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Daily sleep quality affects drug craving, partially through indirect associations with positive affect, in patients in treatment for nonmedical use of prescription drugs

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Abstract

Objective—Sleep disturbance has been identified as a risk factor for relapse in addiction to a range of substances. The relationship between sleep quality and treatment outcome has received relatively little attention in research on nonmedical use of prescription drugs (NMUPD). This study examined the within-person association between sleep quality and craving in medically detoxified patients in residence for the treatment of NMUPD.

Method—Participants (n= 68) provided daily reports of their sleep quality, negative affect (NA), positive affect (PA), and craving for an average of 9.36 (SD= 2.99) days. Within-person associations of sleep quality and craving were examined using multilevel modeling. Within-person mediation analyses were used to evaluate the mediating roles of NA and PA in the relationship between sleep quality and craving.

Results—Greater cravings were observed on days of lower than usual sleep quality (γ_{10} = −0.10, p = .003). Thirty-one percent of the overall association between sleep quality and craving was explained by PA, such that poorer sleep quality was associated with lower PA and, in turn, lower

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Contributions

SCB, HHC, ED, and REM designed the study. ASH, JH, and DS oversaw data collection. DML performed the statistical analyses. All authors contributed to the writing of and approved the final manuscript.

Conflict of Interest

The authors declare that they have no conflicts of interest.

PA was associated with greater craving. No evidence emerged for an indirect association between sleep quality and craving through NA.

Conclusions—Daily fluctuations in sleep quality were associated with fluctuations in craving, an association partially explained by the association between sleep quality and daily PA. These data encourage further research on the relationship between sleep, affect, and craving in NMUPD patients, as well as in patients with other substance use disorders.

Keywords

opioids; affect; sleep; experience sampling; craving

1. INTRODUCTION

The annual quantity of painkillers prescribed in the United States has quadrupled since the year 2000 despite the absence of an increase in reported pain (SAMHSA, 2013). As a consequence, opioid analgesics are often diverted, resulting in nonmedical use of prescription drugs (NMUPD), substance use disorders and overdose deaths (Volkow & McLellan, 2016). Indeed, over the past two decades, the prevalence of prescription opioid dependence in the United States is increasingly recognized as a public health concern (Johnston et al., 2011; SAMHSA, 2013). Sleep disturbance has been identified as a risk factor for relapse in addiction to a range of substances (see Brower & Perron, 2010 for review), including alcohol (Brower, Aldrich, & Hall, 1998), nicotine (Boutou et al., 2008), and cocaine (Sofuoglu et al., 2005). Much less work has documented the role of sleep in relapse in the context of opioid dependence (see Dijkstra et al., 2008 for an exception) despite observations of sleep disruption during opiate withdrawal (Wang & Teichtahl, 2007). To gain further insight into the effects of sleep disruption in patients in treatment for NMUPD, this study examined the effects of sleep quality on craving – a proximal outcome associated with subsequent opioid use (Tsui et al., 2014) – through the indirect associations with positive affect (PA) and negative affect (NA) at the day-to-day, within-person level.

1.1. The Associations Between Sleep, Affect, and Craving

Sleep quality is negatively correlated with craving across a range of substances during drug withdrawal, including alcohol, tobacco, opiates, and cannabis (Serre et al., 2015; Lahti et al., 2011). The precise mechanism by which sleep impacts craving, however, remains unclear. Affective states, such as low PA or high NA, are likely to play a role in the relationship between disturbed sleep and craving.

1.1.1. Affect and Craving—Pervasive changes in affective experience persist following detoxification of patients dependent upon opioids. Persistent, drug dependence-associated changes in reward and memory brain circuitry are associated with sensitivity to drug-related cues and diminished sensitivity to non-drug rewards during drug abstinence (Koob & Mason, 2016; Volkow et al., 2004). In addition, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis with opioid dependence is associated with heightened sensitivity to stressors during drug abstinence (Koob & Kreek, 2007). These abstinence-associated effects on reward and stress response systems likely underlie the subjective experiences that patients

report during protracted abstinence, and might contribute to the persistent desire for drugs even as patients are in residence and living apart from drug-related environmental triggers of craving (Ferguson & Shiffman, 2009; Kober & Mell, 2015).

Against this backdrop of "tonic" desire for drug, episodic craving might emerge, reflected in variability in levels of craving during abstinence in response to external or internal cues (Ferguson & Shiffman, 2009). When perceived, drug cues engender an incentive motivation for drugs (Robinson & Berridge, 2008), even after up to 30-days of abstinence (Childress et al., 1986). Cue-induced craving has a long history (Carter & Tiffany, 1999; Drummond, 2000) but internal states, including affective states (Baker et al., 2004; Otto et al., 2007), also constitute powerful cues or contexts for drug desire (Huhn et al., 2016).

