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Real-time assessment of alcohol drinking and drug use in opioid-dependent polydrug users

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Abstract

We investigated relationships between drinking, other drug use, and drug craving, using ecological momentary assessment (EMA), in a sample of polydrug users who were not heavy drinkers. In a prospective longitudinal cohort study, 114 heroin and cocaine users in methadone-maintenance treatment carried handheld electronic diaries during waking hours and were screened for drug and alcohol use for up to 25 weeks. Individuals who met DSM criteria for alcohol abuse or dependence were excluded. Participants responded to 2–5 random prompts per day to report on their moods, cravings, and activities, and initiated entries when they used or acutely craved heroin or cocaine. Drinking alcohol was assessed in both types of entries. Breath alcohol was measured three times weekly. Participants reported drinking alcohol in 1.6% of random-prompt entries, 3.7% of event-contingent entries when craving cocaine and/or heroin, and 11.6% of event-contingent entries when using cocaine and/or heroin. Alcohol drinking was also associated with higher craving ratings and pre-study alcohol use. More drinking was detected by ambulatory self-report than by in-clinic breath testing. Even though we had screened out heavy drinkers from our sample of polydrug users, drinking was associated with heroin and cocaine craving and actual use.

Keywords

alcohol; cocaine; heroin; craving; drug use; ecological momentary assessment; human

INTRODUCTION

Polydrug use is common among people with substance-use disorders, and it increases morbidity and complicates treatment (Kenna et al., 2007). Alcohol is among the substances most frequently used by patients in opioid-agonist maintenance for heroin dependence (Bickel et al., 1987; Leri et al., 2003). An analysis of studies conducted in the National Institute on Drug Abuse (NIDA) Clinical Trials Network (CTN) found that 38% of opioid treatment seekers enrolled in CTN trials had an alcohol-use disorder (Hartzler et al., 2010). Drinking has been shown to predict poorer treatment outcome (Stapleton & Comiskey, 2010), though this is not always the case (Byrne & Petry, 2011). Staiger and colleagues

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(2013) have reviewed the literature on drinking during recovery from addiction to other substances, and their main conclusion was that the topic is understudied.

For those interested in conducting such research, monitoring alcohol use can be challenging. Although alcohol is detectable in breath and body fluids such as urine, blood and saliva, its half-life and, thus, window of detection are relatively short, on the order of hours (Swift, 2003). With available technology, detection of alcohol use in all but the heaviest alcohol drinkers would require frequent testing, perhaps multiple breath tests per day. For this reason, many alcohol studies, including pivotal clinical trials submitted to the Food and Drug Administration to support medication approval, rely on self-report (Kiluk et al., 2016).

Given the necessity of using self-report, one of the better options may be ecological momentary assessment (EMA), which has been increasingly used to study patterns of alcohol consumption (Wright et al., 2016) and its relationship to comorbid conditions (e.g., Possemato et al., 2015). In EMA, real-time self-report data are collected at randomly prompted times throughout the day and at the time of specific events at which participants initiate an entry. EMA avoids the problem of recall bias and enables multiple times of data collection across the day.

In the analyses reported here, we examined alcohol drinking in a larger natural-history study, in which we used EMA to investigate patterns and triggers of drug use and craving in cocaine- and heroin-using outpatients undergoing opioid-agonist maintenance (Epstein et al., 2009). In this paper we report how drinking is associated with heroin and cocaine use and craving, and on the differential detection of drinking by breath monitoring in clinic versus self-report in EMA entries.

METHODS

Participants and Setting

Participants were cocaine- and heroin-using outpatients; we have previously reported the methods in detail (Epstein et al., 2009, 2010). Inclusion criteria were age 18 to 65 years, physical dependence on opioids, and current use of cocaine and opiates as indicated by self-report and urine screen. Exclusion criteria were current dependence on alcohol or any sedative-hypnotic (by DSM-IV criteria), schizophrenia or any other DSM-IV psychotic disorder, history of bipolar disorder, or current major depressive disorder, inability to give informed consent, or a medical illness that would compromise participation in the study. Screening instruments included the Addiction Severity Index (ASI; McLellan et al., 1985), Diagnostic Interview Schedule for DSM-IV (Robins et al., 1995), and the CAGE (Allen et al., 1995). The study was approved by the NIDA Institutional Review Board, and participants gave written informed consent before being enrolled.

