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Continuous In-The-Field Measurement of Heart Rate: Correlates of Drug Use, Craving, Stress, and Mood in Polydrug Users

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Abstract

Background—Ambulatory physiological monitoring could clarify antecedents and consequences of drug use and could contribute to a sensor-triggered mobile intervention that automatically detects behaviorally risky situations. Our goal was to show that such monitoring is feasible and can produce meaningful data.

Methods—We assessed heart rate (HR) with AutoSense, a suite of biosensors that wirelessly transmits data to a smartphone, for up to four weeks in 40 polydrug users in opioid-agonist maintenance as they went about their daily lives. Participants also self-reported drug use, mood, and activities on electronic diaries. We compared HR with self-report using multilevel modeling (SAS Proc Mixed).

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Author Disclosures

Conflict of Interest

No conflict declared.

Contributors

A.P.K., M.L.J., and D.A. helped design the study and participated in data collection; D.H.E. helped design the study, performed statistical analyses, and contributed to drafting the manuscript; M.T. participated in data management and statistical analyses; K.A.P. helped design the study and oversaw clinical aspects of data collection; A.A.A., R.B., S.M.H., K.H., M.M.R., and E.E. developed the AutoSense hardware and data collection, transmission, and storage software, and analyzed data; S.K. oversaw the development of AutoSense, participated in the design of the study, wrote methods in the manuscript and contributed to the drafting of the manuscript; K.L.P. conceived of the study, oversaw its design, and contributed heavily to the drafting of the manuscript. All authors discussed and commented on the manuscript.

Results—Compliance with AutoSense was good; the data yield from the wireless electrocardiographs was 85.7%. HR was higher when participants reported cocaine use than when they reported heroin use ($F(2,9) = 250.3, p < .0001$) and was also higher as a function of the dose of cocaine reported ($F(1,8) = 207.7, p < .0001$). HR was higher when participants reported craving heroin ($F(1,16) = 230.9, p < .0001$) or cocaine ($F(1,14) = 157.2, p < .0001$) than when they reported of not craving. HR was lower ($p < .05$) in randomly prompted entries in which participants reported feeling relaxed, feeling happy, or watching TV, and was higher when they reported feeling stressed, being hassled, or walking.

Conclusions—High-yield, high-quality heart-rate data can be obtained from drug users in their natural environment as they go about their daily lives, and the resultant data robustly reflect episodes of cocaine and heroin use and other mental and behavioral events of interest.

Keywords

cocaine; heroin; ambulatory physiological monitoring; heart rate; craving

1. INTRODUCTION

As mobile electronic devices become nearly ubiquitous in most of the world, the field of mobile health (mHealth) burgeons, bringing the potential for remote assessments and interventions—if sufficient empirical data are collected first (Collins, 2012). One especially good target for mHealth interventions is drug addiction. Because the risk of relapse persists for years after treatment, there is need for proactive aftercare that does not require heavy continuous use of “brick and mortar” resources. Also, the actual content of addiction treatment is usually amenable to delivery on mobile devices. Efforts are already underway to develop desktop-computer delivery of cognitive-behavioral therapy for addiction (Carroll et al., 2014; Marsch et al., 2014) and internet delivery of contingency management for addiction (Dallery et al., 2013).

As for mobile technology in addiction, researchers have already embraced it as an assessment tool in the form of ecological momentary assessment (EMA; Epstein et al., 2009; Waters et al., 2014). Using EMA, our research clinic has demonstrated that both cocaine craving and exposure to drug-use triggers increase in the hours before cocaine use, and that craving ratings increase as stress ratings increase (Epstein et al., 2009; Preston et al., 2009; Preston and Epstein, 2011). We are now also using real-time geolocation data collected with global positioning system (GPS) devices to assess environmental influences on addiction (Epstein et al., 2014).

The participant burden of EMA, the occasional resultant sparsity of EMA data, and the possibility that some important biological events (such as unconscious physiological responses to stressors) might not be amenable to self-report (Epstein et al., 2014) have led us to augment EMA with continuous physiological monitoring. At least one of the leading theories of addiction posits that behavior can be driven by “unconscious emotions” (Berridge and Winkelman, 2003). Regardless of whether one accepts that term, there is clear evidence that biologically and socially relevant environmental events (e.g., images of facial expressions) that occur too quickly to be consciously detectable can produce

measurable physiological responses (Dimberg, 1990). And regardless of whether one accepts that such physiological responses have important consequences for health or behavior when unaccompanied by subjective responses, the fact remains that physiological monitoring can be done continuously without requiring participants to stop and provide reports. Continuous monitoring increases the likelihood that some data will be available from any given moment of interest, such as a lapse to drug use or an encounter with a stressor. Also, physiological data collected in the field will almost certainly have greater ecological validity than those that have been collected in behavioral-pharmacology laboratories, because ethical and practical considerations limit the doses and combinations of drugs that can be given in a laboratory, as well as the activities that can occur.

In this study, we supplemented EMA with a wireless physiological-monitoring suite called AutoSense (Ertin et al., 2011). AutoSense provides continuous measurements of heart rate, heart-rate variability, respiration, skin conductance, ambient temperature, and physical activity. In prior studies by some of the current authors, AutoSense was used to collect a week's worth of ambulatory physiological data from smokers and social drinkers (Rahman et al., 2012). Here, we report on a field test of AutoSense in 40 illicit-drug users during outpatient treatment. As we discussed in a separate report, each type of physiological data requires extensive processing for quality control (Rahman et al., 2012). For the present analyses, we focused only on heart-rate data. Here we present, for the first time, data on heart-rate changes associated with EMA reports of mood, drug craving, and stress, as well as cocaine and heroin use in polydrug users.

2. METHOD

2.1 Participants

Opioid-dependent treatment seekers underwent screening for medical, psychiatric, and drug-use histories, physical examination, standard laboratory tests, and a battery of assessment instruments, including the Addiction Severity Index (ASI; McLellan et al., 1985), Structured Clinical Interview for DSM-IV (SCID; First et al., 2007), and the Diagnostic Interview Schedule (DIS-IV; Robins et al., 1995). Inclusion criteria were: age 18 to 75; evidence of physical dependence on opioids (by self-report and physical examination); and living or spending time in Baltimore, MD (because the parent study included geolocation tracking in the context of data on city neighborhoods). Exclusion criteria were: history of DSM-IV psychotic disorder or bipolar disorder; current major depressive disorder; current dependence on alcohol or any sedative-hypnotic; cognitive impairment; and medical illness that would compromise study participation. The Institutional Review Board (IRB) of the NIDA Intramural Research Program approved this study ([clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00292136) identifier: NCT00292136). All data were covered by a Federal Certificate of Confidentiality. Participants gave written informed consent prior to starting data collection and were paid for their time completing the research components of the project.

