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Implicit and Explicit Drug-Related Cognitions during Detoxification Treatment are Associated with Drug Relapse: An Ecological Momentary Assessment Study

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Abstract

Objective—Relapse is a major problem in drug addiction treatment. Both drug craving and drug-related cognitions (e.g., attentional bias and implicit attitudes to drugs) may contribute to relapse. Using ecological momentary assessments (EMA), we examined whether craving and cognitions assessed during drug detoxification treatment were associated with relapse.

Method—Participants were 68 heroin-dependent inpatients undergoing clinical detoxification at an addiction treatment center. Participants carried around a personal digital assistant (PDA) for 1-week. Participants completed up to 4 random assessments (RAs) per day. They also completed an assessment when they experienced a temptation to use drugs (TA). At each assessment, participants reported their craving and attitudes to drugs. Implicit cognitions were assessed with a drug Stroop task (attentional bias) and an Implicit Association Test (implicit attitudes).

Results—Individuals who relapsed during the study week exhibited a larger attentional bias and more positive implicit attitudes to drugs than non-relapsers at TAs (but not RAs). In addition, compared to non-relapsers, relapsers reported higher levels of craving and more positive explicit attitudes to drugs at TAs compared to RAs. Additional within-subject analyses revealed that attentional bias for drugs at TAs increased before relapse.

Conclusions—Drug-related cognitive processes assessed using EMA were associated with relapse during drug detoxification. Real-time assessment of craving and cognitions may help to identify individuals at risk of relapse, and when they are at risk of relapse.

Keywords

heroin dependence; ecological momentary assessment; relapse; attentional bias; implicit associations

Relapse prevention is arguably the most important problem in substance dependence treatment. Generally, drug-dependent patients start substance abuse treatment with detoxification. However, more than 50% of patients do not complete detoxification treatment (Franken & Hendriks, 1999; Hättenschwiler, Rüesch, & Hell, 2000; Day & Strang,

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2011) and usually relapse to drug use soon afterwards (Gossop, Green, Phillips, & Bradley, 1987; Gossop, Stewart, Browne, & Marsden, 2002). It is therefore critical to understand the psychological processes underlying treatment drop-out and relapse so that more effective interventions can be developed.

Several theories on the maintenance of substance use and relapse focus on the role of craving (e.g., Ludwig, Wikler, & Stark, 1974; Wise, 1988). Many studies have reported that self-reported craving is a predictor of treatment outcome and relapse (see McKay, 1999). However, not all studies have demonstrated this and its role seems to be dependent on how it is measured (Sayette et al., 2000; Rosenberg, 2009). Studies have also examined the role of self-reported attitudes toward substance use; in the current context this refers to feelings or cognitions towards substance use. Studies that have examined the association between self-reported attitudes towards substances and substance use behavior have yielded mixed findings. For example, Burden and Maisto (2000) reported that self-reported positive attitudes towards alcohol consumption predicted heavier drinking behavior at 1-month follow-up, whereas De Leeuw, Engels, Vermulst, and Scholte (2008) reported that self-reported positive attitudes towards smoking did not predict smoking behavior of adolescents at 1-year follow-up.

Much recent research has also focused on the role of drug-related cognitive processes underlying addiction and relapse (e.g., Franken, 2003). According to these models both implicit (or automatic) and explicit (or controlled) cognitive processes play a role in drug use and relapse. Implicit cognitions are automatic, fast processes that can be measured indirectly using behavioral measures, usually reaction time tasks. Explicit cognitions are more controlled, slower processes and can be measured via self-report (Wiers & Stacy, 2006). An advantage of using implicit measures is that participants are generally unaware of the purpose of the assessment. The implicit measures may therefore be a more objective measure of internal processes (e.g., Fazio & Olson, 2003). In contrast, self-report measures require a certain level of insight into one's own motivational and cognitive processes. Therefore, self-report measurements can be biased by limited insight into these motives or processes and by other biases such as social desirability (Marissen, Franken, Hendriks, & van den Brink, 2005).

In addiction research, the two most studied implicit cognitive processes are attentional bias and implicit memory associations (Wiers & Stacy, 2006). Attentional bias refers to exaggerated attentional processing of drug-related stimuli. It is often assessed using the drug Stroop task in which participants are required to classify the colors of drug-related and neutral words; slower responses on the former indicates an attentional bias to drug-related stimuli (Cox, Fadardi, & Pothos, 2006). Heroin- and cocaine-dependent patients exhibit a robust attentional bias to drug-related words on this task whereas control subjects do not (Franken, Kroon, Wiers, & Jansen, 2000; Hester, Dixon & Garavan, 2006; Constantinou et al., 2010). Implicit memory associations are usually measured with the Implicit Association Test (IAT; Greenwald, Nosek, & Banaji, 2003). Drug users tend to exhibit more positive (less negative) automatic associations with drug-related cues than non-users (see Roefs et al., 2011 for review of IAT and addiction literature).

Most pertinent to the present study, it has been hypothesized that both attentional bias (e.g., Franken, 2003) and implicit associations (e.g., Wiers & Stacy, 2006) can contribute to relapse. Several studies have examined the prospective association between implicit cognitions and substance use or relapse. Specifically, it has been reported that attentional bias predicts substance use and/or relapse in nicotine dependence (Waters et al., 2003; Janes et al., 2010; Powell, Dawkins, West, Powell, & Pickering, 2010), alcohol abuse (Cox, Hogan, Kristian, & Race, 2002; Cox, Pothos, & Hosier, 2007) and heroin or cocaine

dependence (Carpenter, Schreiber, Church, & McDowell, 2006; Marissen et al., 2006). In non-clinical populations it has been reported that implicit attitudes predict use of alcohol (e.g., Wiers, van Woerden, Smulders, & de Jong, 2002), cigarettes (McCarthy & Thompson, 2006) and cannabis (Ames et al., 2007). However, no studies have examined the role of implicit associations in relapse during or after treatment (see also Roefs et al., 2011).

The aforementioned studies have been conducted in laboratory settings. A limitation of laboratory settings is that there may be a long lag between the assessment of cognition (and craving) and the occurrence of relapse. This lag might diminish the reported associations (Shiffman, 2000; Field, Munafo, & Franken, 2009). Moreover, it is uncertain whether craving or cognitions assessed in the laboratory accurately capture craving and cognitions experienced in the natural environment. Finally, in laboratory studies it is difficult to collect extensive longitudinal data from participants, making it difficult to understand how craving and cognition change over time.