Procedure

Participants attended our treatment-research clinic in Baltimore, MD, seven days a week for up to 25 weeks and received daily oral methadone (target dose: 100 mg/day) and weekly individual drug counseling by master's-level counselors. Urine specimens were collected under observation and tested for cocaine, heroin, methadone, amphetamines, barbiturates,

PCP, and cannabinoids three times per week. On the same days, breath alcohol concentration (BAC) was measured with an Alco-Sensor IV (Intoximeters, Inc., St. Louis, MO).

To encourage abstinence, participants received abstinence reinforcement during weeks 7–18, in the form of a voucher given each time their urine drug screens were negative for cocaine. The value of the vouchers began at \$5.00 and increased in value by \$3.00 for each consecutive cocaine-negative urine. For a positive or missed urine, no voucher was given, and the value of the next earned voucher was reset to \$5.00. In addition, for every 3 consecutive cocaine-negative urines, the participant earned an extra voucher worth \$20.00. The maximum possible earnings were \$2,310.

Real-time self-report was collected on personal digital assistant devices (PDAs; Palm Zire or Palm Zire 21) running our Transactional Electronic Diary software (Vahabzadeh et al., 2004). At the end of week 3, each participant was issued a device and trained to make two types of EMA entries. Randomly prompted (RP) entries were triggered by the PDA two to five times per day for 25 weeks, timed to occur only during each participant's typical waking hours. Participants were also instructed to initiate an event-contingent (EC) entry whenever they craved without using or used cocaine or heroin or both drugs. At each EC or RP entry, participants answered a set of questions that included "When the beep occurred, were you drinking alcohol?" in RP entries. "When the craving/use occurred, were you drinking alcohol?" in EC entries. In all entries, participants reported their location ("Where are you now?" with a dropdown list of options, including home, work, vehicle, other, etc.). At each random prompt, participants were also asked to rate their craving for cocaine and heroin on a 4-point Likert scale NO!!, no?!, yes?!, or YES!!. Participants were instructed that only research staff, not counseling staff, would have access to the contents of their EMA entries and that abstinence reinforcement was based solely on the urine drug screens and not on drug use reported via EMA.

Data analysis

To determine the relationships between drinking and cocaine or heroin craving in RP entries, we used repeated-measures logistic regressions (SAS Proc Glimmix) with drinking as the dichotomous dependent variable. The within-subject independent variables were ratings of craving for cocaine and heroin and included control terms for sex, race, age, and location. A first-order autoregressive error structure was used. Contrast coefficients were used to test for linear trends.

To determine relationships between drinking and episodes of craving or use in event-contingent entries, we again used the SAS Proc Glimmix, with event type (drug craving or drug use) as the within-subject independent variable, along with control terms for sex, race, age, and location; again, we specified a first-order autoregressive error structure.

Additional comparisons between event-contingent and random-prompt entries are described in Results.

To evaluate the time course of reports of drinking, we calculated the percent of total entries with and without drinking at each hour between 5 AM and 2 AM for RP entries and craving and drug-use entries.

We compared person-level summary data on cocaine use and drinking (percentage of cocaine-negative urines versus percentage of random-prompt reports in which drinking was reported), with Kendall's tau, a nonparametric measure of correlation, because of the non-normal distribution of each variable. For the same reason, we used Kendall's tau to compare EMA summary measures with baseline measure of alcohol-use history from the ASI.

For comparison between alcohol drinking RP and detection of alcohol in breath tests, we defined "positive BAC" as anything > 0.000 . Each positive detection of alcohol use in an EMA entry and the BAC was compared case by case for a plausible association of a given BAC positive with a recent EMA report of drinking—taking "plausible" as either post-midnight (for a morning positive BAC) or post-6:00am (for an afternoon positive BAC). In most cases, the EMA entry of drinking had been reported just an hour or two prior to the BAC reading, if it was reported at all. We report descriptive statistics on these data.

For all analyses, the criterion for significance was $p = 0.05$, two tailed.