2.2 Standard treatment and drug-use monitoring

Methadone or buprenorphine maintenance began at enrollment and continued for up to 36 weeks at our treatment-research clinic in Baltimore, MD. Participants attended 7 days per

week for oral methadone or sublingual buprenorphine (target doses 100 mg/day or 16–24 mg/day); doses were individualized based on use, opioid withdrawal, and side effects with no ceiling. Individual counseling was available once weekly.

Thrice weekly (usually Mondays, Wednesdays, and Fridays) urine specimens were collected under observation and tested for cocaine (benzoylecgonine equivalents; BZE), opiates (morphine), marijuana, and benzodiazepines (oxazepam). Cutoffs were 300 ng/ml for cocaine, opiates, and benzodiazepines, and 50 ng/ml for marijuana. Breath alcohol was determined with an Alco-Sensor III (Intoximeters, Inc., St. Louis, MO).

2.3 Procedures

2.3.1 EMA—For the parent study, during weeks 3–18 of treatment, participants carried a GPS logger and completed EMA entries on a smartphone programmed with electronic-diary software (Vahabzadeh et al., 2004). Participants were asked to make an EMA entry after each use of a drug for a nonmedical purpose; the EMA questions included drug type, amount, route, and approximate time since the drug was used. For heroin and cocaine, quantity was reported in “dimes” (ten-dollar units; a dime of cocaine may contain about 100 mg of cocaine, and a dime of heroin may contain 10 mg or more of heroin). Participants also received 3 random prompts (RPs) per day, timed to their typical waking hours. In RP entries, participants rated their mood, stress, and craving for opioids and cocaine. Participants rated their mood on 25 adjectives, along with craving and stress, on 5-point Likert scales (1 – not at all to 5 – extremely). Participants also reported on present-location exposure to drug-use triggers at each RP (Marlatt and Gordon, 1985; Epstein et al., 2009), including seeing or being offered drugs or experiencing stressors (e.g., “someone hassling you,” “something violent or disturbing happening nearby”).

2.3.2 Autosense ambulatory physiological monitoring—A volunteer subset of 40 participants also underwent AutoSense monitoring. They each carried a Sony Ericsson Xperia X8 smartphone and wore AutoSense in their daily environments during four one-week periods over up to 7 weeks, with each AutoSense week separated by at least one week. The version of AutoSense used in this study consisted of a flexible chestband with a two-lead electrocardiograph (ECG), a 3-axis accelerometer, and a sensor for galvanic skin response (GSR). The chestband collected respiration data via inductive plethysmography. For ECG, a precision differential amplifier was used to measure electrical potential across the heart using two leads, and a second instrumental amplifier was used to remove the baseline drift that can occur due to the absence of a leg electrode and the possible differences in impedance between the two electrode/skin contact points. The resulting ECG signal was low-pass filtered to remove noise above 60Hz and sampled at 128 Hz with a 14-bit analog-to-digital converter (ADC). The information was then digitally filtered and encoded into wireless packets for the transmission to the smartphone. The smartphone was used to collect additional self-report data and to store the data transmitted by the sensor suite. It could also display heart-rate and respiration data graphically to enhance user interest. Additional details about AutoSense and pictures of the device and data display can be found at <http://web.archive.org/web/20150316160819/https://sites.google.com/site/autosenseproject/>.

Participants were trained to put on the chest electrodes and chestband. At each clinic visit, the placement of the electrodes and chestband was checked by study staff, and participants were asked whether AutoSense was causing problems. Participants were given extra electrodes in case their electrodes detached. At the end of each AutoSense week, participants completed a questionnaire on device acceptability.

2.4. Data analysis

Demographic and drug-use variables were compared between study completers (at least three weeks of AutoSense data collection) and study non-completers using chi-squares and independent-samples t-tests.

Heart-rate data from AutoSense were processed by first determining the acceptability of the ECG signals using the methods described in Plarre et al (2010). Signals were labeled unacceptable if they did not conform to the characteristic morphology of the physiological function being measured. This can result from electrode detachment, drying out of electrode gel, and noise from physical movement. After removing unacceptable ECG signals, we removed the DC offset from each interval to control for baseline drift and applied the Pan-Tompkins algorithm (Pan and Tompkins, 1985) to detect R-peaks. We removed outlier RR intervals using the algorithm in Berntson et al (1990). The resultant series of RR intervals was used to calculate heart rate.

To assess relationships between AutoSense heart-rate data and EMA self-reports, we first converted ratings of mood adjectives, craving, and stress from 5-point Likert scales to binomial 0 (not at all) or 1 (present) because the distributions were right-skewed. For RP entries, our general strategy was to compare heart rates for a given category of response (e.g., a report of heroin craving) to heart rates from all other random prompts. To do so, we used heart-rate data for 30 minutes before and after each random prompt; this time frame was arbitrary, but seemed appropriate for capturing the circumstances surrounding a report of current mood. For event-contingent entries (i.e., participant-initiated reports of drug use), we widened the time frame to 120 minutes before and after the entry, because we had only approximate information on the exact timing of drug use prior to the entry, and we wanted to capture onset and offset of drug effects. Statistical analyses of the heart-rate data were performed using SAS Proc Mixed. The models accounted for the repeated nature of the data and the fact that not every participant contributed every kind of data (e.g., most participants' random-prompt reports included both "yes" and "no" responses for heroin craving, but some consisted entirely of either "yes" or "no" responses). Each model included a time-varying predictor term for response type (typically "yes" or "no" on the EMA item of interest), a term for time relative to the EMA entry (−30 to +30, or −120 to +120, including 0), and an interaction term. The models used an autoregressive error structure and the between-within method for degrees of freedom. Output included F tests and least-squares means, which we used to graph the data. The least-squares means were almost identical to raw, sample-aggregated means from initial descriptive data summaries (not shown), but unlike the sample-aggregated means, were accompanied by appropriate standard errors. In all analyses, we used a two-tailed alpha of .05.

