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# SLEEP DISTURBANCE IN SUBSTANCE USE DISORDERS AND COMORBID CHRONIC VIRAL INFECTIONS

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## Abstract

Sleep disruption is associated with both substance use disorders and chronic viral infections, which commonly co-occur. A greater understanding of how sleep is affected by substance abuse and comorbid chronic viral infections is needed, as fatigue, depression and other neuropsychiatric impairments caused by chronic viral infections can affect response to addiction treatment adversely.

### Keywords

Alcohol; blood; brain barrier; hepatitis C; HIV; neuroinvasion; psychostimulants

The recent study by Irwin *et al*. [1] provides an important step in characterizing sleep disturbances during early abstinence in adults with cocaine or alcohol dependence. However, in an attempt to impose more controlled conditions in their polysomnographic investigation, research participants with evidence of HIV or hepatitis C virus (HCV) were excluded from the study. Their main findings are consistent with previous work in these populations showing increases in rapid eye movement (REM) sleep and profound losses of stage N3 slow wave, otherwise thought of as ‘deep’ sleep [2]. The authors note that: ‘Loss of sleep depth has implications for morbid outcomes associated with cocaine-and alcohol dependence including… infectious disease’ and that: ‘sleep depth is thought to contribute to the maintenance of health and the homeostatic regulation of the autonomic, neuroendocrine and immune systems’, including anti-viral immunity. This commentary goes beyond the discussion by Irwin *et al*. [1] and considers how sleep architecture might be affected in the

**Declaration of interests**

None.

context of substance use disorders and comorbid chronic viral infections. This is an important population to study, as these illnesses commonly co-occur, and chronic viral infections can contribute to central nervous system (CNS) dysfunction (i.e. neuropsychiatric impairments such as fatigue, depression and cognitive deficits) [3–5], which often increase the risk of relapse and impede response to addiction treatments [6,7].

Disrupted sleep alters immune function and is associated with both substance use disorders and chronic viral infections. Studies indicate self-reported sleep disturbances in 44–56% of individuals with HIV [8] and in 60–65% of individuals with HCV [9]. Further, the use of sleep aids was identified recently as a predictor of HCV therapy discontinuation [10], suggesting that sleep disturbances may hinder anti-viral drug therapy outcomes as well as anti-viral immune responses. In addition, research characterizing sleep disturbance in HIV and HCV shows a direct relationship between changes in sleep architecture and CNS function. An early study of patients with HIV found that REM latency was reduced and correlated negatively with depressive symptomatology [11]. More recently, Raison *et al.* [12] reported that patients with HCV (undergoing interferon-based anti-viral therapy and without preexisting sleep disorders) experienced decreases in stages 3/4 sleep and increases in REM latency that were associated with increases in fatigue. Further, both high delta sleep ratio and low alpha power may be indices of resilience to cytokine-induced depression in adults with HCV [13]. These data suggest that proinflammatory cytokines may provide a mechanistic link between disorders associated with chronic inflammation, including substance use disorders and accompanying neuropsychiatric sequelae (e.g. sleep disturbance, cognitive impairment and depression). It has been proposed that immunological biomarkers (leucocyte activation status and cytokine levels) may be useful for clinical monitoring of sleeping quality patterns in HCV patients [14].

Irwin *et al.* [1] discuss how activation of specific inflammatory pathways play a role in the increases in REM sleep observed in substance use disorders, such as increases in mononuclear cell production of interleukin (IL)-6 and tumour necrosis factor (TNF)-α—cytokines that are associated with impairments in mood, cognition and sleep [15,16] as well as with blood–brain barrier integrity [17] and viral neuroinvasion [18]. Indeed, HIV and/or HCV infection of the brain may contribute to sleep disruption and neuropsychiatric impairments, particularly in adults with a history of substance abuse (e.g. [19]).

Sleep disruption has been hypothesized as a ‘universal risk factor for relapse in addiction’ [20] and may represent a biomarker that links the risk factors of an individual (e.g. chronic viral infection) to substance use disorders, via shared molecular pathways. Characterizing the sleep effects of comorbid substance use disorders and chronic viral infection with HIV or HCV could inform the development of novel interventions that target specific sleep parameters (e.g. augmenting slow wave sleep and/or reciprocally decreasing REM sleep, as suggested by Irwin *et al.* [1]) in order to improve substance abuse treatment outcomes. Thus, future studies on sleep and substance use disorders may want to consider inclusion of research participants with HIV and/or HCV, as these are the individuals whose health and quality of life may be most impacted from a lack of slow wave sleep.

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