RESULTS

Participant characteristics

A total of 130 participants enrolled in the main study; EMA data were collected from 114 participants who carried PDAs for 14,918 person-days (mean 130.9 days). Among the 114 participants, 46 reported drinking in an EC or RP entry and 68 did not. Demographic information is shown in Table 1. African American participants were significantly more likely to have reported their detected instances of alcohol use (chi-square = 6.52, $df = 1$, $p = .011$).

EMA self-reports of drinking and heroin and cocaine use and craving

Overall, participants completed 27,413 RP entries, plus 1,026 EC entries reporting heroin or cocaine use and 1,617 EC entries reporting heroin or cocaine craving episodes. Drinking was reported more often during drug-craving EC entries (3.7%) and drug-use EC entries (11.6%) than in RP entries (1.6%) (Figure 1A). In Glimmix models, each of these rates were significantly different: for craving entries versus RP entries, $F(1,94) = 31.05$, $p < 0.001$; for use entries versus RP entries, $F(1,77) = 304.29$, $p < 0.001$; for use entries versus craving entries, $F(1,69) = 32.15$, $p < 0.001$. (Degrees of freedom reflect the numbers of participants contributing data to more than one cell.) Within all RP entries, the likelihood of drinking increased linearly with intensity of ongoing "background" craving for either cocaine (linear trend: $F(1,265) = 106.13$, $p < 0.001$) or heroin (linear trend: $F(1,232) = 22.02$, $p < 0.001$) (Figure 1B).

Among the 46 participants who ever reported drinking in an EMA entry, drinking was reported in 3.8 % of 11,955 RP entries, 8.6% of 685 drug-craving EC entries, and 23.7% of 540 drug-use EC entries.

The hourly distributions of entries with and without reported drinking are shown in Figure 2. Both RP and craving-event entries in which participants reported drinking peaked later in the day relative to reports without drinking. In contrast, the time courses of drug-use entries with and without drinking were similar to each other.

When participants were abstinent from cocaine for at least one week (three consecutive negative urine specimens), drinking was reported in 1.54% of RPs, compared to 1.73% of RPs made during periods of cocaine use (three consecutive positive urine specimens) (Glimmix analysis: $F(1,33) = 18.89$, $p < 0.001$). There was no correlation between overall percent of cocaine-negative urine specimens and the percentage of RP entries in which drinking was reported (Kendall's tau < 0.001 , $p = .99$).

Detection of Alcohol Use: Self-report versus BAC

Drinking was detected by either EMA or BAC in 60 (53%) of 114 participants. Among the 60 participants in whom drinking was detected, it was detected by EMA only in 33 (55%), by BAC only in 14 (23%), and by both methods in 13 (22%). For the 46 participants who ever reported drinking in an EMA entry, the mean number of drinking reports was 13.9 (SD = 29.2, median = 3, range 1 to 157). Positive BACs were infrequent. Only 27 participants ever had a positive BAC, with a mean of 2.8 (SD = 3.1, median = 1, range 1 to 13). There was no relationship between participants' percentage of days with positive BACs and their percentage of RPs in which they reported drinking (tau $< .001$, $p = .99$), although one participant had an especially high percentage of each.

Detection of specific occasions of drinking by both measures was rare. The mean number of drinking reports followed by a positive BAC in a plausible time span was 0.2 (SD = 1.0, median = 0, range 0 to 5). The mean percentage of drinking reports followed by a positive BAC in a plausible time span was 0.9% (SD = 4.9, median = 0%, range 0% to 33.3%). The mean number of positive BACs preceded by an EMA report in a plausible time span was only 0.3 (SD = 1.0, median = 0, range 0 to 5). The mean percentage of positive BACs preceded by an EMA report in a plausible time span was only 5.9% (SD = 20.9, median = 0%, range 0% to 100%).