Ecological momentary assessment (EMA) is an emerging methodology that can obviate these concerns (Stone, Shiffman, Atienza, & Nebeling, 2007). EMA can assess fluctuating and context dependent phenomena in real-time and has been used successfully in a variety of psychiatric populations including the addictions (e.g., Shiffman & Waters, 2004; Epstein et al., 2009). In EMA, assessments are typically completed at random times and when participants experience heightened emotions or motivational states. In addiction research, assessments taken during temptation episodes can be highly informative, because there may be commonalities in the psychological processes underlying temptation episodes and relapse episodes (Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996; Shiffman, 2009; Waters, Marhe, & Franken, 2012). EMA studies also yield rich longitudinal datasets, allowing researchers to investigate how variables such as craving (Shiffman et al., 1997) and negative affect (Shiffman & Waters, 2004) change in the days leading up to relapse.

The recent development of portable electronic devices has facilitated the collection of EMA data in the addictions (e.g., Freedman, Lester, McNamara, Milby, & Schumacher, 2006). For example, Preston et al. (2009) reported an EMA study that examined the association between cocaine craving and cocaine use. During the five hours prior to cocaine relapse, ratings of cocaine craving at random assessments significantly increased. This study provided real-time evidence for the association between self-reported craving and subsequent relapse.

As noted before, implicit cognitions might also be important predictors of relapse (e.g., Marissen et al., 2006). Although it is feasible to administer reaction time tasks on electronic devices in EMA studies (e.g., Tiplady, Oshinowo, Thomson, & Drummond, 2009; Waters & Li, 2008), no previous study has assessed the predictive utility of implicit cognitions administered during EMA.

In sum, the main goal of the study was to examine whether implicit cognitive measures (i.e. attentional bias and implicit associations) and/or self-reported craving and explicit attitudes assessed using EMA were associated with relapse during heroin detoxification treatment. In doing so we also examined whether implicit and explicit cognitions were elevated in the days preceding relapse. We hypothesized that relapsers would report higher levels of self-reported craving and more positive explicit attitudes towards drugs than non-relapsers. We also hypothesized that relapsers would exhibit higher levels of attentional bias for drugs and a more positive implicit association with drugs than non-relapsers. Previous research has revealed that increases in craving are observed during the five hours before a relapse (Preston et al., 2009) and on the morning of the relapse day (Shiffman et al., 1997). Given

that attentional bias may precede (and contribute to) craving (Franken, 2003), we hypothesized that attentional bias may be elevated in the days prior to relapse.

Methods

Participants

Sixty-eight heroin-dependent inpatients (58 males) were recruited from a large addiction treatment center in an urban area (Bouman GGZ, Rotterdam, The Netherlands). Inclusion criteria for this study were: 1) aged between 18 and 65 years; 2) presence of the *DSM-IV* diagnosis for heroin dependence (assessed by both a physician and a research psychologist); and 3) the ability to speak, read, and write in Dutch at an eighth-grade literacy level. Exclusion criteria were: 1) indications of severe psychopathology (i.e., psychosis, severe mood disorder, as assessed by a physician); 2) self-reported color blindness or (non-corrected) defective vision; and 3) pregnant or breast-feeding.

The mean age of the participants was 40.9 years ($SD = 7.7$). Of the total 68 participants, 14.9% completed primary education, 56.7% completed junior secondary education, 25.4% completed senior secondary education, and 3% completed higher education. Of all participants, 51.5% reported Dutch nationality and origin, 33.8% reported Dutch nationality but other origin, and 14.7% reported other nationality and origin. All participants were heroin dependent. Although cocaine dependence was not an inclusion criterion, most participants were also cocaine dependent (88.1%), and those who were not had used cocaine regularly for an average of 10.1 years. Additionally, 95% of all participants had used heroin in the week prior to intake in the detoxification treatment. During the past month, participants reported using heroin on an average of 21.3 days ($SD = 9.1$) and cocaine on 19.0 days ($SD = 10.1$). The mean reported age of first heroin use was 22.3 years ($SD = 6.7$) and the mean reported total years of heroin use was 14.1 years ($SD = 8.7$). The mean reported age of first cocaine use was 22.3 years ($SD = 8.5$) and the mean reported total years of cocaine use was 12.4 years ($SD = 7.9$). Inhalation was endorsed as the main administration route for both heroin (85.3% of all participants) and cocaine (86.8% of all participants).

The study was approved by the Ethics Committee of the Erasmus Medical Center, Rotterdam, The Netherlands. All procedures were carried out with the adequate understanding and written informed consent of the participants.

Treatment Setting

The inpatient detoxification unit where the study was carried out consists of two living and dining rooms, a nicotine smoking room, a small kitchen and a garden. All patients had their own private bedroom. The usual duration of a detoxification treatment in this setting is three weeks. The specific goal of this detoxification treatment is to reduce physical and mental withdrawal symptoms, in this case heroin withdrawal symptoms. In the present study, 63 participants (95%) of participants ($n = 66$, as there were missing data from 2 participants) were placed on methadone maintenance at admission (mean starting dose = 58.9 mg, $SD = 26.8$). The mean number of days of methadone use ($n = 65$, there were missing data from 3 participants) during the study was 6.57 days ($SD = 1.51$). After the 3-week detoxification treatment, the patients started a follow-up treatment. This is a rehabilitation program with a duration between one month and two years, depending on the severity of the problems. Occasionally, the detoxification treatment staff decided to discharge patients after 3-weeks if they had successfully finished detoxification and did not need further treatment.

Procedure

Participants were informed about the study on the second day of detoxification treatment. They had 24 hours to decide whether to participate. Volunteers signed the informed consent form on the third day of detoxification treatment. They then completed several questionnaires (data from questionnaire assessments will be reported elsewhere) and were trained to use the PDA. Participants carried the PDA around for 7 days; that is, from the third day of detoxification treatment until the ninth day of treatment. All study materials were written in Dutch.

The PDA was programmed to beep four times each day at random times (Random Assessment; RA). Participants were also instructed to press a PDA button whenever they experienced an acute rise in urge to use heroin or cocaine or when they felt they were on the brink of acquiring and using heroin or cocaine (Temptation Assessment; TA). At each RA or TA assessment, participants responded to items assessing subjective (e.g., craving), pharmacological (e.g., use of coffee, alcohol and cigarettes), and contextual variables (e.g., the present environment/room, light conditions, presence of others). Subsequently, the PDA administered either a drug Stroop task or a drug IAT (detailed below; see Figure 1). The PDA was programmed to administer the two tasks in an alternating sequence to each participant. After completion of the study, the participant returned the PDA and received financial compensation. Compensation was contingent on the number of completed RAs (max. 50 Euro).