The role for NA as a precipitant to drug craving has received considerable empirical support. Laboratory studies have demonstrated a positive association between NA and drug craving for a number substances, including opiates (Childress et al., 1994), alcohol, cocaine, and cigarettes (Conklin & Perkins, 2005; Litt et al., 1990; Sinha et al., 2000). Studies employing ecological momentary assessment (EMA) have also observed a positive association between NA and craving (Delfino et al., 2001; Epstein et al., 2009; Huhn et al., 2016).

The association between PA and craving, however, appears to be more complex than the association between NA and craving. Low PA has been associated with greater craving (Huhn et al., 2016; McHugh et al., 2013), and high levels of PA have been associated with both higher and lower levels of craving in the laboratory (Mason et al., 2008; Maude-Griffin & Tiffany, 1996; Schlauch et al., 2013; Tiffany & Drobes, 1990) and in the EMA (Bujarski et al., 2015; Epstein & Preston, 2010) literature. Emotional states that produce high PA might place individuals in a celebratory mood, encouraging drug use for hedonic reasons (Baker, Morse, & Sherman, 1987; Robinson & Berridge, 1993). Alternatively, high PA might serve to inhibit craving through the facilitation of self-regulation (Schlauch et al., 2013). Theoretically, among treatment-seeking patients, high relative to low PA might render participants more successful at managing cravings due to increased self-regulatory abilities and the capacity to experience reward from sources other than substances of abuse (Fredrickson, 2004). Consistent with this perspective, high PA has been shown to be associated with reduced cravings and lower urges among patients withdrawing from tobacco and/or alcohol (Schlauch et al., 2013; Zinser et al., 1992).

1.1.2. Sleep and Affect—Subjective sleep quality is associated with lower levels of subjective well-being (Lemola et al., 2013). Furthermore, sleep deprivation in the laboratory is related to greater NA and lower PA relative to normal sleep conditions (Franzen et al., 2008). Experience sampling studies, assessing natural variations in sleep, have observed a positive association between sleep quality and PA, as well as a negative association between sleep quality and NA (de Wild-Hartmann et al., 2013), although this effect has been more consistently observed for PA in EMA studies (e.g., Bower et al., 2010). Mechanisms underlying the association between sleep and affect might reflect an impaired ability to engage in affect regulation strategies following poor sleep quality (Mauss et al., 2012; Yoo et al., 2007).

1.2. The Present Study

To gain insight into the relationship between sleep quality and craving in NMUPD, the present study used EMA to examine the associations between sleep quality and craving at the daily level – both directly and through indirect associations between sleep, NA, and PA. Existing EMA studies have leveraged the method's capacity to reduce retrospective bias (Schwarz, 2007) by asking participants to report emotions and experiences in the moment.

One strength of the intensive repeated measures design that has not yet been leveraged in the context of prescription opioid dependence and sleep, is the ability to disentangle within- and between-person variability. This allows for examination of the associations between day-to-day fluctuations in sleep (within-person) separately from the associations between person-to-person differences in sleep (between-person) and craving. This within-person approach is motivated by calls to increase our understanding of the dynamics involved in substance abuse recovery (McKay et al., 2006; Shiffman, 2009), at the micro, daily level (Zheng et al., 2015). The need for this approach is further underscored by findings of day-to-day variability in the constructs of craving, affect, and sleep (Bei et al., in press; Cleveland & Harris, 2010; Peacock et al., 2015).

In the current study, lower than usual sleep quality on a given night was hypothesized to be associated with higher than usual cravings during the following day, and this effect was predicted to be at least partially explained by an increase in NA and a decrease in PA following lower than usual sleep quality.

2. METHOD

2.1. Participants

Participants in the study were patients (n= 75; 30% female) recruited as part of a larger study at a residential drug and alcohol treatment facility in Wernersville, Pennsylvania. Participants ranged in age from 19 to 56 (M= 28.96, *Range*= 19–56) and had completed medically assisted withdrawal at the treatment center 10–14 days prior to the beginning of data collection. Patients were prescreened based on clinical charts at the residential treatment center; this information was used to initially identify participants that met study criteria who were then invited to take part in the study. Patient inclusion criteria were as follows: (1) capable and willing to comply with the research protocol; (2) met criteria for prescription opioid dependence as determined by clinical staff at the Caron Foundation using the Structured Clinical Interview for DSM-IV-TR (SCID; First et al., 2002), and Form-90D (Westerberg et al., 1998); (3) prescription opioids were the primary drug of choice; (4) over the age of 18; and (5) staying in residential treatment for at least 30 days. Exclusion criteria included (1) any history of serious mental illness (bipolar or schizophrenia) or psychosis, as diagnosed by the SCID; (2) intravenous drug use; (3) history of traumatic brain injury; and (4) because the other arms of the study included neuroimaging, current use of any opiate agonist (methadone or buprenorphine) or antagonist (Naltrexone). After self-selecting into the study, all participants provided written informed consent after a full explanation of the protocol as approved by the Pennsylvania State University College of Medicine Internal Review Board. For the present analyses, patients (n = 2) were excluded because they

