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Prospective study of cannabis withdrawal in cannabis-using adolescents

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To the Editor:

Milin and colleagues are to be commended for conducting “the first published prospective study of cannabis withdrawal in adolescents with cannabis dependence seeking treatment that is not confounded by other co-morbid substance use disorders”¹ (p. 178). The authors tested two hypotheses: 1) “a withdrawal syndrome with clinically significant and measureable symptoms will follow abrupt cessation of cannabis use;” and 2) “the intensity of the withdrawal syndrome will be dependent on the quantity of cannabis used, frequency of exposure, length of cannabis dependence, and/or age at onset of daily cannabis dependence and mental health status”¹ (p. 175). Results showed that adolescents seeking treatment for cannabis dependence exhibit clinically significant withdrawal symptoms and concluded that cannabis-dependent adolescents may be particularly vulnerable to physiological symptoms that occur with cannabis withdrawal.

While these are important findings, the authors also concluded that their second hypothesis was not supported because “the intensity of the withdrawal syndrome was not related to the quantity of cannabis used, frequency of exposure, length of cannabis dependence, and age of onset of daily cannabis use”¹ (p. 178). This latter conclusion may be premature because there are several design considerations that may affect the interpretation of study results, and lead to further questions needing consideration in the future. In contrast to Milin’s negative findings that may be the result of a design involving weekly assessments, other studies with adult cannabis users have found that cannabis withdrawal severity peaks between 3–7 days after initiating abstinence^{2–4}. Furthermore, preliminary findings from our laboratory indicate that adolescents who use cannabis heavily report increases in irritability, trouble concentrating, yawning, decreases in appetite, depression, trouble sleeping, runny eyes and nose, and muscle pains and achy joints during the first week of abstinence⁵. Collectively, the findings from adult studies and our recent findings in adolescents indicate that the most severe cannabis withdrawal symptoms appear during the first week of intentional abstinence, for both adult and adolescent cannabis users. Therefore, the question is raised: Could Milin and colleagues have detected peak cannabis withdrawal severity as a function of cannabis use patterns (e.g., quantity, frequency, duration of cannabis use) if they had conducted more frequent assessments during the first week of abstinence, where others have noted the peak cannabis withdrawal syndrome occurs?

Also, the Milin study results may offer a conservative estimate of the clinical relevance of the cannabis withdrawal syndrome among adolescents. The issue of participant attrition is the bane of researchers and unfortunately endemic in research asking substance abusers to abstain from their drug of choice. Like many other studies, there was participant attrition in the Milin study, with the loss of 8 participants and retention of 13 adolescents who successfully completed the full 4-week study, a loss of 38 percent of participants. The question raised by this loss of participants is to what extent could a cannabis withdrawal syndrome contribute to the observed

attrition, and had those participants been retained would the results have indicated a more severe withdrawal syndrome?

In conclusion, Milin and colleagues are to be praised for providing the first published prospective study of cannabis withdrawal in adolescents with cannabis dependence seeking treatment. However, the design used limited their ability to test their second hypothesis. Our goal is not to criticize Milin and colleagues' study unduly, but instead to raise the above methodological concerns that need to be addressed in future studies in order to more specifically determine the factors that predict severity of cannabis withdrawal and the clinical relevance of abstinence outcomes in cannabis-using adolescents.

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