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Non-Treatment Laboratory Stress-and Cue-Reactivity Studies are Associated with Decreased Substance Use Among Drug-Dependent Individuals

Stacia M. DeSantis *

Department of Biostatistics, Bioinformatics, and Epidemiology, 135 Cannon Street Suite 303, Charleston, SC 29425 USA

Dipankar Bandyopadhyay,

Department of Biostatistics, Bioinformatics, and Epidemiology, 135 Cannon Street Suite 303, Charleston, SC 29425 USA

Sudie E. Back, and

Department of Psychiatry and Behavioral Sciences, Clinical Neuroscience Division, 67 President Street, Charleston, SC 29425 USA

Kathleen T. Brady

Department of Psychiatry and Behavioral Sciences, Clinical Neuroscience Division, 67 President Street, Charleston, SC 29425 USA

Stacia M. DeSantis: desantis@musc.edu; Dipankar Bandyopadhyay: bandyopd@musc.edu; Sudie E. Back: backs@musc.edu; Kathleen T. Brady: bradyk@musc.edu

Abstract

Introduction—Human laboratory paradigms for examining stress-or cue-reactivity in substance-dependent individuals often involve exposure to pharmacological, psychosocial or physical laboratory procedures or drug paraphernalia. This study examines whether participation in such studies alters drug-seeking behavior and which patient attributes contribute to increased use.

Methods—In two separate studies, the relationship between participation and drug use post study were examined. Cocaine-dependent participants received 1µg/kg of corticotropin releasing hormone intravenously, underwent the Trier Social Stress Task, and were exposed to drug cues and various measures obtained. Cocaine use for 90 days prior and 28 days following the study was assessed. Methamphetamine-dependent participants were exposed to drug cues and various measures obtained. Methamphetamine use for 90 days prior and 14 days following the study was assessed.

* author to whom correspondence should be addressed.

Contributors

Authors Kathleen T. Brady and Sudie E. Back designed the study and wrote the protocol. Authors Stacia M. DeSantis, Dipankar Bandyopadhyay, and Sudie E. Back managed the literature searches and summaries of previous related work. Authors Stacia M. DeSantis and Dipankar Bandyopadhyay undertook the statistical analysis, and author Stacia M. DeSantis wrote the 3rd draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of Interest

All authors declare that they have no conflicts of interest.

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Weekly drug use was modeled using a 2-state hidden Markov model assuming two possible underlying states at each week. Bayesian estimation was used. Results are presented as posterior mean odds ratios (OR) and 95% credible intervals (CI).

Results—Participation decreased the odds of remaining in or transitioning to the high use state (cocaine study OR = 0.04 [CI = 0.01, 0.11]; methamphetamine study OR = 0.39 [CI = 0.07, 1.70]). In the cocaine study, older age increased the odds of remaining in or transitioning into the high use state (1.66 [CI = 0.99, 2.96]). In the methamphetamine study, male gender increased the odds (2.70 [CI = 1.10, 6.17]).

Conclusion—Stress and cue exposure paradigms were associated with a decreased odds of drug use following participation.

Keywords

Cue-reactivity; stress-reactivity; substance abuse; substance dependence; cocaine; methamphetamine; time line follow back

1 Introduction

Minimizing risks to human subjects participating in clinical research is of paramount importance. Human laboratory paradigms for examining stress-or cue-reactivity in substance-dependent individuals often involve exposure to short-term pharmacological, psychosocial or physical laboratory-based procedures or drug paraphernalia (Back et al., 2005, 2008; Sinha, et al., 2000; Saladin, et al., 2002; Coffey, et al., 2002; Brady et al., 2009). Clinical research demonstrates that psychosocial stress contributes to drug-seeking behavior and increased risk of relapse (Brown, et al., 1995; Karlsgodt, et al., 2003). It is unclear, however, whether participation in laboratory paradigms which invoke stress or craving could lead to drug-seeking behavior or relapse among individuals with substance use disorders. Clinical research designed to improve treatment of future patients must be designed such that there is minimal risk associated with participation (Brandon, et al., 1995; Dawe and Power, 1995). As such, it is of great interest to determine whether participation in clinical non-treatment research studies designed to induce stress or craving affect subsequent substance use intake.