3. RESULTS

3.1. Participant Characteristics and Urine drug screen results

Forty (73%) of 57 participants who signed consent provided 3 or more weeks of AutoSense data and were considered completers. Of the 17 who did not complete: 3 were dropped from the parent study for noncompliance; 2 were dropped from the AutoSense study for noncompliance; 1 was incarcerated; 6 withdrew from the AutoSense study after starting it (2 because participation was incompatible with their jobs and 4 for unspecified reasons); 5 withdrew from the AutoSense study before starting it (3 for unspecified reasons; 1 disqualified due to a skin condition; 1 withdrawn because the study had ended). Demographics are summarized in Table 1.

Among the 40 participants included in the data analyses, all were physically dependent on opioids at admission; 25 also met DSM criteria for current opioid dependence and 7 met DSM criteria for current cocaine dependence. 25 were maintained on buprenorphine and 15 on methadone. Of 623 urine specimens collected during the AutoSense study, 38.9% were positive for cocaine, and 38.7% were positive for opioids.

3.2. AutoSense data quality and participants' ratings of acceptability

AutoSense data were collected between January 2012 and March 2014. We collected 922 person-days of data from 40 participants; they wore the device 14.57 (SD 2.8) hrs/day. Overall data yield was 85.7% for ECG data: we obtained 11.33 (SD .88) hrs/day of usable ECG data out of the mean 13.22 hrs/day that sensors were on the body. Respiration data yield was marginally higher, with 11.84 (SD 0.52) hrs/day of usable data per participant.

Participants generally found AutoSense acceptable: 39/40 (98%) rated it as very easy or easy to put on, and 39/40 rated the smartphone as very easy or easy to use. AutoSense was rated as very comfortable or comfortable by 28/40 (70%) of participants; the other 30% rated it as uncomfortable or very uncomfortable; 15/40 (38%) reported feeling moderately or very self-conscious while wearing AutoSense, but 35/40 (88%) reported having to make few or no adjustments to their activities while wearing AutoSense.

3.3 Heart rate at reports of drug use

Participants initiated 289 drug-use entries during AutoSense weeks. Most reports were for cocaine (N = 85), heroin (N = 50), or both (N = 108). There were 46 drug-use entries that did not include heroin or cocaine: 15 in which drug type was not specified, and 32 with one or more types of drug (20 marijuana, 11 benzodiazepines, 7 amphetamines, and 5 alcohol). When heroin use was reported on its own, the mean dose was 1.2 (SD 0.5) dimes, primarily (82%) snorted. When cocaine use was reported on its own, the mean dose was 1.7 (SD 0.9) dimes, primarily (78%) smoked. When both were used together, the mean doses were 1.5 (SD 0.8) dimes of heroin and 1.6 (SD 1) dimes of cocaine, taken mostly intravenously (51%) or by snorting (45%). Most cocaine/heroin uses were reported either 5–15 minutes after use (36%) or 15–30 minutes after use (35%); 12% were reported within 5 minutes, and 17% were reported more than 30 minutes later.

To assess associations between drug use and heart rate, we examined the two hours of AutoSense data before and after different types of drug-use entries; these data were available for 35 heroin uses, 59 cocaine uses, and 74 uses of both. AutoSense data were not available for all use events because some drug use occurred while participants were not wearing the device, and some data were lost due to equipment failure (Rahman et al., 2014). The general pattern was that mean heart rate (approximately 84 beats per minute (bpm)) was similar across the three types of drug uses from 1.5 to 2 hours prior to the reported use, and then began to separate. As can be seen in the top panel of Figure 1, heart rate was higher around the time of cocaine-use entries (mean: 85.8, SEM 0.2 bpm) and lower around the time of heroin-use entries (mean: 77.5, SEM 0.3 bpm). The mean differences in heart rate were apparent before the entry (drug use occurred before entries) and continued through the two-hour post-entry period included in the graph. When both drugs were used, heart rates tended to fall between those associated with cocaine-only and heroin-only uses (mean: 82.0, SEM 0.2; for clarity, data not shown). There was a significant main effect of drug type ($F(2,9) = 250.33$, $p < .0001$), with no effect of time ($F(239, 5118) = 0.49$, $p = .99$) and no drug-by-time interaction ($F(478, 1515) = 0.52$, $p = .99$). All three Tukey pairwise comparisons between drug types were significant at $p < .0001$.

For cocaine-use entries, we also found a dose-response effect. Using only entries at which the amount reported was either 1 or 2 dimes of cocaine (Figure 1, bottom panel; data from 20 participants), we found that heart rate was faster around the “2 dimes” reports (mean 87.5, SEM 0.3) than around the “1 dime” reports (mean 82.5, SEM 0.1). There was a significant main effect of dose ($F(1,8) = 207.73$, $p < .0001$), with no effect of time ($F(239, 3913) = 0.42$, $p = .99$) and no dose-by-time interaction ($F(239, 1218) = 0.52$, $p = .99$).

In supplementary analyses (not shown), we compared heart rates in the 30 minutes before and after all random prompts to heart rates around the times of heroin-only and cocaine-only drug-use entries. We chose a 30-min time interval because the number of heart-rate readings in the two hours before and after the random prompts exceeded the memory that SAS could allocate. Heart rates around the times of heroin-only and cocaine-only drug-use entries were significantly lower and higher, respectively, than heart rates around the times of all random prompts (p values $< .0001$).

3.4 Heart rate at random-prompt entries

Heart-rate data were available for 2,329 random-prompt entries. Heart rate was significantly greater 30 minutes before and after participants reported craving heroin or cocaine than when they did not (Figure 2). When participants reported craving heroin, mean (SEM) heart rate was 85.0 (0.2) compared to 82.0 (0.1) at all other RPs. There was a significant main effect of heroin craving ($F(1,16) = 230.86$, $p < .0001$), with no effect of time ($F(60, 2340) = 0.48$, $p = .99$) and no craving-by-time interaction ($F(60, 881) = 0.48$, $p = .99$). When participants reported craving cocaine, mean (SEM) heart rate was 86.4 (0.3) compared to 82.2 (0.1) at all other RPs. There was a significant main effect of cocaine craving ($F(1,14) = 157.18$, $p < .0001$), with no effect of time ($F(60, 2340) = 0.53$, $p = .99$) and no craving-by-time interaction ($F(60, 727) = 0.36$, $p = .99$). Reports of seeing drug triggers were too infrequent to produce reliable results.

