2)	n/a	n/a
Number of Group TAU Sessions Attended	8.3 (13.7)	6.4 (9.5)	9.8 (16.4)	0.92 (0.34)	8.34 (13.2)	6.4 (9.0)	10.0 (15.8)	1.18 (0.28)
Treatment Outcome Measures								
% Urines Negative for Cocaine Within Treatment Period	24.4 (29.7)	29.8 (33.5)	19.5 (25.2)	1.87 (0.18)	22.8 (31.1)	25.4 (34.0)	20.1 (27.9)	0.53 (0.47)
% Days Self-reported Abstinence Within Treatment Period	62.7 (27.9)	65.6 (27.8)	60.0 (28.1)	0.60 (0.44)	59.3 (30.1)	59.6 (31.5)	59.0 (29.2)	0.01 (0.93)
Longest Duration Continuous Abstinence Within Treatment Period (Days)	12.4 (12.9)	14.1 (14.3)	11.0 (11.6)	0.87 (0.35)	11.0 (12.5)	11.3 (13.5)	10.6 (11.6)	0.06 (0.82)
3+ Weeks Continuous Abstinence, (N (%))	11 (18.0)	8 (27.6)	3 (9.4)	3.4 (0.07)	12 (15.2)	8 (21.1)	4 (9.8)	1.95 (0.16)

[1]Days of use in month prior to treatment was out of a possible total of 28 days (i.e., past four weeks) Results are reported as mean (SD) unless otherwise noted, in which case it is reported as N (percent)

SILS=Shipley Institute of Living Scale; RT= response time; ms =milliseconds

Table 2

Drug Stroop Task Performance

I. Drug Stroop Behavior: Means, SD

	Completers (N=61)					
	Total (n=61)		CBT4CBT+TAU (n=29)		TAU (n=32)	
	Mean	SD	Mean	SD	Mean	SD
Ii. Pre-Treatment						
Drug Trials: Mean Correct RT (ms)	817.02	204.75	824.00	217.03	810.69	196.23
Neutral Trials: Mean Correct RT (ms)	778.15	171.26	784.38	156.51	772.50	185.94
Drug Trials: Proportion Correct	0.97	0.04	0.96	0.05	0.98	0.04
Neutral Trials: Proportion Correct	0.97	0.03	0.97	0.03	0.97	0.03
Iii. Post-Treatment						
Drug Trials: Mean Correct RT (ms)	745.22	168.77	699.76	129.60	786.43	190.46
Neutral Trials: Mean Correct RT (ms)	739.54	145.08	722.10	133.62	755.35	155.13
Drug Trials: Proportion Correct	0.94	0.14	0.94	0.11	0.94	0.17
Neutral Trials: Proportion Correct	0.95	0.07	0.95	0.05	0.95	0.08

II. Drug Stroop Statistics

	Completers (N=61)					
	Mean Correct RT			Percent Correct		
IIi. Between Subject Factor: Treatment Group	$F (df=1,59)$	p	η^2_G	$F (df=1,59)$	p	η^2_G
Trial Type (Drug, Neutral)	**5.75**	**0.02**	0.004	1.86	0.18	0.003
Time Point (Pre-, Post-Treatment)	**11.60**	**0.001**	0.027	*2.90*	*0.09*	0.018
Treatment Group (CBT4CBT+TAU; TAU)	0.36	0.55	0.005	*0.14*	*0.07*	0.001
Trial type × time point	**4.51**	**0.04**	0.003	1.00	0.32	0.001
Time point × treatment group	**4.70**	**0.03**	0.011	0.14	0.713	0.001
Trial type × treatment group	2.07	0.16	0.035	0.53	0.47	0.084
Trial type × time point × treatment group	2.85	*0.097*	0.002	0.36	0.55	0.001
IIii. Between Subject Factor: Abstinence Outcome	$F (df=1,59)$	p	η^2_G	$F (df=1,59)$	p	η^2_G
Trial Type (Drug, Neutral)	3.93	0.05	0.003	1.98	0.17	0.003
Time Point (Pre-, Post-Treatment)	**11.78**	**0.001**	0.028	1.21	0.28	0.008

Abstinence Outcome (</>3 weeks abstinence)	0.12	0.73	0.002	0.26	0.61	0.002
Trial type × time point	**10.8**	**0.002**	0.006	0.001	0.98	0.000
Time point × abstinence outcome	2.18	0.15	0.005	0.13	0.72	0.001
Trial type × abstinence outcome	0.03	0.86	0.032	0.37	0.55	0.082
Trial type × time point × abstinence outcome	**6.79**	**0.01**	0.004	1.46	0.23	0.002

CBT4CBT=computer based cognitive behavioral therapy; TAU=treatment as usual; ms=milliseconds. Statistics in bold are significant (p<.05) and in bold italics are trend

η^2G= Generalized Eta Squared

Table 3

Associations between Drug Stroop Effect and Indicators of Treatment Engagement

TREATMENT ENGAGEMENT INDICATORS		CBT4CBT +TAU Treatment Group			TAU Treatment Group		
		Pre-Treatment	Post-Treatment	Change (PostTx - PreTx)	Pre-Treatment	Post-Treatment	Change (PostTx - PreTx)
TAU Treatment Components							
# Group TAU Sessions During Active Treatment	T	−0.061	−0.171	−0.044	0.085	0.041	0.002
	p	0.664	0.221	0.752	0.494	0.738	0.988
	N	29	29	29	35	35	35
Methadone dose	T	0.08	0.101	−0.01	0.1	−0.045	−0.076
	p	0.487	0.384	0.93	0.38	0.69	0.501
	N	38	38	38	41	41	41
CBT4CBT Treatment Components							
# Computerized CBT (CBT4CBT) Sessions Attended	T	0.215	−0.229	−0.463	.	.	.
	p	0.083	0.065	0.0002	.	.	.
	N	38	38	38	.	.	.
# CBT Homework Assignments Done	T	0.199	−0.162	−0.363	.	.	.
	p	0.099	0.179	0.0026	.	.	.
	N	38	38	38	.	.	.
Overall Study Treatment Duration							
Days in treatment protocol	T	0.199	−0.265	−0.488	−0.004	0.016	0.037
	p	0.123	0.04	0.0002	0.974	0.896	0.769
	N	38	38	38	41	41	41

Correlations between Drug Stroop Effect (mean correct RT for drug trials - mean correct RT for neutral trials; at pre-treatment, post-treatment and change (Post- Pre Treatment)) and measures of treatment engagement were run within the randomized sample (N=79), split by treatment group (CBT4CBT+TAU=38; TAU=41). CBT= cognitive behavioral therapy; TAU=treatment as usual; Tx=treatment; T= tau= Kendall's rank correlation coefficient. CBT homework was assigned at CBT4CBT sessions, and the correlation between these two variables was T=0.59 (p<.001). Fifteen correlations were run within the CBT4CBT+TAU group. A Bonferroni-corrected p-value for these multiple comparisons would be pcorrected=0.05/15=0.0033. Therefore, the associations between change in Drug Stroop and number of CBT4CBT sessions, number of CBT homework assignments done, and number of days in treatment protocol within the CBT4CBT+TAU group remain significant following Bonferroni correction (indicated with gray highlights).