During treatment, a patient was permitted to go on leave for a couple of hours upon staff approval. Therefore, participants could lapse (take heroin or cocaine) while offsite (away from the clinic). All reported relapses occurred offsite. To prevent PDA loss, participants were not permitted to take the PDA with them offsite. Therefore, all PDA assessments were completed at the detoxification unit.

EMA measures

Because most participants were cocaine dependent or had used cocaine regularly (as noted earlier) we used both heroin and cocaine versions of all behavioral tasks and subjective measures (where appropriate, see below). Both versions were administered to all participants.

Subjective measures—Participants were asked to respond according to how they feel “at this moment”. Unless otherwise indicated, participants made their responses on seven-point Likert scales (1=strongly disagree to 7=strongly agree). Craving for heroin, craving for cocaine (e.g., “At this moment, I am craving heroin”), explicit attitude to heroin, (“At this moment, please indicate your overall attitude to heroin”; 1=strongly negative to 7=strongly positive), explicit attitude to cocaine, and difficulty concentrating were assessed with single items. Explicit attitudes were only administered on those assessments during which an IAT was administered. Several additional items, not reported here, assessed affect, contextual variables, pharmacological variables and number of interruptions (Waters et al., 2012).

Drug Stroop task

The PDA version of the Stroop task has been described in detail elsewhere (see Waters & Li, 2008; Waters et al., 2012). Briefly, the instructions on the PDA stated that words written in different colors would be presented on the PDA screen one after the other and that the task was to indicate as rapidly and as accurately as possible which color the word was written in by pressing one of the three response buttons on the PDA using the stylus. The response buttons were boxes with color names within them (green, red, and blue). Participants were informed that they should ignore the meaning of the (target) word itself

and just respond to the color. At each assessment, participants responded to a practice sequence of letter strings (33 trials), followed by two test blocks of 33 trials each. Each word was presented in capital letters and remained on the screen until the participant responded or a time-out of three seconds.

Stimulus materials—Participants completed either a heroin-Stroop or a cocaine-Stroop at each Stroop assessment. The Stroop task was randomly selected (without replacement) from one of 24 sequences of words (“lists”). Twelve lists (1-12) contained heroin words and matched neutral words (heroin-Stroop), and the other twelve (13-24) contained cocaine words and matched neutral words (cocaine-Stroop). The positions of the response buttons on the screen varied across lists (e.g., on list 1 they were ordered [Blue] [Green] [Red]; on list 2 they were ordered as [Green] [Red] [Blue]). Order of presentation of neutral words and drug words was counterbalanced across lists.

In the heroin-Stroop, each list contained 11 heroin-related words (score, flash, smack, dope, dealer, junk, shot, ball, heroin, inhale, high) and 11 neutral words drawn from the category “transport” (ticket, metro, tram, moped, bike path, scooter, zebra crossing, asphalt, gasoline, freeway, racing), matched on word length and word frequency from the CELEX database (Baayen, Piepenbrock, & Gulikers, 1995). In the cocaine-Stroop each list contained 11 cocaine words (pipe, puff, crack, smoke, cocaine, blow, line, coke, snort, powder, base) and 11 neutral words drawn from the category “indoor features” (rug, blanket, sofa, oven, lamp, attic, cabinet, armchair, tap, couch, stove), matched on word length and word frequency.

Scoring—Reaction times (RTs) from incorrect responses were discarded (3.5% of trials), as were RTs < 100 ms (0.01% of trials). To reduce the influence of RT outliers caused by interruptions, up to four RTs from assessments with reported interruptions were discarded (0.68% of trials), as described elsewhere (Waters & Li, 2008). A difference score between mean RT on drug Stroop words and mean RT on linked neutral words was computed to create a drug Stroop effect on each assessment. The estimated internal (split-half) reliabilities of the heroin-Stroop and cocaine-Stroop effects were $r = .72$ and $r = .68$, respectively (Waters et al., 2012).

Drug IAT

The IAT consists of two tasks. On Task 1, participants are required to respond rapidly with a key press to items representing two concepts (e.g., heroin + pleasant) and with a different key press to items from two other concepts (e.g., no heroin + unpleasant). In Task 2, the assignment of one concept is switched. In the current case, no heroin + pleasant shared a response, and heroin + unpleasant shared the other response. The main idea is that it is easier to perform the key presses when the two concepts are strongly associated in memory than when the two concepts are unrelated. The IAT effect is a measure of the difference in response times on Task 1 vs Task 2. The IAT effect is an index of the relative strength of automatic associations. In the example above, it indicates whether associations are stronger between heroin and pleasant, and no heroin and unpleasant, than between no heroin and pleasant, and heroin and unpleasant.

The heroin IAT consisted of four blocks: 1) First block of Task 1 (e.g., heroin + pleasant/no heroin + unpleasant); 2) Second block for Task 1; 3) First block of Task 2 (e.g., no heroin + pleasant/heroin + unpleasant); 4) Second block for Task 2. At each assessment, participants were randomly assigned to complete one of four IATs: (a) heroin + pleasant first, pleasant on left; (b) heroin + pleasant first, unpleasant on left; (c) heroin + unpleasant first, pleasant on left; (d) heroin + unpleasant first, unpleasant on left. Analogous procedures were used for cocaine IAT. There were no practice blocks.

On each trial, a stimulus (picture or word) was presented in the center of the PDA screen. On the top of the screen were labels (on each side of the screen) to remind participants of the categories assigned to each key for the current task. Participants responded to the categorization task by pressing either the left or the right key under the screen on the PDA. They were instructed to respond as quickly and as accurately as possible. The program randomly selected items such that the sequence of trials alternated between the presentation of a (heroin/no heroin or cocaine/no cocaine) picture and the presentation of a (pleasant/unpleasant) word. If the participant made an error, a red "X" appeared below the stimulus and remained there until the participant responded correctly. Participants were instructed to correct their errors as quickly as possible. The inter-trial interval was 150 ms.

IAT Stimulus materials—Ten heroin and 10 neutral pictures were used in the heroin IAT and 10 cocaine and 10 (different) neutral pictures in the cocaine IAT. Twelve words were used for pleasant (Dutch equivalent of nice, pleasant, cool, relaxing, soothing, restful, smooth, peaceful, positive, friendly, satisfying, calm) and unpleasant (nasty, unpleasant, dirty, foul, smelly, unhealthy, ugly, negative, antisocial, depressing, harmful, revolting).