violated rules of the treatment center/study protocol after induction into the study, and participants with less than 2 days of sleep, affect, and craving data (n = 5) were also excluded, leaving 540 days nested within 68 persons. Participants provided data for a mean of 9.36 (*SD* = 2.99, *Range* = 2–14) days. In line with the increased rates of psychopathology in patients in treatment of NMUPD relative to normative samples (e.g., Cicero et al., 2008), participants in the sample were diagnosed with a range of mental health disorders, the most prevalent of which were generalized anxiety disorder (38.40%), attention deficit/hyperactivity disorder (29.41%), depressive disorder not otherwise specified (29.41%), and lifetime major depression disorder (23.53%). For further characterization of the sample, participant dependence on a range of substances as well as their use of medications during data collection are presented in Table 1. Notably, 44.12% of participants were prescribed medication to aid with their sleep during data collection.

2.2. Procedure

Participants were equipped with smart phones programmed to administer a survey 4 times daily. On consecutive days, a preset alarm notified participants to complete surveys at morning, midday, mid-afternoon and evening times that did not conflict with their treatment program. Real time data were streamed to a secure server at the University campus to monitor compliance and data quality. The surveys took approximately 2–3 minutes each to complete. Research staff also used brief, in-person meetings to build rapport, answer participant questions, and manage any technical difficulties.

2.3. Measures

2.3.1. Craving—Craving was measured four times daily. Three items were employed with a five-point scale ranging from “strongly disagree” to “strongly agree”: 1) “Since last data entry, the idea of using drugs has intruded upon my thoughts”; 2) “Since last data entry, I have missed the feeling drugs can give me”; 3) “Since last data entry, I have thought about how satisfying drugs can be”. The stem for each item took the form of “Since waking” rather than “Since last data entry” for the morning assessments. An average craving score was created for each participant for each day of the study. A reliability analysis using a generalizability theory approach appropriate for intensive repeated measures data (see Bolger & Laurenceau, 2013) demonstrated that the reliable change score for the daily craving scale was .89, indicating that within-person change in craving could be assessed reliably with this scale.

2.3.2. Negative Affect—Participants rated their experience of NA 4 times per day with 8 items on a touchpoint scale ranging from 0 (Not at all) to 100 (Very): “angry,” “irritable,” “lonely,” “sad,” “guilty,” “ashamed,” “anxious,” “stressed”. An average daily negative affect score was created for each participant for each day of the study with at least one completed measurement occasion. The reliable change score for the daily negative affect variable was . 89, indicating that within-person change in NA could be assessed reliably.

2.3.3. Positive Affect—Participants rated their experience of PA 4 times per day with 8 items on a touchpoint scale ranging from 0 (Not at all) to 100 (Very): “warmhearted,” “joyful,” “enthusiastic,” “happy,” “affectionate,” “loving,” “relaxed,” “calm”. An average

daily PA score was created for each participant for each day of the study with at least one completed measurement occasion. The reliable change score for the daily negative affect variable was .91, indicating that within-person change in PA could be assessed reliably.

2.3.4. Sleep Quality—Sleep quality was measured during the morning assessment survey using an item adapted for daily reporting of sleep from conventional retrospective scales indexing subjective sleep quality (e.g., Ellis et al., 1981). Participants answered "How would you evaluate your sleep last night?" on a seven-point scale ranging from "Extremely light" to "Extremely deep." Such daily, self-report sleep measures are more strongly correlated with objective sleep measures than retrospective, previous month reports (Lauderdale et al., 2008). They are also practical when frequent measurements are made to reduce participant burden, and have demonstrated favorable psychometric properties (e.g., Cappelleri et al., 2009). Daily sleep quality was significantly related to daily tiredness ($\beta = -1.80$) and drowsiness ($\beta = -1.70$) with days of better than usual sleep quality associated with lower than usual tiredness and drowsiness, suggesting that the item was a valid measure of sleep quality (further details on these supplementary analyses are available on request from the authors).

2.4. Data Analysis

The intensive repeated measures data were analyzed using multilevel models (Snijders & Bosker, 1999) to account for the nested nature of the data. A person-level sleep quality variable was calculated as the arithmetic mean across each individual's repeated measures. A day-level sleep quality variable was calculated as deviations from these person-level means (Bolger & Laurenceau, 2013). Time, in the form of day in the study, was sample-mean centered.

