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## Self-reported Sleep disturbances during Cannabis Withdrawal in Cannabis-dependent Outpatients With and Without Opioid-Dependence

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### To the Editor

A cannabis withdrawal syndrome (at least two symptoms) occurs in more than 50% of dependent smokers after cessation (1). The typical withdrawal pattern is composed of 6 symptoms: anger or aggression, decreased appetite or weight loss, irritability, nervousness/anxiety, restlessness, and sleep difficulties (1). The rate of sleep disturbances during cannabis cessation was found to be 32% in non-treatment seeking dependent smokers (2). The two most frequent sleep symptoms are reduced sleep duration and strange or vivid dreams. These have been related to longer sleep onset latency, reduced slow wave sleep, and REM rebound (3).

Cannabis use is more frequent among opioid-dependent patients than in the general population. Opioid dependence might be expected to influence cannabis withdrawal, given the known interactions of the endogenous opioid and cannabinoid systems in the central nervous system (CNS). Cannabinoid CB1 and mu-opioid receptors are often co-localized in the same post-synaptic neurons in the nucleus accumbens and in the dorsal striatum.

We compared the frequency of self-reported cannabis withdrawal symptoms using questionnaires in 43 cannabis-dependent outpatients with current opioid dependence and 56 cannabis-dependent outpatients without history of opioid dependence (Table 1 in online supplementary material).

The two groups are comparable in terms of sex ratio (male 70%,  $\chi^2 p=.51$ ), age of first cannabis use ( $16 \pm 4$  years, ANOVA  $p=.09$ ), and number of cannabis joints smoked at the time

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of the cannabis cessation attempt ( $5 \pm 4$ , ANOVA  $p = .75$ ). But subjects with opioid dependence were older ( $37 \pm 7$  vs.  $27 \pm 8$  years ANOVA  $p < .001$ ) and more frequently current tobacco smokers (97% vs. 66%,  $\chi^2 p = .001$ ). They are significantly more likely (79.1%) to report sleep disturbances than subjects without opioid dependence (53.6%). The types of reported sleep disturbances include trouble falling asleep (55%), frequent night awakenings (44%), early morning awakening (39%), sleeping more (27%), sleeping less (37%), strange dreams (37%), vivid dreams (41%), others (9%). The median duration of these symptoms' post-cessation is 19 days.

The two groups do not differ significantly in the proportion of subjects with  $\geq 2$  symptoms (65%) or frequency of the 5 other symptoms: appetite or weight loss (30.8%), irritability (45.1%), anxiety (56%), aggression (36.3%), restlessness (45.1%).

We conclude that sleep disturbance is the only withdrawal symptom which is more prevalent in patients with concurrent opioid dependence (79.1% vs. 53.6%). This fact could be due to several mechanisms: interactions between cannabinoid and opioid systems, poor sleep quality and sleep disturbances already associated with opioid dependence (4), or high rate of smoking (97%) in the opioid-dependent group which has been associated with unpleasant dreams during cannabis withdrawal in the general population (5). Use of cannabis as a self-medication for sleep disturbances in such patients may increase the risk of relapse.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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