EMA and BAC and alcohol history at intake

The number of RP reports of alcohol drinking was correlated with the number of days that alcohol had been consumed in the 30 prior to treatment entry on the ASI (tau = 0.28, $p < 0.001$) and with the amount of money spent on alcohol in the same 30 days (tau = 0.23, $p < 0.005$). There was no association between number of EMA reports of alcohol drinking and number of DSM symptoms of alcohol dependence (tau = -0.01, n.s.) or alcohol abuse (tau = -0.03, n.s.), or with number of prior treatments for alcohol abuse (tau = -0.14, ns), years of alcohol use (tau = .03, ns), days of alcohol intoxication (tau = -0.13, n.s.), or years of alcohol intoxication (tau = -0.08, n.s.).

The percentage of positive BACs, despite the lack of overlap between BAC positives and EMA reports, was significantly correlated with some of the same baseline measures: number of days that alcohol had been consumed in the 30 prior to treatment entry on the ASI (tau = 0.32, $p < 0.001$) and amount of money spent on alcohol in the same 30 days (tau = 0.18, $p <$

0.03). The percentage of positive BACs was, if anything, negatively correlated with the number of alcohol abuse symptoms, though not at our .05 alpha cutoff ($\tau = -0.15$, $p = .06$).

DISCUSSION

Even though we enrolled only people who did not have an alcohol-use disorder, alcohol consumption was significantly, though modestly, associated with craving and use of other drugs. Participants were approximately two times more likely to report drinking during discrete drug-craving episodes than at randomly prompted assessments, and almost eight times more likely during drug-use episodes. Among participants who ever reported drinking in an EMA entry, drinking was reported on nearly one quarter of drug-use occasions. Drinking reports were more likely to occur later in the day in random-prompt and craving entries relative to entries in which drinking was not reported, though the time course of use reports with drinking was not delayed relative to those without drinking. In random-prompt entries, the likelihood of drinking increased linearly with intensity of ongoing “background” drug craving. Drinking was significantly less likely on days when participants were abstinent from cocaine than when they were actively using. The number of EMA drinking reports was also positively associated with study-intake measures of recent days of alcohol use and amount recently spent on alcohol. These findings support a momentary-level association between drinking and use of (or craving for) other drugs, even in people without an alcohol-use disorder.

To put into perspective the rates of drinking reported by our participants, we can compare them to those seen in an experience-sampling study reported by Hofmann and colleagues (2012) in a healthy-volunteer sample (150 university students and 55 nonstudents): in that sample, drinking was reported at 8% of random prompts. Drinking among our participants was well below this rate (it was reported in 1.6% of random prompts and 3.7% of craving reports), except at moments that they were also using other drugs, when it rose to 11.6%. The rates of drinking in our sample may have been slightly higher than suggested by the overall 1.6% in random-prompt entries, because the initiation and peak alcohol use was shifted later in the day relative to the distribution of random prompts, which we delivered only within each participant’s stated waking hours. The initiation and peaking of drinking later in the day in our random-prompt and craving-event data (Figure 2) are consistent with typical drinking patterns in the United States (Arfken, 1988; Liang and Chikritzhs, 2015). However many late-night instances of drinking we may have missed in random prompts, it is unlikely that this could account for the two-fold and seven-fold higher rates seen in craving and drug-use event entries.

The Hoffman study also showed that the ability to resist drinking decreased and the magnitude of desire for alcohol increased when participants reported high levels of drinking, compared to little or no drinking (Hoffman et al., 2012). Our study results are consistent with higher craving, and perhaps greater likelihood of using other drugs, when participants were drinking, though we assessed only the presence or absence of drinking and not the quantity.

In prior studies (one of which was from our research clinic) comparing drug-screen results and self-reported use of illicit drugs in an interview format, rates of disclosure were lower in African Americans participants than in white participants (Ghitza et al., 2007; Fendrich and Johnson, 2005). Such findings have been ascribed to a lower level of trust or communication when giving sensitive, illegal information to a person of another race (Cooper-Patrick et al., 1999; Collins et al., 2002; Richardson et al., 2003; Tassiopoulous et al., 2006). Yet in the present study, African Americans were disproportionately more likely to disclose their drinking. It is not clear whether this was due to the legal and socially acceptable nature of alcohol use or to the use of electronic diaries for data collection in our current study.