A model for the association between sleep quality and craving was constructed as:

$$\mathrm{Craving}_{\mathrm{it}}=\beta_{0i}+\beta_{1i}\mathrm{Day'sSleepQuality}_{\mathrm{it}}+\beta_{2i}\mathrm{Time}_{\mathrm{it}}+e_{\mathrm{it}} \quad (1)$$

where craving$_{it}$ is the craving variable for person i on day t; β_{0i} indicates the expected *craving* in the middle of the study for an individual experiencing an average level of sleep quality for that person; β_{1i} indicates within-person differences in craving associated with the day's sleep quality; β_{2i} indicates the effect of time in study on craving in order to account for time as a third variable (see Bolger & Laurenceau, 2013); and e_{it} are day-specific residuals that were allowed to autocorrelate (AR1).

Person-specific intercepts and associations from the Level 1 model were specified at Level 2 as:

$$\beta_{0i}=\gamma_{00}+\gamma_{01}\mathrm{UsualSleepQuality}_i+\gamma_{02}\mathrm{Age}_i+\gamma_{03}\mathrm{Gender}_i+u_{0i}$$

$$\beta_{1i}=\gamma_{10}+\gamma_{11}\mathrm{UsualSleepQuality}_i+\gamma_{12}\mathrm{Age}_i+\gamma_{13}\mathrm{Gender}_i+u_{1i}$$

$$\beta_{2i}=\gamma_{20} \quad (2)$$

where the γs are sample-level parameters and the μs are residual between-person differences that may be correlated, but are uncorrelated with e_{it}. Parameters γ_{11} through γ_{13} indicate how between-person differences in the within-person associations of day's craving and sleep quality were moderated by usual sleep quality, age, and gender. The model was fit using the nlme package in R (Pinheiro et al., 2015) using maximum likelihood estimation, with incomplete data treated using missing at random assumptions. Statistical significance was evaluated at $\alpha = .05$.

Other associations were tested but on finding no significant associations with craving, as well as unchanged results for the association between sleep quality and craving, the more parsimonious models were retained. These associations include a quadratic effect of time in addition to the linear effect of time; age at first use of opiates; and whether or not participants were prescribed medication to aid with their sleep during the study. Further, as mean scores across measurement occasions within days were used for the affect and craving variables, with days with at least one completed measurement occasion included, multilevel models predicting levels of positive affect, negative affect, and craving by within-person and between-person versions of the number of surveys completed per day, as well as a within- by between-person interaction, were used to test whether the number of surveys completed by participants was significantly associated with affect and craving scores. No significant differences emerged. As such, days with any data on affect and craving were included in the models.

Building from this model, two separate 1-1-1 multilevel mediation models (in which all three variables of interest are within-person, Level 1 variables) were employed to examine the role of sleep quality (X) on craving (Y) through the mediating pathway of affect (M; both PA and NA were tested in separate models). Mediation followed procedures described in Bolger and Laurenceau (2013). Person-mean deviated versions of sleep quality, NA, PA, and craving were created and the models were estimated in Mplus (Muthen & Muthen, 1998–2010). As per Bolger and Laurenceau (2013), possible linear time trends in the craving and affect outcomes during the study days were controlled for by regressing them on time. Quadratic effects of time on craving and affect were tested in addition to the linear effect of time but these effects were not significant. As such, the more parsimonious models were retained. The total effect was calculated using the formula from Kenny et al. (2003):

$$c=c'+\mathrm{ab}+\sigma_{a_j b_j} \quad (3)$$

where c' is the average direct effect of sleep quality on craving, *ab* is the product of the average X-to-M and M-to-Y effects, and $\sigma_{a_j b_j}$ is the covariance of between-person differences in the X-to-M and M-to-Y effects.

3. RESULTS

3.1. Descriptive statistics

On average, participants reported a mean sleep quality of 3.99 (*SD*= 1.36) and craving with a mean rating of 2.00 (*SD*= 1.75). Previous analyses have shown high inter-item reliability for the PA and NA factors (standardized Chronbach's alpha for NA=0.93, and PA=0.95; Huhn et al., 2016). The Pearson's r correlation between the PA and NA factors was *r*= −0.13. On average, participants reported a mean PA of 43.28 (*SD*= 18.57) and a mean NA of 33.13 (*SD*= 19.82).

3.2. Associations between Sleep Quality and Craving

Results from the multilevel model examining the effects of sleep quality on craving are shown in Table 2. In line with the hypothesis that the day's sleep quality would affect craving, the within-person association between day's sleep quality and craving was significant (γ_{10}= −0.10, *p*= .003). That is, on days when participants' sleep quality was higher than usual, their craving was lower than usual. Although a relatively small effect on average with an effect size of 0.13 (estimate for the within-person association divided by the within-person residual standard deviation, γ_{10}/σ_e = 0.10/sqrt(0.60)), this within-person association ranged from −0.21 to 0.01 across persons. This within-person association between sleep quality and craving was not moderated by individuals' usual sleep quality, age, or gender (γ_{11} to γ_{13}, *ps*> .05).