Heart rates for six representative EMA questions are shown in Figure 3. Heart rates were significantly lower around RPs in which participants reported feeling relaxed, feeling happy, or doing sedentary activities such as watching TV, compared to all other RPs; means (SEM) were: relaxed 81.2 (0.1), not relaxed 83.9 (0.1) ($F(1, 39) = 428.13, p < .0001$); happy 81.6 (0.1), not happy 83.3 (0.1) ($F(1, 37) = 154.85, p < .0001$); watching TV 80.0 (0.2), not watching TV 83.0 (0.1) ($F(1, 33) = 331.46, p < .0001$). Heart rates were significantly higher around RPs in which participants reported physical activity, feeling stressed, or being hassled; means (SEM) were: walking 86.4 (0.2), not walking 81.4 (0.1) ($F(1, 35) = 991.61, p < .0001$); feeling stressed 85.0 (0.1), not stressed 81.4 (0.1) ($F(1, 35) = 609.93, p < .0001$); being hassled 87.3 (0.3), not being hassled 82.2 (0.1) ($F(1, 9) = 214.82, p < .0001$). There were no significant effects of time ($p = .60-.99$) or interactions with time ($p = .19-.99$).

4. DISCUSSION

Our most important finding, immediately apparent in each of the figures, was that our AutoSense device captured ambulatory measures of heart rate that clearly changed in the expected directions with real-time self-reported changes in mood, craving, stress, and drug use. The robustness of the associations supports the credibility of both our ambulatory heart-rate monitoring and the real-time self-report data with which we compared it.

Our intention is a practical one: to use these findings as the basis for a live mHealth intervention that detects and intervenes in behaviorally risky situations with minimal input needed from the user. To reach that practical end, we need to be conceptually clear about what we have and have not achieved.

What we have achieved is continuous field monitoring of heart rate in a manner that seems to be sensitive to behavioral and mental events of interest, such as drug craving and drug use. Laboratory studies have shown that heart rate is decreased by heroin (Tress and El-Sobky, 1980), increased by cocaine (Preston et al., 1992; Foltin et al., 1995; Preston et al., 1996; Walsh et al., 1996), and generally increased when the two are given together (Foltin and Fischman, 1992; Walsh et al., 1996). We found the same pattern in our ambulatory data during cocaine and heroin uses, including a dose-response effect between reports of having used one versus two “dimes” of cocaine. These effects were seen despite many sources of noise: the variable durations by which drug uses preceded self-reports, the variability of doses used, and the unaccounted-for (in our analyses) differences in physical activity. The lack of time effects on heart rate, for example, are likely due to variability in the time between the use and EMA entry. Accelerometer data, which are continuously collected by AutoSense, can be used to filter out data from intervals in which participants were physically active. We chose not to do that here because periods of physical activity might also have been periods of cocaine use and other activities of interest. However, we plan to incorporate such measures as we develop more detailed models.

We found that heart rates were higher when participants reported craving. Again, this is consistent with laboratory findings (Sideroff and Jarvik, 1980; Preston et al., 1996; Carter and Tiffany, 1999; Sinha et al., 2000; Hyman et al., 2007). We can rule out the possibility that our participants showed ambulatory increases in heart rate when they had *anything* to

report, because we saw decreases in heart rate when participants reported other moods (such as “relaxed” or “happy”) and sedentary activities (such as watching TV). Prior laboratory studies have shown that heart-rate variability increases with craving and exposure to cues in alcohol-dependent individuals (Garland et al., 2011; Ingjaldson et al., 2002; Quintana et al., 2013). Assessment of heart-rate variability in future studies may permit a more nuanced evaluation of exposure to cues in the natural environment.

It might seem surprising that we did not see heart-rate changes over time within the windows we examined around each entry. This was probably the result of our randomly timed method of collecting self-reports: there is no reason to expect our random sampling to relate systematically to the onset or offset of craving, moods, or activities. The durations of moods and activities presumably varied across people and occasions, so relationships washed out in the aggregated data.

To clarify what we have not yet achieved, we refer readers to literature on the search for physiological “fingerprints” of specific emotions, most recently reviewed by Quigley and colleagues (2014). Emotions are the relatively discrete, individually labeled states (e.g., happiness, anger, boredom, etc.) that occupy particular positions in two dimensions in affective space: arousal (high to low) and valence (positive to negative). Physiological measures, including ours, are generally better at detecting variations along the “arousal” dimension than the “valence” dimension (Kuppens et al., 2012). One task that lies ahead in the AutoSense project is to capture valence. Other investigators have detected changes in affective valence using facial electromyography (Dimberg, 1990) or spectral analysis of speech (Lin et al., 2014). A larger task, which may not yet be possible, is to detect not merely affective arousal and valence, but specific nameable emotions. To our knowledge, the most successful example of bodily emotion detection was a study in which participants drew maps indicating which parts of their bodies felt activated and deactivated during states that included love, pride, shame, envy, and contempt; the resultant “bodily maps” were consistent across West European and East Asian samples (Nummenmaa et al., 2014). But these were not physiological measures; they were participants’ self-reports about their perceptions of their physiology. Like other investigators (Quigley et al., 2014), we suspect that detection of specific emotions—especially ones as nuanced as love or contempt—may require self-report.

What we have already done with AutoSense in other samples, however, is detect psychological stress. We combined 13 readouts from ECG and respiration signals to infer instances of stress with high accuracy in a laboratory and in daily life (Plarre et al., 2011). What we are labeling “stress” in our AutoSense data might be more accurately called one example of a high-arousal, negatively valenced affective state. In ongoing work, we will try to develop models with which AutoSense can detect shifts into other parts of affective space, such as the low-arousal, negatively valenced states that would include boredom—a known predictor of lapses to cocaine use (Epstein et al., 2009). We have already demonstrated, as well, that we can infer instances of cocaine use in daily life by decomposing the activation effects of cocaine from the natural trajectory of heart-rate recovery after physical activity (Hossain et al., in press).

In the AutoSense work just cited (Plarre et al., 2011; Hossain et al., in press), we developed models that detected specific events in individual participants. One limitation of the heart-rate analyses presented here are that they are based on aggregated data. We have not tried to address individual differences in the physiological correlates of affective states. We intend to do so as we accumulate more data.

