Potent questions about cannabis and mental health

Lancet Psychiatry 2015
Published Online
February 18, 2015
http://dx.doi.org/10.1016/S2215-0366(14)00130-8
See Online/Articles
http://dx.doi.org/10.1016/S2215-0366(14)00117-5

The association between cannabis use and psychosis is well established, with estimated odds ratios (ORs) of 1·4 for lifetime exposure and 2·1 for frequent use according to longitudinal population-based cohorts.[1] These results seem to show a dose-response effect,[1] but have not taken account of a key component of cannabis—its potency. In *The Lancet Psychiatry,* Marta Di Forti and colleagues[2] address this gap with a case-control analysis of first-episode psychosis. Strengths of the study include the large sample of patients (n=410), an impressive response rate for participation (461 [76%] of 606 individuals) and appropriate control for confounding by gender, ethnicity, education, employment status, and other drug use.

Consistent with previous reports,[1] patients with first-episode psychosis were more likely than controls to have used cannabis on a daily basis. More importantly, however, this effect was strongly dependent on the type of cannabis used. The investigators identified no associations between low-potency (hash) cannabis and psychosis, even with daily use. By contrast, the risk increased substantially for high-potency (skunk) cannabis, with ORs of 1·9 (95% CI 1·08–2·62) for use less than once per week, 2·7 (1·4–9·1) for use at weekends, and 5·4 (2·8–11·3) for use every day.

These findings make a notable contribution to the existing literature on cannabis and psychosis. Previous studies[1] reporting a stronger association in frequent users, have been unable to separate heaviness of use from some of its correlates. For example, as frequency of cannabis use rises, so does the regularity with which an individual carries out a stigmatised and widely illegal activity, which has important social and developmental implications. Simultaneously, time spent on other recreational activities, education, or work will typically decrease. Furthermore, cannabis is almost always smoked with tobacco in many countries, including the UK. This fact makes separation of the effects of tobacco co-administration from those of cannabis itself challenging.[3] These factors cannot explain the differential associations between cannabis type and psychosis reported by Di Forti and colleagues,[2] if skunk and hash are assumed to be used by similar populations in a similar manner.

Replication of these findings in longitudinal cohorts will be important. Ideally these studies should biologically quantify cannabinoid exposure in addition to self-reported use. These measures could account for individual patterns of use, such as titrating (using less cannabis) as potency increases.[4] Skunk is not only characterised by high concentrations of Δ-9-tetrahydrocannabinol (THC; about 15%), but also by scarcity of cannabidiol (<0·1%). By contrast, hash usually contains roughly 5% THC and about 4% cannabidiol.[5] Examination of cumulative exposure to these cannabinoids could determine whether the results reported by Di Forti and colleagues might be explained by propsychotic effects of THC,[6] anti-psychotic effects of cannabidiol,[7] or interactions between the two.[8,9] Identification of the contribution of different cannabinoids might have implications for other mental health problems linked to cannabis, such as addiction.[10]

Di Forti and colleagues correctly state that causality cannot be established on the basis of their study, and this consideration is important. If causality exists, they calculate that 24% of first-episode cases in their South London catchment area might be attributable to high potency cannabis. This figure is higher than their estimate for daily use in general (19%). If this interpretation is correct, cannabis potency is more

Tom P Freeman

important than frequency of use in prediction of risk of psychosis, and could have a substantial effect on public health.

Tom P Freeman
Clinical Psychopharmacology Unit, University College London, London WC1E 6BT, UK
tom.freeman@ucl.ac.uk

I declare no competing interests.

1 Moore THM, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet* 2007; **370:** 319–28.
2 Di Forti M, Marconi A, Carra E, et al. Proportion of patients with first-episode psychosis attributable to use of high potency cannabis: the example of South London. *Lancet Psychiatry* 2015; published online Feb 18. http://dx.doi.org/10.1016/S2215-0366(14)00117-5
3 Gage S, Hickman M, Heron J, et al. Associations of cannabis and cigarette use with psychotic experiences at age 18: findings from the Avon Longitudinal Study of Parents and Children. *Psychol Medicine* 2014; **44:** 1–10.
4 Freeman TP, Morgan CJ, Hindocha C, Schafer G, Das RK, Curran HV. Just say 'know': how do cannabinoid concentrations influence users' estimates of cannabis potency and the amount they roll in joints? *Addiction* 2014; **109:** 1686–94.
5 Hardwick S, King LA. Home Office cannabis potency study 2008. London: Home Office Scientific Development Branch, 2008.
6 D'Souza DC, Perry E, MacDougall L, et al. The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: implications for psychosis. *Neuropsychopharmacology* 2004; **29:** 1558–72.
7 Leweke F, Piomelli D, Pahlisch F, et al. Cannabidiol enhances anandamide signaling and alleviates psychotic symptoms of schizophrenia. *Transl Psychiatry* 2012; **2:** e94.
8 Morgan CJA, Curran HV. Effects of cannabidiol on schizophrenia-like symptoms in people who use cannabis. *Br J Psychiatry* 2008; **192:** 306–07.
9 Englund A, Morrison PD, Nottage J, et al. Cannabidiol inhibits THC-elicited paranoid symptoms and hippocampal-dependent memory impairment. *J Psychopharmacol* 2013; **27:** 19–27.
10 Morgan CJA, Freeman TP, Schafer GL, Curran HV. Cannabidiol attenuates the appetitive effects of Delta 9-tetrahydrocannabinol in humans smoking their chosen cannabis. *Neuropsychopharmacology* 2010; **35:** 1879–85.