The between-person association between usual sleep quality and craving was not significant (γ_{01}= 0.04, *p*= .77). The other between-person variables, age and gender, were also not significant predictors of craving (γ_{02} to γ_{03}, *ps*> .05). Finally, there was a significant effect of time, such that craving decreased during the course of the study (γ_{20}= −0.03, *p*< .001).

3.3. Associations between Sleep Quality, Negative Affect, and Craving

Results of the within-person mediation model are presented in figure 1. For the typical individual, sleep quality (X) did not significantly predict NA (M), *B*= −1.06, *SE*= 0.57, *z*= −1.86, *p*= .06. The NA (M) to craving (Y) slope for the average participant was 0.02, *SE*= 0.003, *z*= 5.23, *p*< .0001, indicating that on days when NA was higher than usual for that individual, craving was also higher than usual. There was also evidence of a direct association between sleep quality (X) and craving (Y) for the average participant, *B*= −0.10, *SE*= 0.03, *z*= −2.94, *p* <.01.

The total average effect of sleep quality on craving for the average participant was −0.12. Seventeen percent of the overall average relationship between sleep quality and craving was explained by NA but this effect had a standard error of 0.14 and was not statistically significant, *z*= 1.23, *p*= .22. Thus, NA did not mediate the association between sleep quality and craving.

3.4. Associations between Sleep Quality, Positive Affect, and Craving

Results of the within-person mediation model are presented in figure 2. For the typical individual, sleep quality (X) significantly predicted PA (M), *B*= 1.60, *SE*= 0.63, *z*= 2.52,

p= .01, indicating that days of higher than usual sleep quality were associated with higher than usual PA relative to days of lower than usual sleep quality. The PA (M) to craving (Y) slope for the average participant was −0.01, SE= 0.004, z= 2.15, p= .03, indicating that on days when PA was higher than usual for that individual, craving was lower than usual. There was also evidence of a direct association between sleep quality (X) and craving (Y) for the average participant, B= −0.08, SE= 0.04, z= −2.31, p=.02, such that, after adjusting for the association between PA and craving, better than usual sleep quality was associated with lower than usual craving.

The total average effect of sleep quality on craving for the average participant was −0.12. Thirty-one percent of the overall average relationship between sleep quality and craving was explained by PA. This effect had a standard error of 0.16 with a statistical significance of z= 2.00, p= .046. Thus, PA partially mediated the effect of sleep quality on craving.

4. DISCUSSION

4.1. Within-Person Association Between Sleep Quality and Craving

The present study found evidence for an association between sleep quality and craving among patients in residential treatment for prescription opioid dependence. A negative, within-person association between sleep quality and craving was observed when using EMA to assess these constructs in close temporal proximity to their occurrence. On days with better than usual sleep quality, participants reported less craving; this finding is consistent with research in other substance use disorders (e.g., Lahti et al., 2011) and extends previous research by considering NMUPD.

4.2. Sleep, Positive Affect, and Craving

Two separate mediation models were employed to gain insight into the relationship between sleep quality, affect, and craving. As hypothesized, day-level sleep quality was positively associated with daily PA, with PA partially mediating the association between sleep quality and craving. This finding is in line with previous research indicating an association between sleep quality and PA (Franzen et al., 2008) and PA and craving (Schlauch et al., 2013) and extends them to the NMUPD literature by explicitly testing the indirect path from sleep quality to craving through PA at the within-person level.

These findings are relevant to treatment of NMUPD in that clinicians might look for a combination of symptoms such as low PA and sleep disturbance as risk factors for high levels of drug craving, and thus, relapse. Opioid dependent patients in the early stages of recovery are likely to be at increased risk for craving on days when they experience sleep disturbance due partially to associated reductions in PA. From a clinical standpoint, this might call for a more personalized approach to patient care, e.g. medical treatments that target sleep disturbance to reduce the risk of relapse.

4.3. Sleep, Negative Affect, and Craving

Day-level NA was associated with craving such that craving was higher on days when NA was higher than usual. However, day-level sleep quality was not significantly associated with

day-level NA. These findings were not in line with the hypothesis that sleep quality would be associated with NA. Due to the lack of EMA studies examining day to day variability in sleep and NA at the within-person level, our hypotheses were drawn from findings emerging primarily from laboratory studies and thus, the associations between less extreme, naturalistic variability in sleep and NA *in situ* might be of a different nature relative to the associations observed using sleep deprivation paradigms (e.g., Franzen et al., 2008). In line with this supposition, Bower and colleagues (2010) observed associations between sleep quality and PA, but not NA, in an EMA study. Such findings call for greater consideration of the associations between sleep and affect in naturalistic contexts.