Our participants generally found AutoSense acceptable; accordingly, the proportion of “hours of usable data” to “hours of wear time” was high, approximately 85%. Nevertheless, participants were not enthusiastic about wearing AutoSense (except for its ability to display their heart rates and breathing patterns) and could not wear it while sleeping or bathing. We have also examined the reasons for data loss, some due to participant non-compliance, and some due to equipment limitations (Rahman et al., 2014). Ongoing improvements in sensor technology are being incorporated into AutoSense that improve the quality and quantity of the data and are contactless, thus eliminating the need for ECG electrodes and improving patient comfort (Gao et al., 2013).

The present study demonstrated that continuous field monitoring of heart rate is remarkably sensitive, at the aggregate level, to behavioral and mental events such as drug use, drug craving, and positive and negative changes in mood. Additional work is needed for live detection of these events at the individual level in mobile applications that predict behavior and deliver treatment as needed. To achieve this goal, we will need to improve the comfort, convenience, and reliability of physiological data collection and continue developing analytic methods to identify individual instances of vulnerability to drug use.

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REFERENCES

- Berntson GG, Quigley KS, Jang JF, Boysen ST. An approach to artifact identification: application to heart period data. *Psychophysiology*. 1990; 27:586–598. [PubMed: 2274622]
- Berridge KC, Winkielman P. What is an unconscious emotion? (The case for unconscious “liking”). *Cogn. Emot.* 2003; 17:181–211.
- Carroll KM, Kiluk BD, Nich C, Gordon MA, Portnoy GA, Marino DR, Ball SA. Computer-assisted delivery of cognitive-behavioral therapy: efficacy and durability of CBT4CBT among cocaine-dependent individuals maintained on methadone. *Am. J. Psychiatry*. 2014; 171:436–444. [PubMed: 24577287]
- Carter BL, Tiffany ST. Cue-reactivity and the future of addiction research. *Addiction*. 1999; 94:349–351. [PubMed: 10605863]
- Collins F. How to fulfill the true promise of “mHealth”: mobile devices have the potential to become powerful medical tools. *Sci. Am.* 2012; 307:16. [PubMed: 22779258]

- Dallery J, Raiff BR, Grabinski MJ. Internet-based contingency management to promote smoking cessation: a randomized controlled study. *J. Appl. Behav. Anal.* 2013; 46:750–764. [PubMed: 24114862]
- Dimberg U. Perceived unpleasantness and facial reactions to auditory stimuli. *Scand. J. Psychol.* 1990; 31:70–75. [PubMed: 2333489]
- Epstein DH, Willner-Reid J, Vahabzadeh M, Mezghanni M, Lin JL, Preston KL. Real-time electronic diary reports of cue exposure and mood in the hours before cocaine and heroin craving and use. *Arch. Gen. Psychiatry.* 2009; 66:88–94. [PubMed: 19124692]
- Epstein DH, Tyburski M, Craig IM, Phillips KA, Jobes ML, Vahabzadeh M, Mezghanni M, Lin JL, Furr-Holden CD, Preston KL. Real-time tracking of neighborhood surroundings and mood in urban drug misusers: application of a new method to study behavior in its geographical context. *Drug Alcohol Depend.* 2014; 134:22–29. [PubMed: 24332365]
- Ertin, E.; Stohs, N.; Kumar, S.; Raji, AB.; al'Absi, M.; Kwon, T.; Mitra, S.; Shah, S.; Jeong, JW. Autosense: Unobtrusively Wearable Sensor Suite For Inferencing Of Onset, Causality, And Consequences Of Stress In The Field; Proceedings of the 9th ACM International Conference on Embedded Networked Systems (SenSys); 2011.
- First, MB.; Williams, JBW.; Spitzer, RL.; Gibbon, M. Biometrics Research. New York: New York State Psychiatric Institute; 2007. Structured Clinical Interview for DSM-IV TR Axis I Disorders, Clinical Trials Version (SCID-CT).
- Foltin RW, Fischman MW. The cardiovascular and subjective effects of intravenous cocaine and morphine combinations in humans. *J. Pharmacol. Exp. Ther.* 1992; 261:623–632. [PubMed: 1578376]
- Foltin RW, Fischman MW, Levin FR. Cardiovascular effects of cocaine in humans: laboratory studies. *Drug Alcohol Depend.* 1995; 37:193–210. [PubMed: 7796714]
- Gao, J.; Ertin, E.; Kumar, S.; al'Absi, M. Contactless Sensing Of Physiological Signals Using Wideband RF Probes; Asilomar Conference on Signals, Systems, and Computers; 2013.
- Hossain SM, Ali AA, Rahman MM, Ertin E, Epstein DH, Kennedy A, Preston KL, Umbricht A, Chen Y, Kumar S. Identifying Drug (Cocaine) Intake Events From Acute Physiological Response In The Presence Of Free-Living Physical Activity. *Information Processing in Sensor Networks (IPSN)*, 11th International Conference. in press.
- Hyman SM, Fox H, Hong KI, Doebrick C, Sinha R. Stress and drug-cue-induced craving in opioid-dependent individuals in naltrexone treatment. *Exp. Clin. Psychopharmacol.* 2007; 15:134–143. [PubMed: 17469937]
- Kuppens P, Tuerlinckx F, Russell JA, Barrett LF. The relation between valence and arousal in subjective experience. *Psychol. Bull.* 2012; 139:917–940. [PubMed: 23231533]
- Lin CH, Liao WK, Hsieh WC, Liao WJ, Wang JC. Emotion identification using extremely low frequency components of speech feature contours. *ScientificWorldJournal.* 2014; 2014:1–7.
- Marlatt, GA.; Gordon, JRE. Relapse Prevention: Maintenance Strategies in the Treatment of Addictive Behaviors. New York: Guilford Press; 1985.
- Marsch LA, Guarino H, Acosta M, Aponte-Melendez Y, Cleland C, Grabinski M, Brady R, Edwards J. Web-based behavioral treatment for substance use disorders as a partial replacement of standard methadone maintenance treatment. *J. Subst. Abuse Treat.* 2014; 46:43–51. [PubMed: 24060350]
- McLellan AT, Luborsky L, Cacciola J, Griffith J, Evans F, Barr HL, O'Brien CP. New data from the Addiction Severity Index: reliability and validity in three centers. *J. Nerv. Ment. Dis.* 1985; 173:412–423. [PubMed: 4009158]
- Nummenmaa L, Glerean E, Hari R, Hietanen JK. Bodily maps of emotions. *Proc. Natl. Acad. Sci. U. S. A.* 2014; 111:646–651. [PubMed: 24379370]
- Pan J, Tompkins WJ. A real-time QRS detection algorithm. *IEEE Trans. Biomed. Eng.* 1985; 32:230–236. [PubMed: 3997178]
- Plarre, K.; Raij, A.; Hossain, SM.; Ali, AA.; Nakajima, M.; al'Absi, M.; Ertin, E.; Kamarck, T.; Kumar, S.; Scott, M.; Siewiorek, D.; Smailagic, A.; Wittmers, LE. Continuous Inference Of Psychological Stress From Sensory Measurements Collected In The Natural Environment; Proceedings of the 10th IEEE/ACM International Conference on Information Processing in Sensor Networks (IPSN); 2011. p. 97-108.