Ethical issues in substance abuse research have been widely studied, mainly with respect to coercion, ability to consent, and the influence of monetary reward on drug-seeking behavior (Striley, et al., 2008; Frestinger, et al., 2005; Dempsey, et al., 2008; Anderson and Dubois, 2007). Using Time-Line Follow-Back data, Dempsey et al. (2008) showed that compensating cocaine-dependent participants with cash, as opposed to a money order, did not result in increased rates of cocaine use during a one-month follow-up period. In fact, monetary compensation has been shown to double the abstinence rate in smoking studies (Kaper, et al., 2005). Several studies have documented that cocaine-dependent individuals show increased craving and signs of physiological arousal when presented with drug cues in a laboratory setting (Childress, et al., 1988; Ehrman, et al., 1992; Brady, et al., 2008). In addition among cocaine-dependent individuals, it has been shown that increased cue-elicited craving predicts shorter time to drug relapse during follow-up (Sinha, et al., 2006; Back, et al., unpublished). In an outpatient cocaine cue-reactivity study, Ehrman et al. (1998) showed that 90% of patients had the same urine test results before and 3 days after cocaine cues were presented. To date, none of these studies have provided specific insight into longitudinal drug using behavior as a response to participating in non-treatment outpatient clinical research.

Therefore, the purpose of this study was to expand upon previous research by determining whether drug use (i.e., numbers of days of drug use per week) was affected by participation in non-treatment stress-and cue-reactivity studies. Participation in two separate studies of

cocaine-and methamphetamine-dependent individuals was examined. We selected the methamphetamine study because there is very little literature regarding methamphetamine cue-reactivity; thus, the risk to benefit ratio has not been adequately addressed. We selected the cocaine study because cocaine cue-reactivity is currently and has been widely studied and, therefore, uncovering potential risks and benefits would be of great interest. The null hypothesis is that participation increases post-study compared to pre-study drug use while the alternative hypothesis is that there is no change or a decrease in post-study use.

As previous research indicates that several demographic characteristics may represent risk or protection factors for drug use, covariate effects are also explored. For example, gender differences in substance use initiation, treatment efficacy, and relapse are well-documented (Elton and Kilts, 2009). Similarly, racial differences in maintenance of drug-seeking behavior, which may be driven by more difficult social situations or higher-stress environments, have been explored (e.g., Castellani, et al., 1997; Walton, et al., 2001).

2 Cocaine Study

2.1 Participants

Participants in the cocaine study were 45 adults (25 men, 20 women) who met DSM-IV criteria for current cocaine dependence. They were part of a larger, non-treatment study examining the relationship between stress reactivity, hypothalamic pituitary adrenal (HPA) axis functioning, and cocaine dependence. Exclusion criteria included psychiatric conditions known to affect HPA-axis functioning, pregnancy, obesity, or other major medical disorders that could affect the HPA axis. Participants were recruited via newspaper and other media advertisements. The study was approved by the Medical University of South Carolina (MUSC) Institutional Review Board (IRB). Participants with elevated craving following testing procedures were required to stay in the hospital until craving subsided, and all participants were provided with resources for treatment programs in the community prior to discharge.