The findings also point to the potential role of the circadian system in the regulation of affect and sleep. Circadian cycles are linked with PA more than NA (Clark et al., 1989; Murray et al., 2002) as noted by Bower et al. (2010) in interpreting the findings of associations between PA and sleep quality but not NA and sleep quality in their EMA study. Similar processes may also be at play in the current study. Indeed, disruptions in circadian rhythms have been observed across substance abusing samples (Birchler-Pedross et al., 2009; Ogeil et al., 2012; see Hasler et al., 2012, for review) with continued disruptions observed up to 30 days of abstinence in heroin-using samples for example (Li et al., 2009). Examining the contribution of the circadian system to affect and craving will require the use of specialized protocols capable of parsing out the effects of circadian timing from homeostatic sleep drive in future studies.

4.4. Limitations and Considerations for Future Research

Since the data in this study were collected from patients in a residential treatment facility, findings might not generalize beyond this context. Furthermore, the current study examined the association between sleep and craving, and not treatment outcome. Participants exhibited dependence for a range of substances and some were on medications (Table 1), including substances that exert influences on affect and sleep (Lydon et al., 2016; Oberndorfer et al., 2000; Weddington et al., 1990). While this polydrug and medication use does not allow conclusions to be drawn on associations between sleep, craving, affect, and NMUPD specifically, it is representative of NMUPD in the context of other drugs observed in nationally representative samples (McCabe et al., 2008; McCabe et al., 2007).

This study used a subjective measure of sleep quality. Although previous studies demonstrating effects of sleep on affect have used subjective sleep measures (e.g., Prather et al., 2013), a fuller understanding of the role of sleep on craving might be achieved by considering other measures of sleep dysregulation (for example, actigraphy-based measures which can provide information on sleep onset latency which is difficult to obtain through self-report) or alternative subjective measures of sleep that provide information on a number of facets of sleep (e.g., sleep duration and sleep disturbances; Buysse et al., 1989). Further, findings that rapid eye movement (REM) sleep is involved in emotional brain regulation (e.g., Gujar et al., 2011) are relevant to findings of associations between variations in sleep and affect and argue for the use of sleep measures capable of distinguishing different components of sleep physiology (e.g., polysomnography).

The focus on composite positive and negative affective states in the present study is in line with previous studies examining the association between affect and craving in NMUPD (e.g., Huhn et al., 2016), as well as studies that have examined the association between affect and drug craving more generally(e.g., McHugh et al., 2013; Schlauch et al., 2013). Future studies might gain further insight into the association between affect and craving by focusing on discrete affective states (e.g., Epstein et al., 2010).

Finally, drug craving decreased during the course of the study. This finding is in line with decreases in craving over the course of drug withdrawal observed in other studies across a range of substances (e.g., Shi et al., 2009; Wang et al., 2013; Weddington et al., 1990). This decrease in craving may reflect re-regulation of HPA axis and brain reward systems during prolonged drug abstinence, evidence for which has emerged in patients in treatment for heroin (Shi et al., 2009) and, more recently, prescription opioid-dependent patients (Bunce et al., 2015). Future research with intensive repeated measures will allow a characterization of the time course of drug craving through abstinence and to identify the relevance of changes in the functioning of the HPA axis and the brain reward systems in these changes.

4.5. Conclusion

This study demonstrated a within-person coupling between sleep quality and craving that was partially mediated by PA. The findings underscore the role of sleep disturbance as a risk factor for poor treatment outcomes in substance use (Brower & Perron, 2010), extending the findings to NMUPD, taking a within-person approach, and taking steps to identify the mechanisms through which sleep disturbances might affect craving. Future research is warranted to further elucidate the relationship between affect and sleep disturbance, particularly as it relates to the early stages of recovery from NMUPD.

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Highlights

- Better than usual sleep quality was associated with lower than usual drug craving
- Higher than usual positive affect was associated with lower than usual drug craving
- The association between sleep quality and drug craving was partly mediated through positive affect