- Preston KL, Sullivan JT, Strain EC, Bigelow GE. Effects of cocaine alone and in combination with bromocriptine in human cocaine abusers. *J. Pharmacol. Exp. Ther.* 1992; 262:279–291. [PubMed: 1625204]
- Preston KL, Sullivan JT, Strain EC, Bigelow GE. Enhancement of cocaine's abuse liability in methadone maintenance patients. *Psychopharmacology.* 1996; 123:15–25. [PubMed: 8741950]
- Preston KL, Vahabzadeh M, Schmittner J, Lin JL, Gorelick DA, Epstein DH. Cocaine craving and use during daily life. *Psychopharmacology.* 2009; 207:291–301. [PubMed: 19777216]
- Preston KL, Epstein DH. Stress in the daily lives of cocaine and heroin users: relationship to mood, craving, relapse triggers, and cocaine use. *Psychopharmacology.* 2011; 218:29–37. [PubMed: 21336579]
- Quigley, KS.; Lindquist, KA.; Barrett, LF. Inducing and measuring emotion and affect: tips, tricks, and secrets. In: Reis, H.; Judd, C., editors. *Handbook of Research Methods in Personality and Social Psychology.* New York: Oxford University Press; 2014.
- Rahman, MM.; Hossain, SM.; Ali, AA.; Raij, A.; Hovsepian, K.; al'Absi, M.; Beck, JG.; Ertin, E.; Kedia, S.; Scott, M.; Tempelman, L.; Ward, KD.; Kumar, S. Technical report CS-12-001. Memphis: University of Memphis; 2012. Bringing The Lab To The Field: A Week-Long Wireless Mhealth Field Study With An Addictive Population.
- Robins, LN.; Cottler, LB.; Bucholz, KK.; Compton, WM, III. The Diagnostic Interview Schedule, version IV. St. Louis, MO: Washington University; 1995.
- Sideroff SI, Jarvik ME. Conditioned responses to a videotape showing heroin-related stimuli. *Int. J. Addict.* 1980; 15:529–536. [PubMed: 7409946]
- Sinha R, Fuse T, Aubin LR, O'Malley SS. Psychological stress, drug-related cues and cocaine craving. *Psychopharmacology.* 2000; 152:140–148. [PubMed: 11057517]
- Tress KH, El-Sobky AA. Cardiovascular, respiratory and temperature responses to intravenous heroin (diamorphine) in dependent and non-dependent humans. *Br. J. Clin. Pharmacol.* 1980; 10:477–485. [PubMed: 7437259]
- Vahabzadeh, M.; Epstein, DH.; Mezghanni, M.; Lin, J-H.; Preston, KP. An Electronic Diary Software For Ecological Momentary Assessment (EMA) In Clinical Trials; Proceedings of the 17th IEEE Symposium on Computer-Based Medical Systems (CBMS); 2004. p. 167-172.
- Walsh SL, Sullivan JT, Preston KL, Garner JE, Bigelow GE. Effects of naltrexone on response to intravenous cocaine, hydromorphone and their combination in humans. *J. Pharmacol. Exp. Ther.* 1996; 279:524–538. [PubMed: 8930154]
- Waters AJ, Szeto EH, Wetter DW, Cinciripini PM, Robinson JD, Li Y. Cognition and craving during smoking cessation: an ecological momentary assessment study. *Nicotine Tob. Res.* 2014; 16(Suppl. 2):S111–S118. [PubMed: 23901053]

Highlights

High-quality heart-rate data can be obtained from drug users in the field.

Drug craving is associated with increased heart rate in the natural environment.

Dose-related effects of cocaine on heart rate were detectable in the field data.