Scoring—The error rate on the IAT was 13.0%. The IAT D score recommended by Greenwald and colleagues was used to derive the IAT effect (Greenwald et al., 2003, Table 4). The untransformed IAT effect (in ms) is also reported to assist in interpretation. The estimated internal (split-half) reliability of the IAT effect was .64 (ms score) and .72 (D score) for the heroin IAT and .72 (ms score) and .77 (D score) for the cocaine IAT (Waters et al., 2012).

Relapse measures

The primary relapse measure was relapse during the PDA study week (i.e., from day three to day nine of treatment; termed "Early Relapse"). On the fourth day of the study week, and at the end of the study week, a researcher asked the participant to report whether or not he or she had used heroin or cocaine during the study. If they reported use, they were asked to recall on which day or days of the study week they had used heroin or cocaine. Participants were assured that their report was confidential and was only to be used for research purposes. Early Relapse was defined as at least one reported heroin or cocaine use during the PDA study week and was coded dichotomously (early relapsers vs. non-EMA relapsers). Treatment dropouts were coded as early relapsers because research has shown that dropouts from residential treatment usually relapse to drug use soon afterwards (Gossop et al., 1987, 2002).

The secondary relapse measure was relapse after the study (termed "Late Relapse"). Late Relapse was assessed until the end of detoxification treatment (i.e., two weeks after the PDA study). Self-reported relapse was assessed for one week after the PDA study. Late Relapse was defined as at least one reported heroin or cocaine use during detoxification treatment but occurring after the PDA study week, or the presence of at least one positive urine screen, and was coded dichotomously (late relapsers vs. never-relapsers). Treatment dropouts during this period (between the end of the PDA study and end of detoxification) were also coded as late relapsers (Gossop et al., 1987, 2002).

PDA hardware and software

Study procedures were implemented on a HP iPAQ Pocket PC running the Microsoft Windows Pocket PC operating system (Waters et al., 2012). The iPAQ uses a pen-based, touch-screen system. Participants could prevent the PDA from presenting RAs for up to 2 hours ("suspend" function). Participants could also delay RAs by 5 minutes (up to four times

per RA). Participants were encouraged to use the suspend and delay functions as infrequently as possible.

Data Reduction and Analysis

Of the 68 participants, 64 contributed data to the study. Data from 2 participants were lost due to PDA error. One participant dropped out immediately following the PDA training because he did not comprehend the procedures, and 1 participant relapsed prior to completing any assessments. Of the remaining 64 participants, 10 were early relapsers (relapsed during study) and 54 were non-EMA relapsers (did not relapse during study)¹. The 10 early relapsers completed 147 assessments prior to relapse (38 TAs, 109 RAs). The 54 non-EMA relapsers completed 1290 assessments (301 TAs, 989 RAs). A relapse (or drop-out) date was known for all 10 early relapsers. Of the 54 non-EMA relapsers, 25 participants were late relapsers (relapsed after study). They completed 583 assessments (118 TAs, 465 RAs). A relapse date was known for 9 late relapsers. There were 29 never-relapsers. They completed 707 assessments (183 TAs, 524 RAs).

Linear mixed models (LMM) were used for the relapse analyses using SAS PROC MIXED. LMM analyses take into account the dependence between observations due to clustering of the data by participants. The analyses also allow for different numbers of observations across participants. To select an appropriate working correlation structure, we first ran LMM analyses under two commonly used correlation structures (compound symmetry and first-order autocorrelation) and compared the resulting Akaike/Schwartz information criteria (AIC/BIC). Based on the reported AIC/BIC (smaller is better), we selected the more appropriate working correlation structure for each dependent variable. For significant results, parameter estimates from the mixed model were reported as an (unstandardized) measure of effect size (Wilkinson, 1999). For the analyses of relapse status, the dependent variables were: craving for heroin; craving for cocaine; difficulty concentrating; explicit attitude to heroin; explicit attitude to cocaine; drug Stroop; and drug IAT.

First, we examined the associations between relapse and the number of temptations reported. The dependent variable was the number of temptations reported on each day. In separate models using data from 400 days ($n = 64$ participants) and 358 days ($n = 54$ participants) respectively, we examined whether Early Relapse Status and Late Relapse Status was associated with number of temptations. To control for the effect of time, day in study was included as a covariate in these models. These analyses address the question “Do individuals who subsequently relapse report more temptations than those who do not relapse?”

Second, we examined the association between Early Relapse status and the dependent variables listed above ($n = 64$ participants, 1437 assessments). Assessment Type (TA vs RA) was entered as a class (categorical) variable. To control for the effect of time, day in study was entered as a continuous variable. Number of assessments within each day was entered as a continuous variable. For analyses on the drug Stroop or drug IAT, drug type (heroin- vs. cocaine-Stroop; heroin- vs. cocaine-IAT) was entered as a class variable. The primary independent variable, Early Relapse Status, was entered as a class variable (early relapser vs. non-EMA relapser). Given that many study measures were significantly elevated during temptation episodes (Waters et al., 2012), and given that relapse risk might arguably be best assessed from responses in temptation episodes, we tested the interaction term between Early Relapse Status and Assessment Type (a detailed analysis of the comparison between TAs and RAs is reported in Waters et al., 2012). If a significant Early Relapse Status and

¹Of the 10 early relapsers, 9 reported at least one relapse and 1 dropped out of treatment during the study week. Of the 25 late relapsers, 9 reported at least one relapse during the first week after the PDA study; of the remaining 16, 11 dropped out of treatment and 5 had at least one positive urine during the last week of treatment.

Assessment Type was observed, follow-up analyses tested the effect of Early Relapse Status at TAs and RAs separately (using LMM). If a significant interaction was not observed, the interaction term was dropped from the model, and the F values from the reduced model were reported. The analyses described above address the question “Do individuals who subsequently relapse (during the PDA study) differ in craving and cognition at TAs and RAs from individuals who do not relapse?” To bolster the LMM analyses, for the variables where a significant interaction or main effect was observed with LMM, we used logistic regression to test whether craving and cognition at TAs and RAs were associated with relapse. In these subject-level analyses, measures of craving and cognition (aggregated over all TAs and RAs) were the independent variables, and relapse was the dependent variable. These analyses address the question “Is craving and cognition at TAs and RAs (during the PDA study) prospectively associated with relapse (during the PDA study)?”