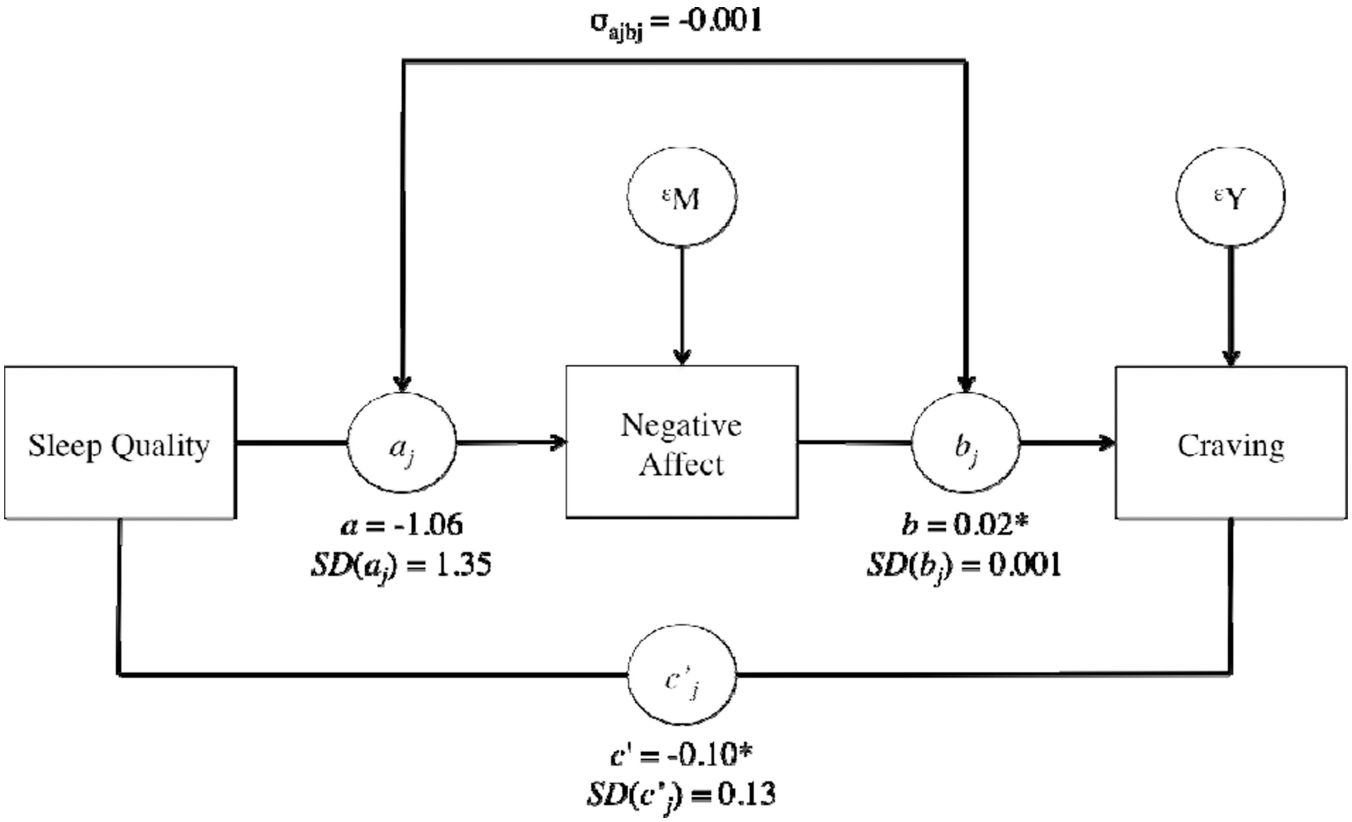

Figure 1.

Results for the within-person mediation for negative affect (see Bolger & Laurenceau, 2013). For ease of interpretability, we have omitted time as a predictor from the figure. Note: *SD* values indicate the between-person variability in the fixed effects. $\sigma_{a_j b_j}$ is the covariance of between-person differences in the X-to-M and M-to-Y effects *$p < .05$.