2.2 Procedures

Following baseline assessment, participants underwent an overnight stay at the General Clinical Research Center (GCRC) where they were exposed to pharmacological and psychosocial laboratory stress tests. During the two-day hospital stay, three tasks were conducted: 1) the Trier Social Stress Task, 2) a pharmacological provocation (i.e., administration of corticotrophin releasing hormone; CRH), and 3) a drug cue exposure paradigm (i.e., drug paraphernalia and a video depicting cocaine use) (Kirschbaum, et al., 1993). In order to control extraneous variables that may affect stress reactivity (e.g., nutrition, caffeine, sleep), participants were admitted to the hospital at approximately 2000h the evening prior to the first day of testing. Participants were discharged 2 hours following the last test. The follow-up visit was conducted 30 days after discharge during which participants were asked to provide detailed information about drug use since the testing.

2.3 Measures

The Structured Clinical Interview for DSM-IV was used to diagnose cocaine dependence (First, et al., 2002). The Time-Line Follow-Back (TLFB), a calendar-based instrument used to assess daily self-reported substance use, was used to assess the dollar value and frequency of cocaine use approximately 90 days before and 28 days after the study (Sobell and Sobell, 1996). Before, during and after each stress task, neuroendocrine (e.g., cortisol) and physiological measures (e.g., heart rate) were obtained along with subjective reports of stress and craving.

2.4 Statistical Methods

Wang, et al. (2002) discuss why simple summary statistics are not adequate for modeling substance use over time. For example, the average use per using day does not differentiate one subject who uses moderately every day and another subject who binges only on the weekend, and the percent days used does not differentiate between light and heavy use. Therefore, it is optimal to model the observed data at high resolution (i.e., via daily or weekly observations) as opposed to a lower dimensional commonly used summary statistics. This allows for patient-specific predictions and in the current case, allows us to incorporate time dependent covariate effects.

The TLFB data represent serial binary correlated measures of drug use, which were summarized into weekly counts. For each subject at each week, it was hypothesized that there exist two underlying latent substance using states corresponding to “high use” and “low use.” These terms are unrelated to the DSM-IV criteria for substance abuse; they are simply latent indicators for high and low levels of substance use in the current sample. The probability of high use for a subject in a given week was assumed to depend on the subject’s prior state, fixed demographics variables (e.g., gender, smoking status, age, race) and the time-varying covariate, participation in the clinical study. Counts were assumed to arise from a Poisson distribution. A 2-state Hidden Markov model (HMM) to reflect these latent abuse states was proposed. A schematic HMM diagram is shown in Figure 1. Such latent constructs have been previously proposed for counts in the psychiatric and drug abuse literature. For example, in a longitudinal clinical trial of alcohol use disorders, based on daily usage data, Shirley et al. (unpublished) hypothesized three underlying drinking states representing no drinking, heavy drinking, and light drinking. Wall and Li (2008) used a similar approach, hypothesizing the existence of an underlying healthy or unhealthy state based on the frequency of alcohol-related hospital visits. Similarly, Scott et al. (2005) modeled underlying health states of schizophrenic patients in a longitudinal drug treatment study. The common thread underlying all of these studies is the desire to model health or drug use status over time at high resolution.

We adopted a Bayesian approach to fitting the model because of its simplicity of exposition and ability to incorporate prior information. Analyses were implemented in WinBUGS Version 14.3 (Spiegelhalter et al., 2008). All results evaluating the effect of the non-treatment study and demographic variables on drug use are presented in terms of posterior mean odds ratios and 95% credible intervals (OR [95% CI]). In the Bayesian paradigm, significance tests are not used because the reported odds ratios and CI are obtained from the true distribution of the parameter; however, Bayesian credible intervals, which represent the 2.5th and 97.5th percentiles, are akin to 95% confidence intervals. Where these intervals exclude or nearly exclude 1, the effects of that covariate are reported as relevant. Where means are presented, they represent posterior means and posterior standard errors (SE).

After fitting the model, each patient at each week was assigned to a latent state: high or low use. Given the states inferred by the model, post hoc Chi-square tests for independence were conducted to determine which variables were predictive of state membership.