Third, we examined the association between Late Relapse status and dependent variables listed above ($n = 54$ participants, 1290 assessments). Thus, these analyses used data from the 54 participants who did not relapse during the PDA study. As before, day in study, number of assessments, and drug type were entered into the model. The primary independent variable, Late Relapse Status (late relapser vs. never-relapser) was entered as a class variable. As above, using LMM, we tested the Late Relapse by Assessment Type interaction term. If a significant Late Relapse Status by Assessment Type interaction was observed, follow-up analyses tested the effect of Late Relapse Status at TAs and RAs separately (using LMM). If a significant interaction was not observed, the interaction term was dropped from the model, and the F values from the reduced model were reported. These analyses address the question “Do individuals who subsequently relapse (after the PDA study) differ in craving and cognition at TAs and RAs from individuals who never relapse?” As before, for the variables where a significant interaction or main effect was observed, we used logistic regression to test whether craving and cognition at TAs and RAs were associated with subsequent relapse. These analyses address the question “Is craving and cognition at TAs and RAs (during the PDA study) prospectively associated with relapse after the study?”

The analyses described above are between-subject analyses that compared craving and cognition in relapsers and non-relapsers. The analyses examine “who” is at risk of relapse. Additionally, to examine the precipitants of relapse during the PDA study, we used mixed model logistic regression analyses. These analyses compared craving and cognition at the RA and TA most proximal to the relapse with craving and cognition at all other RAs and TAs completed by the participant (control cases that were not followed by relapse). In these analyses, relapse was the dependent variable, and the measures of craving and cognition were the predictor variables.

This was a within-subjects comparison that addressed the question “Is relapse more likely to occur following elevated craving and cognition at RAs and TAs?” They examine “when” an individual is at risk of relapse. Following the methods of Cooney et al. (2007), we used Generalized Estimating Equations (GEE; PROC GENMOD in SAS) and restricted analyses to data from the 10 PDA relapsers, who completed 76 and 71 assessments on the drug Stroop and drug IAT tasks respectively. We selected the appropriate working correlation structure based on the reported QIC (smaller is better), a goodness-of-fit statistic for GEE models. For TAs, the proximal assessment occurred on average 2.11 days and 2.14 days before relapse for the Drug Stroop and Drug IAT assessments respectively; for RAs the proximal assessments occurred on average 0.20 days and 0.78 days before relapse. Consistent with the LMM analyses, Assessment Type, and the interaction term between Assessment Type and the predictor variable were included in the GEE models, as were the variables day, number of assessment (in day), and drug material type (if appropriate). If a

significant interaction was not observed, the interaction term was dropped from the model, and the Chi Square values from the reduced model were reported.

In secondary analyses, we recomputed LMMs when including three study methadone-related variables as covariates: starting dose of methadone (a subject-level continuous variable); detoxification status (a subject-level dichotomous variable that indicated whether or not the participant underwent detoxification during the PDA study); and methadone status (an assessment-level dichotomous variable that indicated whether or not the assessment occurred while the participant was on methadone). Due to missing data for methadone-related variables, these analyses used data from 62 and 53 participants for the early relapse and late relapse analyses respectively. These analyses yielded similar findings to the primary analyses, and are not reported here.

For all analyses, only assessments completed before reported relapse were included. Given the study focus on two implicit measures, and given the large number of tests, alpha was set at .025 for the multi-level analyses (LMMs and GEEs); p values $< .025$ are interpreted, and p values $< .05$ are also noted. For logistic regression analyses, which were fewer in number because they were only conducted following significant effects in LMMs, alpha was set at .05. All tests were 2-tailed.

Results

Number of Temptations

Early relapsers ($n = 10$) reported on average 0.90 temptations per day ($SD = 1.10$) prior to relapse ($n = 42$ days). Non-EMA relapsers ($n = 54$) reported on average 0.84 temptations per day ($SD = 1.29$; $n = 358$ days). The effect of Early Relapse Status on number of temptations was not significant ($p > .1$). Late relapsers ($n = 25$) reported on average 0.70 temptations per day ($SD = 1.17$; $n = 169$ days). Never-relapsers ($n=29$) reported on average 0.97 temptations per day ($SD = 1.38$; $n = 189$ days). The effect of Late Relapse Status on number of temptations was not significant ($p > .1$).

Primary outcome: Early Relapse

Summary statistics are reported in Table 1 and results from LMMs are reported in Table 2. The Early Relapse Status by Assessment Type interaction was significant for the following variables: craving for heroin; craving for cocaine; explicit attitude to heroin; explicit attitude to cocaine; drug Stroop effect; and drug IAT effect (ms score and D score)². For the drug Stroop effect, the Early Relapse Status by Assessment Type interaction remained significant when craving for heroin and craving for cocaine were added as covariates to the model ($F(1, 688) = 5.61$, $PE = 108.0$, $SE = 45.6$, $p < .025$). For the drug IAT effect, the Early Relapse Status by Assessment Type interaction remained significant when explicit attitude to heroin and explicit attitude to cocaine were added as covariates to the model (ms score: $F(1, 610) = 8.52$, $PE = 490.5$, $SE = 168.0$, $p < .01$; D score: $F(1, 610) = 4.98$, $PE = 0.30$, $SE = 0.13$, $p < .05$). Explicit attitudes were associated with craving ratings across subjects (heroin craving and explicit attitude to heroin, $r = .73$ and $.50$, $ps < .001$ at RAs and TAs respectively; cocaine craving and explicit attitude to cocaine, $r = .79$ and $.59$, $ps < .001$, at RAs and TAs respectively) and within subjects (mean within-subject correlation: heroin craving and explicit attitude to heroin: $r = .44$, $p < .001$, cocaine craving and explicit attitude to cocaine, $r = .47$, $p < .001$). However, the Early Relapse status by Assessment Type interaction for

²For the implicit assessments, we also examined whether the Early Relapse Status by Assessment Type interaction was moderated by Drug Type (heroin vs. cocaine Stroop and heroin vs. cocaine IAT). There were no significant Drug Type by Early Relapse Status by Assessment Type interactions ($p > .1$).

explicit attitude to heroin ($F(1, 612) = 11.67$, $PE = 1.27$, $SE = 0.37$, $p < .01$) and cocaine ($F(1, 612) = 9.94$, $PE = 1.22$, $SE = 0.39$, $p < .01$) persisted when controlling for the craving for heroin and craving for cocaine respectively.