The low degree of overlap between BAC-detected drinking and EMA-reported drinking does not impugn either measure and does not reflect on the participants' honesty. Neither the EMA prompts nor the thrice-weekly BACs were intended to capture every episode of drinking, nor were they timed to reflect one another. Random spot checks via EMA identified more drinking than thrice-weekly in-clinic breath tests (although for 14 participants, 12% of the whole sample, drinking was detected *only* by the in-clinic breath tests). This lower rate of BAC positives is likely due to alcohol's rapid elimination from blood and relatively brief window of detection in the breath (Jones, 2010), along with our clinic's safety policy of withholding the day's dose of methadone from any participant who appears intoxicated on sedative-hypnotics. Our findings show that opioid-maintained outpatients are willing to report at least some of their drinking via EMA, despite two factors that might militate against reporting: drinking was not the focus of their treatment-seeking, and they probably knew that any drinking during addiction recovery is typically frowned on by treatment providers.

Investigators who want to detect every instance of drinking with EMA will probably need to ask participants either to make an EC entry for each occurrence of drinking or include a randomly prompted item such as "did you drink since the previous entry?" These methods have been successfully used in EMA primarily directed toward studying alcohol use (Collins et al., 1998; Beckjord & Shiffman, 2014). A recent study showed good correspondence between EMA reports and transdermal assessment of alcohol use in young adults (Simons et al., 2015). Our own goal, which we achieved here, was only to assess drinking as one of many kinds of behavior that might or might not be associated with craving and use; to get that information with EMA, investigators need only perform "spot checks" at random prompts to estimate the base rate of drinking for comparison with the rates of drinking at specific times (such as use of other drugs).

A limitation of our data is that we do not know whether a given instance of drinking was a cause or consequence of an associated instance of heroin or cocaine use, and the association was modest, with alcohol use reported in only 11% of drug-use events. Nevertheless, our findings may have treatment implications. Alcohol use may indicate occasions of vulnerability to relapse, or may be a signal that relapse has already occurred. Its use could be prospectively addressed with behavioral or pharmacological interventions. For example, treatment with disulfiram has been shown to decrease cocaine use in methadone-maintained patients, even among those who are not heavy alcohol users (Petrakis et al., 2000).

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Figure 1.

A. Overall percentages of random-prompt entries, craving-episode entries, and use entries in which alcohol drinking was reported; * denotes a significant difference between entry types, $p < 0.001$. B. Adjusted percentages of reports of drinking in random-prompt entries and intensity of ongoing drug craving from a Glimmix model controlling for age, sex, race, and location.

Figure 2.

Distribution of random-prompt entries, craving-episode entries, and use entries with and without reports of alcohol drinking, in one-hour bins across the day.

Table 1

Characteristics of participants who did and did not report alcohol drinking in EMA

Measure	alcohol reporters	nonreporters
N	46	68
Men	31 (67%)	40 (59%)
African American	34 (74%)	34 (50%)
White	11 (24%)	32 (47%)
Age (years)	40.1 (<i>SEM</i> 1.1, range 26–54)	41.6 (<i>SEM</i> 1.0, range 20–58)
Education (years)	11.9 (<i>SEM</i> 0.2, range 7–15)	11.7 (<i>SEM</i> 0.2, range 7–15)
Employment		
Unemployed	30%	39%
employed part time	28%	25%
employed full time	39%	32%
Cocaine-Use History		
Lifetime use (years)	9.7 (<i>SEM</i> 8.5, range 0–37)	12.8 (<i>SEM</i> 8.6, range 0–30)
Past 30 days (days)	20.2 (<i>SEM</i> 9.2, range 5–30)	19.6 (<i>SEM</i> 9.1, range 4–30)
Heroin-Use History		
Lifetime use (years)	13.0 (<i>SEM</i> 1.3, range 0–37)	14.0 (<i>SEM</i> 1.0, range 2–36)
Past 30 days (days)	29.3 (<i>SEM</i> 0.6, range 5–30)	29.2 (<i>SEM</i> 0.3, range 15–30)
Alcohol-Use History		
Lifetime use (years)	3.1 (<i>SEM</i> 0.8, range 0–25)	5.4 (<i>SEM</i> 1.0, range 0–31)
Past 30 days (days)	6.1 (<i>SEM</i> 1.2, range 0–30)	2.6 (<i>SEM</i> 0.5, range 0–16)