Results

Historical data were complete in 45 subjects while follow-up data were missing on average, less than 10% of days. The mean [range] age in the study was 38 [20–53], 44.4% were female, 46.7% were African American, 45.5% were employed, 54.5% attended some college, 80.0% were smokers, and 33.3% were married. Figure 2, top panel, represents TLFB daily usage for the 12 weeks prior to and 4 weeks after completion of the 2-day study. The estimated mean number of days used per week for participants in the high use state was 5.5 (SE = 1.1) versus 0.9 (SE = 1.0) days in the low use state. Table 1 illustrates posterior mean and median odds

ratios (95% CI) obtained by fitting the hidden Markov model to the weekly count data. The odds of transitioning to or remaining in a high use state in any given week after participation in the study was 0.04 [0.01, 0.11] of what it was in the 12 weeks prior to the research study. As this 95% CI excludes 1, it provides evidence of a substantially protective effect of study participation on subsequent drug use. This effect is illustrated in the bottom panel of Figure 2. This panel shows the assigned latent state for the individual, where black represents the low use and white represents the high use state. Accounting for covariate effects, the study-specific benefit (seen after week 12) in reducing drug using behavior is evident by the preponderance of black rectangles in the figure. The odds of remaining in or transitioning to the high use state increased 1.66 [0.99, 2.96] times for every standardized increase in age. This CI barely covers the value 1 indicating that increasing age is an important predictor of remaining in or transitioning to the high use state.

Of note, in Figure 2, the first 20 patients are female while the last 25 are male. The fitted model visually implies that in general, there is more variability in abuse among the females; i.e., females are more likely than males to switch between high and low use states.

As expected, due to serial autocorrelation of weekly counts, an individual's pre-study use state was highly predictive of their post-study state, thus the odds of transitioning between high and low states were small in this population. Alternatively stated, the odds of remaining in the high use state at time t given that a participant was in the high use state at time $t-1$, is 305.82. This characterizes the very strong week-to-week dependence of cocaine abuse behavior and provides a strong rationale for the implementation of the Markov model.

For the purpose of this analysis, a "full study effect" was defined, a priori, as being in the high use state every single week for all 4 weeks immediately prior to the study, and for zero weeks after the study. According to their latent state, 12/45 (26.7%) participants exhibited a full study effect. Furthermore, 17/45 (37.8%) who exhibited high use for at least one of the twelve weeks prior to the study, did not exhibit high use in any of the four follow-up weeks. Note that this does not mean that they did not use cocaine; it means that they were not assigned to an underlying high use state in that time frame. Almost half (21/45; 46.7%) never exhibited high use throughout the 16 weeks. Five participants (11.1%) demonstrated follow-up use that was either moderately improved or consistent with prior behavior, and 1 (2.2%) participant who was considered low use for all weeks prior to the study, transitioned to high use following study completion. Thus, a detrimental study effect was observed in only 1 out of 45 participants.

In a post hoc analysis, we considered whether gender, smoking, race, or age could distinguish the 39 participants who experienced a decrease in use (favorable) from the 6 participants who experienced no change or increased use (unfavorable). Smoking was significantly predictive of a favorable effect (Chi square = 17.4, p -value = 0.0001).

4 Methamphetamine Study

4.1 Participants

Participants in the methamphetamine study were 40 people (10 men, 30 women) aged 18–50 who met the criteria for methamphetamine dependence ($N=38$) or methamphetamine abuse ($N=2$) in the past six months. Participants were recruited via newspaper and other media advertisements. All participants were required to maintain abstinence from methamphetamine, alcohol, and all other drugs of abuse except nicotine as confirmed by breathalyzer and urine drug screening on the day of test assessments. Exclusion criteria included a history of or current psychotic disorder, bipolar affective disorder, or major depressive disorder requiring antidepressant pharmacotherapy or presenting with significant suicidal risk. Participants with current severe anxiety disorders including panic disorder, posttraumatic disorder, generalized

anxiety disorder, or currently treated with benzodiazepines, beta-blockers, anti-arrhythmic agents, psychostimulants or any other agents known to interfere with heart rate and skin conductance monitoring were excluded. The study was approved by the IRB of MUSC. All participants provided written informed consent after being fully informed of potential risks of participation.