Because the Early Relapse Status by Assessment Type interaction was significant for the aforementioned variables, we tested the effect of Early Relapse Status at TAs and RAs separately (Table 2). At TAs, the effect of Early Relapse Status was significant for the drug Stroop effect (Figure 2), indicating that the attentional bias of early relapsers (at TAs) was 111 ms greater than the attentional bias of non-EMA relapsers (at TAs). Similarly, at TAs the effect of Early Relapse Status was significant for the drug IAT effect (Figure 2) indicating that the IAT effect of early relapsers (at TAs) was 654 ms (ms score) more positive than the IAT effect of non-EMA relapsers (at TAs). At TAs, the effect of Early Relapse Status was not significant ($p > .1$) for the other variables (i.e., craving for heroin, craving for cocaine, explicit attitude to heroin, and explicit attitude to cocaine). At RAs, the effect of Early Relapse Status was not significant ($p > .1$) for any of the following variables: craving for heroin; craving for cocaine; explicit attitude to heroin; explicit attitude to cocaine; drug Stroop effect; and drug IAT effect.

The Early Relapse Status by Assessment Type interaction was not significant for difficulty concentrating (Table 2). Similarly, the main effect of Early Relapse status (reduced model) was not significant ($p > .1$) for this variable.

Using logistic regression, the drug Stroop effect at TAs was prospectively associated with relapse ($PE = 0.0053$, $SE = 0.0027$, $Wald = 3.95$, $p < .05$). The effect remained significant when craving for heroin and craving for cocaine were added as covariates to the model ($PE = 0.0056$, $SE = 0.0030$, $Wald = 3.98$, $p < .05$). The IAT ms score at TAs was also prospectively associated with relapse ($PE = 0.0012$, $SE = 0.00055$, $Wald = 4.65$, $p < .05$). The effect remained significant when explicit attitude to heroin and explicit attitude to cocaine were added as covariates to the model ($PE = 0.0014$, $SE = 0.00062$, $Wald = 4.94$, $p < .05$). The association for the IAT D score approached significance ($PE = 1.42$, $SE = 0.82$, $Wald = 3.00$, $p = .08$). There were no significant effects at TAs for the following variables: craving for heroin; craving for cocaine; explicit attitude to heroin; explicit attitude to cocaine (all $p > .1$). There were no significant effects for any variable at RAs (all $p > .1$).

Secondary outcome: Late Relapse

Summary statistics are reported in Table 3 and results from LMMs are reported in Table 4. The Late Relapse Status by Assessment Type Status interaction was significant for the following variables: explicit attitude to heroin and explicit attitude to cocaine. Follow-up analyses revealed that there were no significant effects of Late Relapse Status (no differences between late and never-relapsers) at TAs or RAs (Table 4).

The Late Relapse Status by Assessment Type Status interaction was not significant ($p > .1$) for the other variables: craving for heroin; craving for cocaine; difficulty concentrating; drug Stroop effect; and drug IAT effect (Table 4). Similarly, the main effect of Late Relapse status (reduced model) was not significant (all $p > .1$) for any of these variables.

Using logistic regression there were no significant effects at TAs or RAs for any study variable (all $p > .1$).

Within-Subject Analyses

Results from GEE analyses (Table 5) revealed that the Assessment Type by Drug Stroop interaction was significant. As the drug Stroop effect increased, the risk of subsequent relapse increased following TAs relative to the risk of subsequent relapse following RAs.

This effect persisted when including self-reported craving for heroin and craving for cocaine in the model (Wald Statistic (1) = 5.61, PE = -0.009, SE = 0.004, $p < .025$). As the drug Stroop effect increased at TAs (but not RAs), the risk of subsequent relapse tended to increase (Table 5). This finding is illustrated in Figure 2. Although early relapsers generally exhibited elevated drug Stroop effect at TAs compared to non-relapsers (as reported earlier), the drug Stroop effect of early relapsers was particularly elevated at the proximal assessment.

For the drug IAT, the Assessment Type by Drug Stroop interaction was not significant. The same was true for craving for heroin, craving for cocaine, difficulty concentrating, explicit attitude to heroin, and explicit attitude to cocaine (Table 5). Similarly, the main effect of the predictor variable (reduced model) was not significant (all $ps > .1$) for any of these variables.

Discussion

This study examined whether implicit and explicit cognitive assessments administered during EMA were associated with relapse during drug detoxification. The main findings were as follows. First, both early and late relapsers did not report more temptation episodes than non-EMA and never-relapsers. Second, and most important, early relapsers exhibited higher levels of attentional bias and more positive implicit attitudes towards drugs than non-EMA relapsers at temptation episodes (but not at random assessments). Attentional bias and positive implicit attitudes at temptation episodes were prospectively associated with relapse during the study. Third, when compared to non-EMA relapsers, early relapsers reported relatively higher levels of craving and more positive explicit attitudes towards drugs at temptation assessments compared to random assessments. Furthermore, when compared to never-relapsers, late relapsers (who relapsed after the PDA study) reported relatively more positive explicit attitudes towards drugs at temptation assessments than at random assessments. Last, there was evidence from the within-subject analyses that elevated attentional bias during temptations was a precipitant of relapse.

Overall, therefore, it appears that early relapsers do not report more temptations than non-EMA relapsers. However, they experience more “severe” temptation episodes than non-EMA relapsers. The association between attentional bias at temptation episodes and relapse provides support for theoretical models that posit a relationship between attentional bias and relapse (e.g., Franken, 2003). As noted earlier, a number of laboratory studies have similarly reported prospective association between attentional bias and subsequent drug use (Cox et al., 2002; Cox et al., 2007; Carpenter et al., 2006; Janes et al., 2010; Marissen et al., 2006; Powell et al., 2010; Waters et al., 2003). The present study also revealed that individuals with more positive implicit attitudes to drugs during temptation episodes were at risk for early relapse. This finding is consistent with data from non-clinical populations. For example, McCarthy and Thompsen (2006) reported that positive implicit associations with alcohol or smoking predicted alcohol use or smoking behavior. Wiers et al. (2002) found that having less negative implicit associations with alcohol was associated with more alcohol use. In general, individuals with more positive (or less negative) implicit associations with drugs are at risk for subsequent use or relapse.

As noted above, the associations between cognition and relapse were only found at temptation assessments; they were not found at the random assessments. It seems likely that cognitive processes assessed during temptations may better reflect cognitive processes just prior to relapse than cognitions assessed at random times. For example, during both temptation episodes and relapse episodes, automatic processes such as attentional bias may drive the individual toward drug use; during temptation episodes the individual is able to prevent actual use (relapse) by inhibiting the output of these processes. However,

individuals who experience more “cognitively severe” temptations may be less able to prevent drug use. Therefore, it is not surprising that cognitions assessed during temptations are more strongly related to risk of relapse than cognitions assessed at random assessments. It is noteworthy that, in some of the laboratory studies cited earlier, attentional bias was assessed under conditions of drug deprivation or shortly after cue exposure (Waters et al., 2003; Janes et al., 2010; Marissen et al., 2006; Powell et al., 2010). These testing conditions may have elicited temptations in some participants.

