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## Addictive Behaviors

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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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## 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.

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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 ( $\gamma_{10} = -0.10, p = 0.003$ ). 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 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.

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## 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 (SAMHSA, 2013). Sleep disturbance has been identified as a risk factor for relapse in addiction to a range of substances (see Brower and Perron, 2010 for review), including alcohol (Brower, Aldrich, and Hall, 1998), nicotine (Boutou et al., 2008), and cocaine (Sofuoglu, Dudish-Pulsen, Poling, Mooney, and Hatsukami, 2005). Much less work has documented the role of sleep in relapse in

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the context of opioid dependence (see Dijkstra, De Jong, Krabbe, and van der Staak, 2008 for an exception) despite observations of sleep disruption during opiate withdrawal (Wang and 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, Anderson, Strong, and Stein, 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 (Seere, Fatseas, Swendsen, and Auriacombe, 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 and 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 and 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 and Shiffman, 2009; Kober and 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 and Shiffman, 2009). When perceived, drug cues engender an incentive motivation for drugs (Robinson and Berridge, 2008), even after up to 30-days of abstinence (Childress, McLellan, and O'Brien, 1986). Cue-induced craving has a long history (Carter and Tiffany, 1999; Drummond, 2000) but internal states, including affective states (Baker, Piper, McCarthy, Majeskie, and Fiore, 2004; Otto, O'Leirigh, and Pollack, 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 of substances, including opiates (Childress et al., 1994), alcohol, cocaine, and cigarettes (Conklin and Perkins, 2005; Litt, Cooney, Kadden, and Gaupp, 1990; Sinha, Fuse, Aubin, and O'Malley, 2000). Studies employing ecological momentary assessment (EMA) have also observed a positive association between NA and craving (Delfino, Jamner, and Whalen, 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, Kaufman, Frost, Fitzmaurice, and Weiss, 2013), and high levels of PA have been associated with both higher and lower levels of craving in the laboratory (Mason, Light, Escher, and Drobos, 2008; Maude-Griffin and Tiffany, 1996; Schlauch, Gwynn-Shapiro, Stasiewicz, Molnar, and Lang, 2013; Tiffany and Drobos, 1990) and in the EMA (Bujarski et al., 2015; Epstein and Preston, 2010) literature. Emotional states that produce high PA might place individuals in a celebratory mood, encouraging drug use for hedonic reasons (Baker, Morse, and Sherman, 1986;

Robinson and 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, Baker, Sherman, and Cannon, 1992).

#### 1.1.2. Sleep and affect

Subjective sleep quality is associated with lower levels of subjective well-being (Lemola, Lederman, and Friedman, 2013). Furthermore, sleep deprivation in the laboratory is related to greater NA and lower PA relative to normal sleep conditions (Franzen, Siegle, and Buysse, 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, Bylisma, Morris, and Rottenberg, 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, Troy, and LeBourgeois, 2012; Yoo, Gujar, Hu, Jolesz, and Walker, 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, Franklin, Patapis, and Lynch, 2006; Shiffman, 2009), at the micro, daily level (Zheng, Cleveland, Molenaar, and Harris, 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, Wiley, Trinder, and Manber, 2016; Cleveland and Harris, 2010; Peacock, Cash, Bruno, and Ferguson, 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

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