4.2 Procedures

Study procedures were conducted at the research clinic of Behavioral Health Services in Pickens, South Carolina, a member site of the NIDA Clinical Trials Network. Participants were screened using the MINI International Neuropsychiatric Interview (Sheehan et al. 2003), a structured interview based on the DSM-IV for assessment of psychiatric and substance use symptoms. A subset of participants was asked to read an evocative guided imagery script related to personal memories of methamphetamine use prior to the cue exposure procedure.

Methamphetamine cues consisted of: (1) 30–35 still photographs of individuals procuring and using methamphetamine (2) a 7–8 minute video depicting methamphetamine use in a variety of settings, and (3) "in vivo" paraphernalia and simulated methamphetamine placed directly on a table in front of the subject for 5 minutes. Physiological and subjective measures were obtained during and immediately after exposure to each cue modality.

4.3 Measures

The Time-Line Follow-Back (TLFB) was used to assess the dollar value and frequency of cocaine use approximately 90 days before and 28 days after the study (of which data were available for 14). Before, during and after each cue exposure physiological measures (e.g., heart rate) were obtained along with subjective reports of craving.

4.4 Results

Historical data were complete in 40 subjects while follow-up data were missing on 15 subjects. The mean [range] age in the study was 31 [19–49], 26.2% were male, 100% were caucasian, 35.7% were employed, 50.0% had a high school degree or greater, 88.1% were smokers, 16.7% were married, 33.3% had an income greater than \$10,000, and 69.0% were seeking treatment at the time of the study. Figure 3, top panel, represents TLFB daily usage for the 12 weeks prior to and 2 weeks after completion of the 2-day study.

The estimated mean number of days used per week for those in the high use state was 3.0 (1.7) versus 1.0 (1.0) days in the low use state. The bottom half of Table 1 illustrates posterior mean and median odds ratios (95% CI) obtained by fitting the hidden Markov model to the weekly count data. The odds of transitioning to or remaining in a high use state in any given month after participation in the study was 0.39 [0.07, 1.70] of what it was in the 12 weeks prior to the research study. While this Bayesian estimate shows substantial evidence of reduced odds of use after the study, the 95% CI does not exclude 1. However the clear reduction in methamphetamine use is illustrated in the bottom panel of Figure 3, which has the same interpretation as Figure 2. Accounting for covariate effects, the study-specific benefit (seen after week 12) in reducing drug using behavior is evident by the preponderance of black rectangles in the figure. In fact, none of the 25 patients for whom follow-up data were available used methamphetamine in the two weeks after participation in the study.

The odds of remaining in or transitioning to the high use state in males versus females was 2.70 [1.10, 6.17]. This CI, exclusive of 1, indicates that male gender was an important predictor of remaining in or transitioning to the high use state. Of additional note is also the effect of employment status on transitioning; those who were employed had a decreased odds of remaining in or transitioning to the high use state (OR = 0.42, [0.13, 1.25]). For all other

covariates considered, odds ratios were near 1 and credible intervals covered 1, thus these demographic variables were not predictive of use behavior. Interestingly, whether a person was enrolled in treatment had no effect on transitioning to or remaining in the high use state (OR = 1.07, [0.34, 3.22]).

As with the cocaine study, due to serial autocorrelation of weekly counts, an individual's pre-study state was highly predictive of their post-study state, thus the odds of transitioning between high and low states were small in this population. This characterizes the very strong week-to-week dependence of methamphetamine use behavior.