We also found that greater craving/more positive attitude at temptations (compared to random assessments) were associated with relapse. Previous EMA studies have also reported associations between craving/urge to use and substance use or relapse (e.g., Preston et al., 2009; Shiffman et al., 1997; Cooney et al., 2007). No previous study has examined associations between explicit attitudes assessed during EMA and relapse. However, several laboratory studies have reported an association between explicit attitudes and substance use or relapse (e.g., Wiers et al., 2002; McCarthy & Thompson, 2006; Chassin, Presson, Sherman, Seo, & Macy, 2010). In the current study, a more positive explicit attitude at temptations (compared to random assessments) was associated with both early and late relapse. This suggests that the single item measure of attitudes used in this study is a useful marker for relapse risk if assessed at temptations and random assessments.

Interestingly, we did not find an association between implicit cognitions and late relapse. This may be because the EMA assessments were more proximal to early relapse episodes than the later relapse episodes (see also McKay, Franklin, Patapis, & Lynch, 2006). For attentional bias, confidence for this interpretation is bolstered by the observation that it was most elevated in the proximal assessment before relapse.

The present data also indicated that early and late relapsers do not report more temptation episodes than non-EMA and never-relapsers. Similarly, Shiffman et al. (1997) reported that number of temptations did not predict smoking relapse. Interestingly, duration of temptations did predict relapse, and, in lapsers, the peak reported urge during temptations (a measure of temptation intensity) increased in the days prior to lapse (Shiffman et al., 1997).

Results from the within-subject analyses suggest that elevated attentional bias during temptations - but not random assessments - is a precipitant for subsequent relapse. When an individual exhibits an elevated attentional bias during a temptation, that individual is at risk of relapse in the short term. In contrast, we did not find that more positive implicit attitudes (during temptations) were elevated just prior to relapse. This was one difference in the pattern of data for attentional bias and implicit attitudes. Individuals who exhibit an elevated IAT effect during temptations are generally at greater risk of subsequent relapse during the study week, but there is not yet evidence that a highly positive implicit attitude at a given time-point provides information about the timing of relapse.

Our findings have implications for treatment during drug detoxification. The data suggest that attentional bias (and implicit attitudes) may be an appropriate cognitive target for intervention. If further research reveals that the association between attentional bias and relapse is causal, an attentional retraining intervention, perhaps delivered on the PDA during treatment, would be a logical approach. If the association between attentional bias and relapse is not causal, the EMA data may still reveal which individuals are at risk of relapse and perhaps when they are at risk of relapse. These data may facilitate drug detoxification treatment. For example, more therapy time or instant intervention at a critical temptation period might be allocated to those individuals at greater risk of relapse.

The present study had limitations. First, because all PDA assessments occurred in the detoxification clinic, and because relapses occurred off-site, we were not able to examine

how craving and cognition changed in the hours and minutes before relapse. Second, due to clinic procedures, the self-reports of early relapse were not biochemically verified (late relapse was biochemically validated). Third, although we used an alpha level of .025 for the multi-level analyses, the large number of tests increases the probability that one or more of our findings are type I errors. However, the consistency in the findings across analyses for the early relapse outcome bolsters confidence that the reported effects are real. Fourth, EMA data are correlational. It therefore remains uncertain whether cognitions cause relapse. Fifth, given that we always assessed implicit attitudes (and not the drug Stroop) after the explicit attitude measure, we cannot rule out the possibility that the explicit attitude question differentially influenced responses on the IAT, e.g., by increasing the salience of the cues in the IAT task. Last, we do not know whether the findings would generalize to users in outpatient or more naturalistic settings. However, the findings would still be of significant clinical interest if they generalized to other detoxification settings.

The study also had strengths. Most importantly, our methodology enabled us to measure implicit cognitions at the moment temptations occurred as well as at random times. The study revealed more specific information on the association between cognition and relapse than has been previously reported.

In sum, our data revealed that real-time assessment of implicit and explicit cognitions may help to identify those individuals who are at risk for relapse during drug detoxification, and, perhaps, when they are at risk of relapse.

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Figure 1.
PDA versions of the drug Stroop task (left) and the IAT (right).

Figure 2.

Means and error bars (1 SE) of the drug Stroop effect (A), and drug IAT effect (B) for early relapsers (control and proximal assessments) at RAs and TAs (see text). Data from Non-EMA relapsers are also shown for comparison purposes.

Table 1
Explicit and Implicit Measures by Early Relapse Status and Assessment Type

	Early Relapsers (n = 10)						Non-EMA relapsers (n = 54)					
	TAs			RAs			TAs			RAs		
	n	M	SD	n	M	SD	n	M	SD	n	M	SD
Heroin Craving (1-7)	38	4.32	1.73	109	2.48	1.50	301	3.79	2.26	989	2.65	1.84
Cocaine Craving (1-7)	38	4.29	2.25	109	2.26	1.48	301	3.49	2.46	989	2.39	1.91
Difficulty Concentrating (1-7)	38	4.34	1.60	109	3.83	1.31	301	4.44	1.91	989	3.86	1.87
Heroin Explicit Attitude (1-7)	19	4.05	1.35	52	2.27	1.27	143	3.20	1.93	464	2.65	1.79
Cocaine Explicit Attitude (1-7)	19	4.26	1.56	52	1.94	1.07	143	2.97	2.10	464	2.47	1.90
Drug Stroop (ms)	19	159.0	171.7	57	26.3	179.0	158	57.8	178.3	525	36.4	156.1
Drug IAT (ms)	19	686.9	969.7	52	185.3	565.9	143	106.0	809.3	464	84.8	628.4
Drug IAT (D score)	19	0.50	0.62	52	0.26	0.70	143	0.12	0.58	464	0.13	0.54

Note. n = no. of observations; M and SD were computed by aggregation across observations. Drug Stroop data were aggregated over heroin and cocaine Stroop tasks. Similarly, drug IAT data were aggregated over heroin and cocaine IAT tasks. Mixed-model based estimates of the mean and standard deviation, that account for the fact that participants differ in the number of observations they contribute, are available on request.