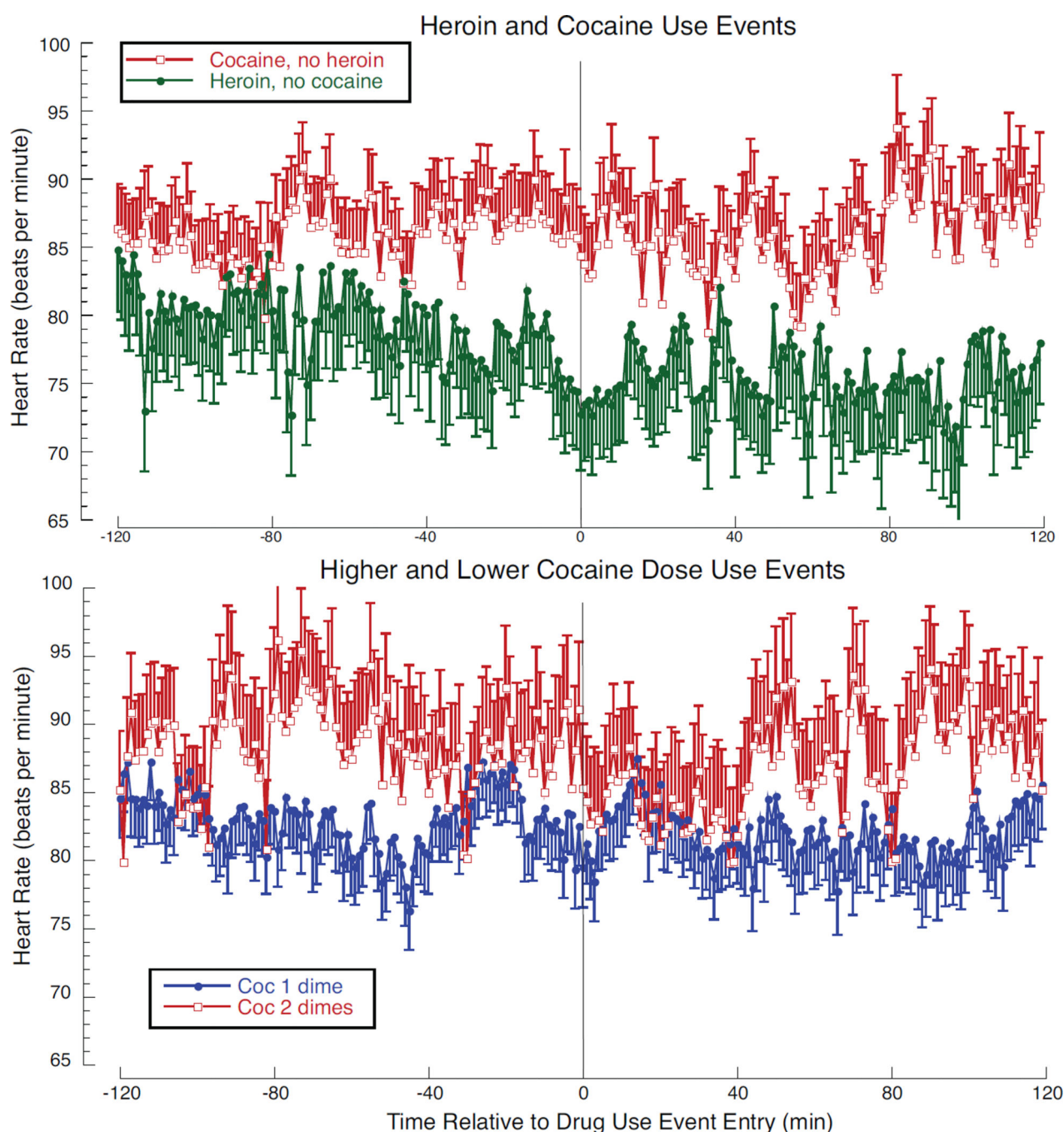


Figure 1.

Mean heart rate in the 120 minutes before and after event-contingent (i.e., participant-initiated) EMA entries reporting the use of heroin or cocaine (top panel, N=28) and after EMA entries reporting the use of 1 or 2 “dimes” of cocaine (bottom panel, N=20). For clarity, we do not show data from events in which both heroin and cocaine were used. Error bars indicate standard errors of the mean. In all cases, drug use occurred prior to the time of entry, indicated by a vertical line at time 0. The denominator degrees of freedom in this and all other EMA analyses reflect the number of participants who contributed data to more than

one line in the graph, though the analyses include data from all participants who contributed data to any line in the graph.

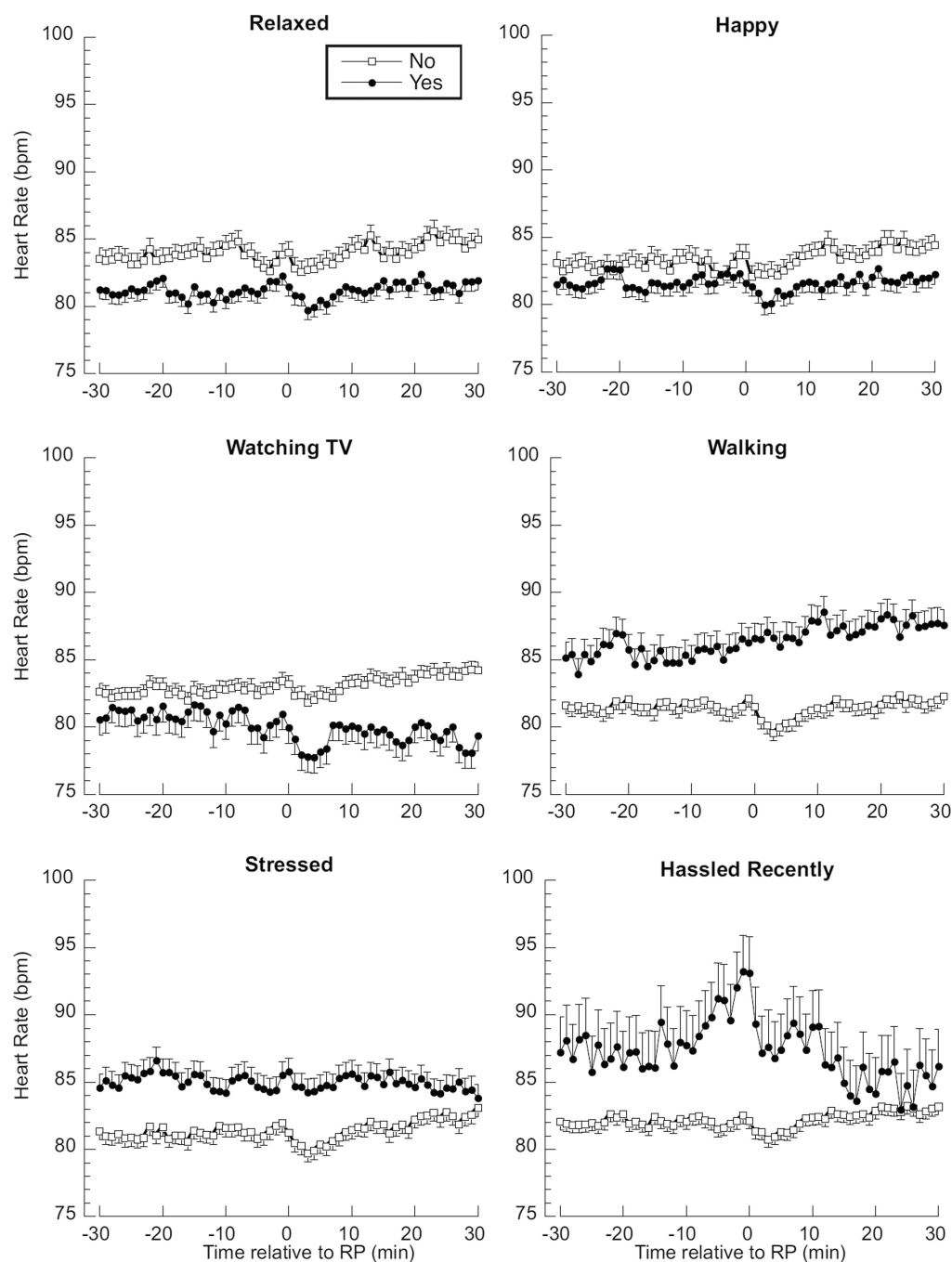


Figure 2.