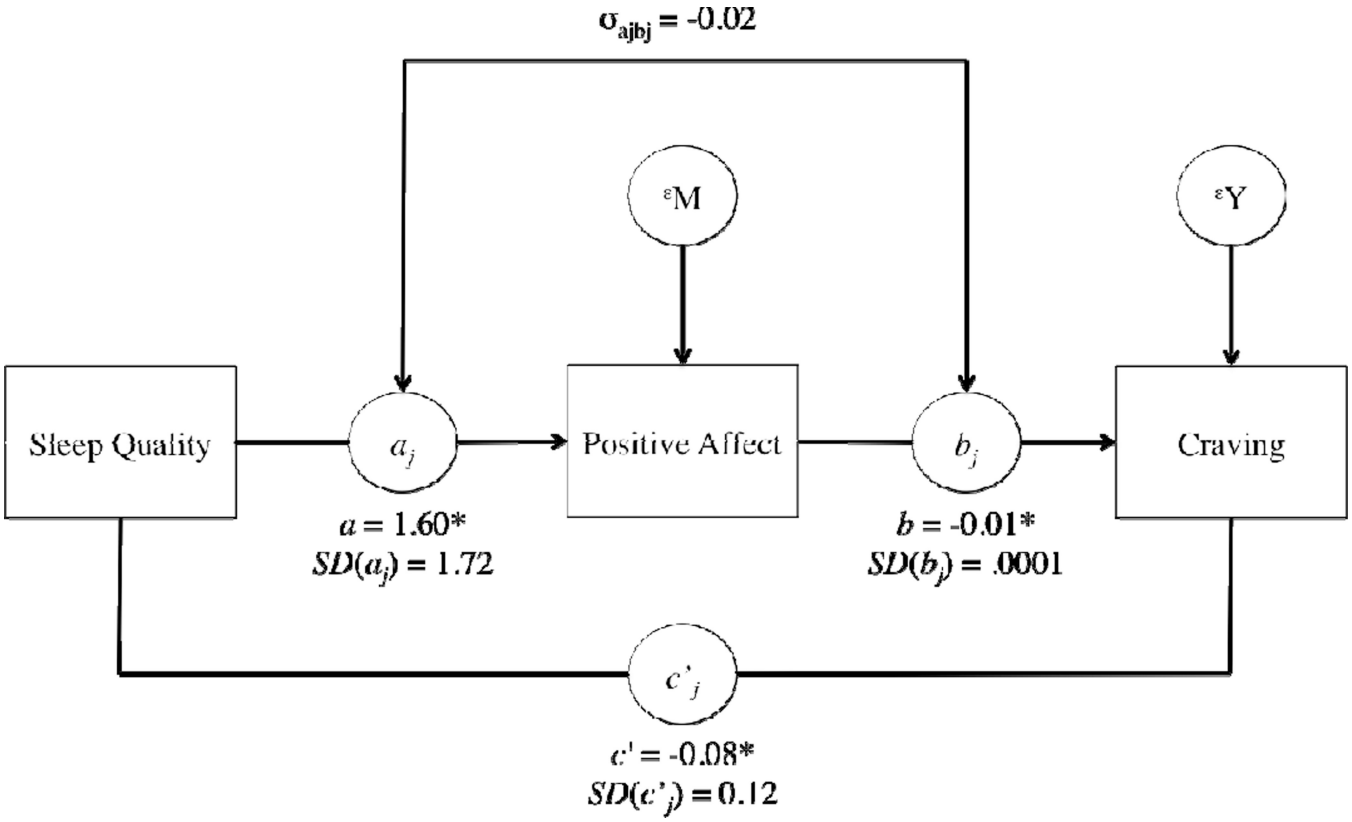

Figure 2.

Results for the within-person mediation for positive affect (see Bolger & Laurenceau, 2013). For ease of interpretability, we have omitted time as a predictor from the figure. Note: *SD* values indicate the between-person variability in the fixed effects. $\sigma_{a_j b_j}$ is the covariance of between-person differences in the X-to-M and M-to-Y effects $^*p < .05$.

Table 1

Drug Dependence of Participants at Treatment Intake and Medication Use During the Study

Participant Drug Dependence		
	N	**%**
Poly-Substance Drug User	31	45.59
Alcohol Current Dependence	10	14.71
Tobacco Current Dependence	28	41.18
Cannabis Current Dependence	24	35.29
Tranquilizer Current Dependence	0	0.00
Sedative Current Dependence	14	20.59
Steroid Current Dependence	0	0.00
Stimulant Current Dependence	8	11.76
Cocaine Current Dependence	6	8.82
Hallucinogen Current Dependence	0	0.00
Inhalant Current Dependence	1	1.47
Opiate Current Dependence	68	100.00
Medications Administered During Data Collection		
	N	%
Antidepressant	34	50.00
Muscle Relaxant	2	2.94
Opiate Antagonist	12	17.65
Narcotic Analgesic	2	2.94
Anticonvulsant	8	11.76
Antipsychotic	6	8.82
Alpha-2 Adrenergic Agonist	21	30.88
Melatonin	10	14.71
Norepinephrine Reuptake Inhibitor	1	1.47
Anxiolytic	2	2.94
Anticholinergic	3	4.41
Sleep Medication	30	44.12

Table 2

Results of the Multilevel Model Examining the Association Between Sleep Quality and Craving

Fixed Effects	***Estimate***	***Standard Error***
Intercept (γ_{00})	2.08*	0.11
Day-Level Sleep Quality (γ_{10})	−0.10*	0.03
Time (γ_{20})	−0.03*	0.01
Person-Level Sleep Quality (γ_{01})	0.04	0.12
Age (γ_{02})	−0.02	0.01
Gender (γ_{03})	−0.52	0.27
Day-level Sleep Quality X Person-Level Sleep Quality (γ_{11})	−0.03	0.04
Day-Level Sleep Quality X Age (γ_{12})	0.004	0.005
Day-Level Sleep Quality X Gender (γ_{13})	0.09	0.08
Random Effects	*Estimate*	*Confidence Interval*
Intercept (σ^2_{u0})	0.83	0.56 – 1.21
Day-Level Sleep Quality (σ^2_{u1})	0.01	0.001 – 0.12
Correlation (r_{u0u1})	−0.11	−0.71 – 0.58
AR(1)	0.13	0.02 – 0.24
Residual (σ^2_e)	0.60	0.56 – 0.65
Fit Indices		
AIC	1232.93	
BIC	1292.78	

Note: $N_{observations}$ =540 days nested within 68 persons; AIC = Akaike information criteria; BIC = Bayesian information criteria.

* $p < .05$.