Conclusion

The goal of this study was to determine whether participation in human laboratory stress or cue-reactivity research was associated with longitudinal increased drug use in cocaine- and methamphetamine-dependent individuals, and to determine relevant demographic predictors of use. To our knowledge, this is the first study to assess effects up to 4 weeks after study completion, as well as the first to examine methamphetamine users (up to 2 weeks). The current investigation builds on previous research by Ehrman, et al. (1998), who demonstrated no deleterious effects of outpatient cue reactivity on cocaine-dependent subjects in the 3 days following the study. The current study demonstrates the absence of deleterious effects of study participation on long term drug use parameters, and provides evidence of significantly decreased use following study participation. However, as neither study had an independent control group of participants, further studies are needed to make such assertions.

According to the hidden Markov model of underlying use, 26.7% of cocaine participants exhibited high use behavior before the study but low use behavior in the four weeks after the study, and 37.8% of participants consistently exhibited low use behavior after they consented to participation. This translates to a 64.5% low use rate in the 4 weeks of follow-up in the cocaine study. These rates mirror the abstinence rates reported following treatment for cocaine addiction (Brodie, et al., 2003; Dackis, et al., 2005; Stein, et al., 2009). Stein, et al (2009) observed a 33% and 26% one-month abstinence rate in intervention versus nonintervention cocaine groups; Brodie, et al. (2003) showed that 40% of cocaine-dependent participants who entered the study regardless of treatment group, completed a 4 week follow-up period without relapse. Our findings suggest that over a similar time frame, stress- and cue-reactivity research in drug-dependent individuals is safe and is associated with a clinically significant decreased odds of drug use following study participation.

Sixty percent of methamphetamine users for whom follow-up data were available exhibited high use behavior before the study but complete abstinence in the two weeks after the study. In a clinical trial of bupropion to treat methamphetamine dependence, Shoptaw, et al. (2008) reported a 39% and 38% 2-week abstinence rate in treatment and placebo arms, respectively. Again, the estimates observed in the current methamphetamine study mirror those observed in treatment studies.

The current analysis employed a latent variable model because of its ability to analyze use data at high resolution, as well as to simultaneously incorporate time-dependent covariate effects. Unlike summary measures, it also allows researchers to visualize exactly when patients relapse. However, standard approaches in the substance abuse literature consider percent days used as the primary outcome. An analysis comparing the percent days used before versus after participation in the cocaine study was therefore performed for comparison purposes, using a paired T-test. Linear regression was then implemented on the post-pre percent days used differences scores to see which covariate effects were predictive of differential use. The paired t-test was highly significant ($p < 0.0001$), indicating that participation in the cocaine study

decreased the percent of days used, but no covariate effects were found to effect the post-pre difference scores. This is in contrast to results from fitting the latent variable model, where both age and gender were shown to be predictors of state membership. The more complex model is justified here, as modeling the data as correlated weekly counts uncovered covariate effects on use behavior.

There are several potential explanations for the observed findings. As people enter a clinical study, assessments are collected and self-monitoring of behavior alone often leads to a behavioral change. It has been demonstrated that self-monitoring alone can have significantly influence behavioral change leading to weight loss in obesity (Butryn, et al., 2007) and decreased smoking in non-treatment seeking smokers (Peters and Hughes, in press). Also, drug-dependent individuals willing to enter a study, even a non-treatment study, may be implicitly expressing willingness to change or examine their drug use behaviors. Finally, the safe environment and motivational materials provided by the clinic may increase therapeutic behaviors among participants.

In general, it is of interest to determine demographic predictors of drug abuse. Of note are the different predictors of abusive behavior in cocaine versus methamphetamine users. Male methamphetamine users were more likely to transition to or remain in a high use state, while these gender findings were not upheld by the cocaine data. In addition, while smoking cigarettes was associated with decreased odds of transitioning to or remaining in the high use state among cocaine study participants, this association with smoking was not seen for methamphetamine use. Finally and most surprisingly, those who were actively seeking methamphetamine treatment at the time of the study did not appear to benefit from it in terms of decreased use (note, data on treatment seeking were not collected for cocaine participants).