Mean heart rate in the 30 minutes before and after random-prompt EMA entries in which participants are reporting either the presence or absence of cravings for heroin or cocaine. Data are shown for 40 participants. Other details are the same as in Figure 1.

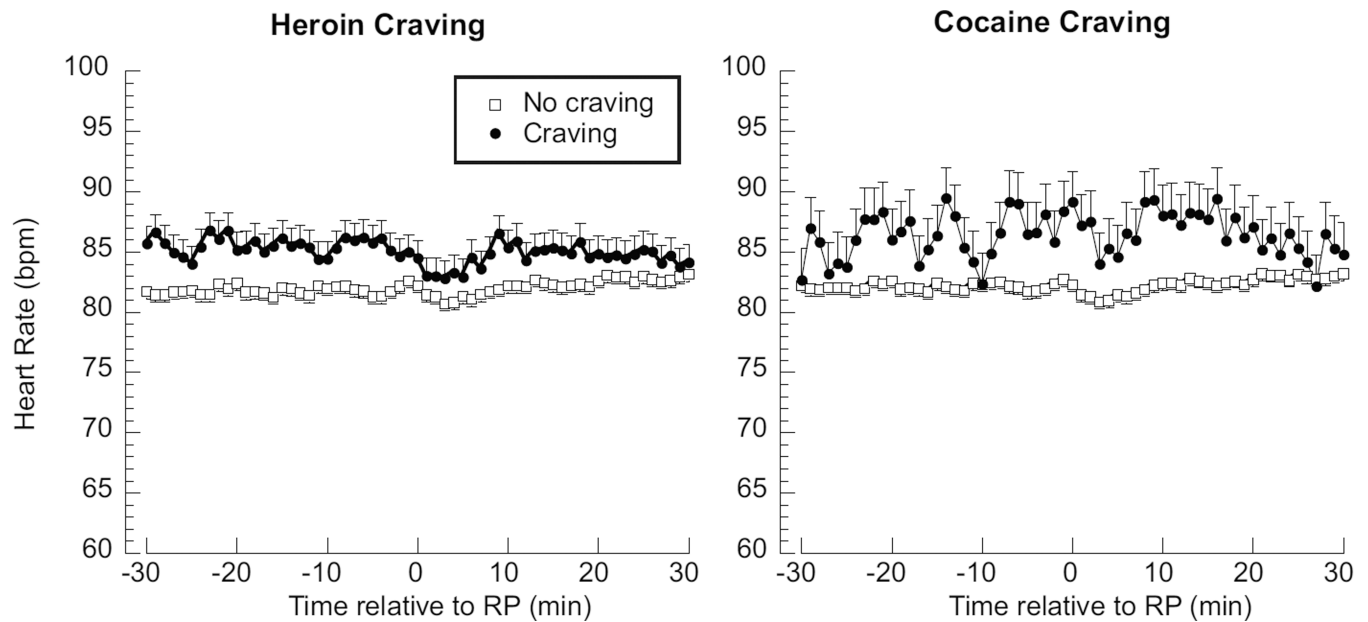


Figure 3.

Mean heart rate in the 30 minutes before and after random-prompt EMA entries in which participants reported the presence or absence of feeling relaxed, feeling happy, watching TV, walking, feeling stressed, and having recently been hassled. Data are shown for 40 participants. Other details are the same as in Figure 1.

Table 1

Clinical and demographic characteristics of study participants

Demographic	Completers (n=40)	Noncompleters (n=17)	Statistics
Yrs of education ^a	12.0 (1.3)	11.9 (1.5)	T(55) = -2.13, p=.82
Sex ^b Men	30 (75%)	10 (59%)	X ² (1)=1.49, p=.22
Age ^a (years)	41.4 (8.3)	41.1 (11.7)	T(55)=-0.10, p=.92
Race/ethnicity ^b			exact p=.89
Black/African American	22 (55%)	9 (53%)	
White	16 (40%)	8 (47%)	
Hispanic	1 (2.5%)		
Multiple race	1 (2.5%)		
Marital Status ^b			exact p=.05
Married	10 (26%)	0	
Never Married	22 (56%)	13 (76%)	
Other	7 (17.5%)	4 (24%)	
Employment ^b			exact p=.42
Full Time	18 (46%)	6 (35%)	
Part Time/Other	10 (25%)	5 (29%)	
Unemployed	11 (28%)	3 (18%)	
Heroin			
Days used in last 30 ^a	16.5 (11.8)	16.3 (14.0)	t(55)=-0.06, p=.95
Years using ^a	14.1 (9.6)	11.9 (9.8)	t(55)=-0.79, p=.43
Route of administration ^b			X ² (1)=0.02, p=.89
Intravenous	15 (41%)	7 (44%)	
Nasal	21 (58%)	9 (56%)	
Other Opioids			
Days used in last 30 ^a	12.0 (12.6)	10.9 (12.5)	t(55)=-0.31, p=.75
Years using ^a	1.8 (3.1)	1.9 (3.5)	t(55)=-0.16, p=.88
Route of administration ^b			exact p=.53
Oral	30 (97%)	13 (93%)	
Nasal	1 (3%)	1 (7%)	
Cocaine			
Days used in last 30 ^a	6.1 (9.6)	4.9 (8.0)	t(55)=-0.45, p=.66
Years using ^a	5.5 (6.9)	5.8 (7.9)	t(55)=0.13, p=.90
Route of administration ^b			exact p=.90
Intravenous	7 (22%)	2 (14%)	
Nasal	7 (22%)	3 (22%)	
Smoked	18 (56%)	9 (64%)	
DSM diagnoses ^b			

Demographic	Completers (n=40)	Noncompleters (n=17)	Statistics
Cocaine dependence	20 (50%)	5 (30%)	exact p=.24
Opioid dependence	37 (92.5%)	17 (100%)	exact p=.55
Alcohol dependence	7 (17.5%)	3 (17.6%)	exact p=.99
Marijuana dependence	1 (2.5%)	3 (17.6%)	exact p=.07
Sedative dependence	1 (2.5%)	2 (11.8%)	exact p=.21
Obsessive Compulsive	2 (5%)	1 (6%)	exact p=.99
Antisocial Personality	20 (50%)	7 (41%)	exact p=.58

^a mean (SD);

^b N (%)