Table 2

Results of LMMs for Early Relapse Status

	Interaction					TAs					RAs				
	dfs	F	PE	SE	dfs	F	PE	SE	dfs	F	PE	SE	dfs	F	PE
Heroin Craving	1, 1368	8.19***	0.75	0.26	1, 277	0.04	-0.12	0.60	1, 1032	0.64	0.41	0.51	1, 1032	0.64	0.41
Cocaine Craving	1, 1368	6.82***	0.61	0.23	1, 277	0.06	-0.18	0.78	1, 1032	0.09	0.18	0.59	1, 1032	0.09	0.18
Difficulty Concentrating	1, 1368	0.56	0.21	0.28	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Heroin Explicit Attitude	1, 612	11.67***	1.27	0.37	1, 111	0.92	-0.61	0.64	1, 453	1.86	0.69	0.51	1, 453	1.86	0.69
Cocaine Explicit Attitude	1, 612	9.94***	1.22	0.39	1, 111	1.69	-0.94	0.72	1, 453	0.99	0.53	0.54	1, 453	0.99	0.53
Drug Stroop	1, 690	5.63**	108.1	45.5	1, 120	5.70**	-111.0	46.7	1, 517	0.16	17.3	24.9	1, 517	0.16	17.3
Drug IAT (ms score)	1, 612	9.34***	508.2	166.3	1, 111	5.19**	-654.2	287.1	1, 453	0.67	-120.8	140.1	1, 453	0.67	-120.8
Drug IAT (D score)	1, 612	5.26**	0.30	0.13	1, 111	4.02*	-0.41	0.20	1, 453	0.36	-0.09	0.15	1, 453	0.36	-0.09

Note. Column labeled Interaction reports Early Relapse Status by Assessment Type interaction term from LMM. Column labeled TAs reports effect of Early Relapse status at TAs; negative parameter estimates mean higher (more positive) values for Relapsers vs. Non-Relapsers. Column labeled RAs reports effect of Early Relapse status at RAs; positive parameter estimates mean lower (more negative) values for Relapsers vs. Non-Relapsers. n/a = not assessed, due to absence of significant interaction term (see text)

* p < .05,

** p < .025

*** p < .01

Table 3
Explicit and Implicit Measures by Late Release Status and Assessment Type

	Late Relapsers (n = 25)						Never-relapsers (n = 29)					
	TAs			RAs			TAs			RAs		
	n	M	SD	n	M	SD	n	M	SD	n	M	SD
Heroin Craving (1-7)	118	4.04	2.07	465	2.41	1.67	183	3.63	2.36	524	2.87	1.96
Cocaine Craving (1-7)	118	3.81	2.43	465	2.45	1.89	183	3.28	2.46	524	2.33	1.93
Difficulty Concentrating (1-7)	118	4.32	2.08	465	3.93	1.89	183	4.52	1.79	524	3.79	1.85
Heroin Explicit Attitude (1-7)	56	3.93	1.85	217	2.49	1.75	87	2.74	1.85	247	2.78	1.81
Cocaine Explicit Attitude (1-7)	56	3.96	2.02	217	2.57	1.94	87	2.32	1.89	247	2.38	1.87
Drug Stroop (ms)	62	51.3	181.4	248	30.9	162.3	96	62.0	177.3	277	41.4	150.4
Drug IAT (ms)	56	299.7	1015.4	217	156.8	642.7	87	-18.7	618.1	247	21.6	609.9
Drug IAT (D ascore)	56	0.25	0.66	217	0.17	0.53	87	0.03	0.51	247	0.10	0.55

Note. n = no. of observations; M and SD were computed by aggregation across observations. Drug Stroop data were aggregated over heroin and cocaine Stroop tasks. Similarly, drug IAT data were aggregated over heroin and cocaine IAT tasks. Mixed-model based estimates of the mean and standard deviation, that account for the fact that participants differ in the number of observations they contribute, are available on request.

Table 4

Results of LMMs for Late Relapse Status

	Interaction				TAs				RAs			
	dfs	F	PE	SE	dfs	F	PE	SE	dfs	F	PE	SE
Heroin Craving	1, 1231	0.00	0.00	0.19	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Cocaine Craving	1, 1231	0.99	-0.17	0.17	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Difficulty Concentrating	1, 1231	0.40	0.13	0.21	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Heroin Explicit Attitude	1, 550	6.10 ^{***}	0.69	0.28	1, 99	1.05	-0.52	0.51	1, 410	0.69	0.32	0.38
Cocaine Explicit Attitude	1, 550	5.99 ^{**}	0.72	0.29	1, 99	2.08	-0.80	0.55	1, 410	0.37	-0.25	0.41
Drug Stroop	1, 624	0.11	-10.3	30.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Drug IAT (ms score)	1, 550	0.46	-0.01	0.10	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Drug IAT (D score)	1, 550	0.07	33.0	123.4	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Note. Column labeled Interaction reports Late Relapse Status by Assessment Type interaction term from LMM. Column labeled TAs reports effect of Late Relapse status at TAs; negative parameter estimates mean higher (more positive) values for Relapsers vs. Non-Relapsers. Column labeled RAs reports effect of Late Relapse status at RAs; positive parameter estimates mean lower (more negative) values for Relapsers vs. Non-Relapsers. n/a = not assessed, due to absence of significant interaction term.

*
p < .05

**
p < .025

p < .01

Table 5

Results of GEE Within Subjects Analyses

	Interaction				TAs				RAs			
	df	Wald Statistic	PE	SE	df	Wald Statistic	PE	SE	df	Wald Statistic	PE	SE
Heroin Craving	1	1.18	0.46	0.43	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Cocaine Craving	1	1.60	0.14	0.11	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Difficulty Concentrating	1	2.23	0.30	0.20	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Heroin Explicit Attitude	1	1.46	-0.55	0.46	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Cocaine Explicit Attitude	1	0.70	0.34	0.41	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Drug Stroop	1	7.44***	-0.01	0.004	1	3.86*	0.01	0.006	1	0.05	0.0005	0.0023
Drug IAT (ms score)	1	1.07	-0.0008	0.0008	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Drug IAT (D score)	1	1.88	-1.20	0.92	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Note. Column labeled Interaction reports the Predictor Variable by Assessment Type interaction term from GEE. Column labeled TAs reports effect of the Predictor Variable at TAs; positive parameter estimates mean that as values of the predictor variable become more positive there is a greater risk of subsequent relapse. Column labeled RAs reports effect of the Predictor Variable at RA. n/a = not assessed, due to absence of significant interaction term (see text). Predictor variables were tested in separate models.

* p < .05

** p < .025

*** p < .01