

# Cannabis bliss?

## Perhaps not?

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The effectiveness of cannabis use in treating multiple sclerosis (MS) symptoms has been mixed. On the one hand, it has been shown to be effective in treating lower urinary tract symptoms<sup>1</sup> as well as pain<sup>2</sup> in these patients. In addition, significant numbers of patients with MS support the use of cannabis for symptom management.<sup>3,4</sup> In contrast, other research has shown that cannabis use does not positively impact symptoms of spasticity.<sup>5</sup> Two common MS sequelae for which the impact of cannabis use has not been systematically examined are cognitive and psychiatric problems. Such exploration is especially important given the known psychoactive properties of cannabis and its possible effect on cognition.

In this issue of *Neurology*®, Ghaffar and Feinstein<sup>6</sup> report their evaluation of the cognitive and psychiatric consequences of cannabis use in patients with MS. The study presents interesting findings that make an important contribution to the MS literature. Specifically, the authors compared 10 patients with MS who reported smoking cannabis regularly (at least once per month) to 40 well-matched control patients with MS who denied cannabis use. Results showed that cannabis users were significantly more likely to meet criteria for a lifetime DSM-IV psychiatric diagnosis. Users were also more impaired on one neuropsychological test measuring speeded visual attentional functioning and working memory. The groups did not differ significantly on current anxiety or depression, nor did they differ significantly on tests measuring verbal and visual memory, speeded auditory attention, or verbal fluency. However, the direction of mean differences on neuropsychological testing was uniformly in the direction of worse performance by cannabis users. The failure of such differences to reach statistical significance was likely due to reduced statistical power because of small sample size. In summary, compared with controls, cannabis users were found to have more lifetime psychiatric and current speeded visual attention deficits.

The study makes significant contributions. First, by showing that cannabis users are characterized by

greater speeded visual attention deficits, an area of cognitive functioning that has already been widely shown to be impaired in MS patients generally, the results suggest that inhaled cannabis may exacerbate such difficulties. The authors rightly point out that 40–65% of patients with MS show evidence of cognitive impairment and that cognitive difficulties are associated with decreased quality of life in patients and caregivers. Given this high prevalence and association with real-world functioning, cannabis use in patients with MS may compound existing problems. Second, with evidence for greater lifetime psychiatric difficulties in MS patients who use cannabis, the authors' study illustrates an analogous problem with psychiatric difficulties in MS. Because lifetime prevalence of psychopathology, especially depression, is at least 50% in patients with MS,<sup>7</sup> the study results suggest that inhaled cannabis use may exacerbate such psychiatric difficulties.

Regarding the implications for practice, the study involves too small a sample to justify any firm clinical guidelines. With that said, the authors' data suggest that it would at least be advisable for clinicians to inform patients who use cannabis that there may be undesirable cognitive and psychiatric consequences. Patients with significant cognitive or psychiatric difficulties might be especially vulnerable to the potential negative impact of cannabis use on their functioning.

Cannabinoids have been shown to have neuroprotective and immunosuppressive benefits in preclinical MS models.<sup>8</sup> However, given the potential cognitive and psychiatric risks, combined with the fact that such effects are only seen at cannabinoid levels beyond what is practicable in clinical practice, these data are not sufficient to support recommending the off-label use of cannabis for MS. The most prudent course of action would be to await clinical trials of neuroprotection in MS using CBR2 agonists.

The most important limitation of the study concerns the causal interpretation of the results. It is

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tempting to conclude that cannabis use leads to greater cognitive and psychiatric difficulties in patients with MS. However, given the correlational nature of the study design, it is equally plausible that those with psychiatric or cognitive problems were more likely to use cannabis as a way of self-medicating. To tease such causal issues out more definitively, a future study could examine whether cannabis users vs controls had any history of psychiatric problems before they began their cannabis use. If they did, then this would suggest that psychiatric problems lead to cannabis use. If they did not, then the data would suggest that cannabis use leads to psychiatric difficulties. A future study using a longitudinal design would also help to clarify causal issues. Another limitation to the study (acknowledged by the authors) is that determination of cannabis use was based upon self-report and there was no confirmation of such use with urine toxicology data. A future study could include such confirmation, and also involve more systematic administration of cannabis.

These limitations aside, Ghaffar and Feinstein's study<sup>6</sup> raises the important question: Do MS patients who use cannabis show increased psychiatric and cognitive difficulties? The answer seems to be yes. The difficulty arises in making causal inferences, something that future work will need to address.

Nonetheless, this important study underscores the clear clinical importance of this question.

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