Limitations of the study must also be recognized. Firstly, the study would have benefited from a control group comparison; that is, a group of substance-dependent individuals who did not undergo any testing but reported to a laboratory and from whom self-reported use was obtained. Secondly, the cocaine and methamphetamine follow-up periods consisted of four and two weeks respectively, which may preclude capturing a long-term effect. While this is longer than the 3-day follow-up considered in previous research (Ehrman, et al., 1998), treatment intervention trials generally allow 4–8 weeks of follow-up, though notably, most (e.g., Brodie, et al., 2003) also have a sizeable amount of loss to follow-up. While the methamphetamine users in the current study had a high rate of attrition, the attrition rate in the cocaine study was less than 10%, which is indeed a strength of the study. Thirdly, self report is often subject to measurement error. While some of this measurement error was accounted for by the choice of statistical model, it is still possible that participants were not forthcoming about their drug use behavior, although it is important to note that TLFB data have been shown to provide reliable estimates of use in cocaine subjects (Ehrman and Robbins, 1997). Comparisons between the current observed effects and the effects resulting from placebo-controlled clinical trials should be interpreted cautiously as clinical trials do not solely rely on self-report but also on drug urine screens. Finally, the sample size consisted of 45 cocaine and 25 methamphetamine subjects, which limits generalizeability of the findings, especially for methamphetamine users. On the other hand, strengths of the study include the duration of follow-up, the robust statistical model, and the inclusion of methamphetamine users.

Future research will benefit from the fact that stress and craving induced via participation in non-treatment studies does not appear to increase post-study use, as long as appropriate precautions are implemented. In fact, such research studies may be protective. Additional empirical studies of with larger samples and ideally with recruitment of a control group are needed to confirm findings in other drug-dependent populations.

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FIGURE 1.

Hidden Markov model for weekly drug use data. Weekly use is observed for each patient and a latent high/low use state is assumed to exist. $P(hh)$, $P(hl)$, $P(lh)$, and $P(ll)$ are the probabilities of transitioning between states (l=low use, h=high use). These probabilities are allowed to depend on study participation and covariates.

FIGURE 2. Matrix of weekly drug use counts for cocaine users (top) and estimated latent state (bottom).

FIGURE 3. Matrix of weekly drug use counts for methamphetamine users (top) and estimated latent state (bottom).

Table 1

Odds ratios illustrating the odds of remaining in or transitioning to the high use state by study (cocaine or methamphetamine) and demographic variables

Variable (Cocaine Study)	Mean Odds Ratio	Median Odds Ratio	95% Credible Interval
Study (Y:N)	0.04	0.04	0.01, 0.11 [*]
Gender(M:F)	0.72	0.72	0.30, 1.63
Age	1.66	1.65	0.99, 2.94
Race (AA:White)	1.28	1.28	0.53, 3.11
Smoker (Y:N)	0.47	0.47	0.18, 1.22
State (high use:low use)	305.82	292.66	102.82, 1170.28 [*]
Variable (Methamphetamine Study)			
Study (Y:N)	0.38	0.39	0.07, 1.70
Gender(M:F)	2.70	2.78	1.10, 6.17 [*]
Age	1.05	1.05	0.64, 1.72
Marital status (Married:Single)	0.91	0.91	0.32, 2.58
Education ($\geq$ HS:< HS)	1.14	1.14	0.49, 2.65
Income ($\geq$ 10K:< 10K)	1.11	1.12	0.42, 2.96
Employment (Y:N)	0.41	0.42	0.13, 1.25
Smoker (Y:N)	0.85	0.86	0.25, 3.08
Treatment (Y:N)	1.07	1.05	0.34, 3.22
State (high use:low use)	162.1	160.0	63.2, 443.2 [*]

^{*} 95% Credible Interval excludes 1

[†] Odds ratio for a 1 standard deviation increase