

Psychosis associated with cannabis withdrawal: case series and systematic review

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Introduction

Cannabis is the most commonly used recreational drug in the UK,¹ and regular use is associated with an increased risk of developing psychosis. This is especially true for high-potency cannabis strains.²

A recent meta-analysis indicates that among individuals who develop a first episode of psychosis, 36% also meet diagnostic criteria for a cannabis use disorder.³

Both the intoxicating (euphoria, relaxation) and the adverse effects of cannabis (anxiety, cognitive impairment and paranoia) are attributable to its main psychoactive constituent, delta-9-tetrahydrocannabinol (THC).⁴

In regular users, abrupt cessation or rapid reduction of cannabis can produce a withdrawal syndrome, characterised by anxiety, restlessness, irritability and insomnia.⁵

Recently, there have been case reports of acute psychosis developing in the context of cannabis withdrawal.⁶

Aims

Therefore, our aim was to examine the association between cannabis withdrawal and psychosis in two large patient samples.

Firstly, we would conduct a retrospective case series using anonymised electronic healthcare records from South London to newly identify cases of psychosis associated with cannabis withdrawal.

Additionally, we set out to undertake a systematic review of all published cases of cannabis withdrawal associated with psychosis in the literature.

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Methods

Cases from Electronic Health Records

Setting and Search Strategy:

Cases were found using the South London and Maudsley NHS Foundation Trust Biomedical Research Centre Case Register, which contains anonymized records of over 400,000 patients.⁷ We searched for patients with clinical entries that contained terms related to both cannabis withdrawal and to psychosis.

Eligibility:

Possible cases were reviewed by two psychiatrists and were included if both agreed that the patient had an episode of psychosis which was 'probably' or 'definitely' associated with cannabis withdrawal.

Data Extraction:

To identify psychotic symptoms the Operational Criteria in Studies of Psychotic Illness (OPCRIT) symptom checklist was utilised.⁸ The presence of DSM-5 cannabis withdrawal symptoms was also recorded.

Systematic Review

Eligibility:

All studies describing cases of psychosis or mania triggered by acute withdrawal from cannabis or synthetic cannabinoids were included.

Search Strategy:

PsycINFO, Embase, and MEDLINE were searched from the date of inception until 20/07/2023 using appropriately constructed search terms. Reference lists were also reviewed to identify missed studies.

Data Extraction:

Two authors independently extracted demographic and clinical outcome data.

Statistical Analysis:

Continuous outcomes were reported as means with standard deviation (SD), or medians with interquartile range (IQR). Categorical outcomes were reported as frequencies. Psychosis relapse was analysed according to cannabis use trajectory with a Chi-squared test. The threshold for statistical significance was $p < 0.05$.

Results

Cases from Electronic Health Records

69 cases of psychosis associated with cannabis withdrawal were identified. The mean age was 27.3 years and 57 (82.6%) were male. 48 (75%) cases involved a first-presentation of psychosis and 21 (30.4%) concerned relapse of an established psychotic disorder.

The quality of information on cannabis use history was variable, but 60 (87%) were daily users and, where recorded, 70.6% (36) used high-potency cannabis.

The majority of participants (56; 81%) had stopped using cannabis abruptly. The frequency of each cannabis withdrawal symptom is shown in **Figure 1**. The time from discontinuation of cannabis to the emergence of frank psychosis ranged from 2 days to 4 weeks.

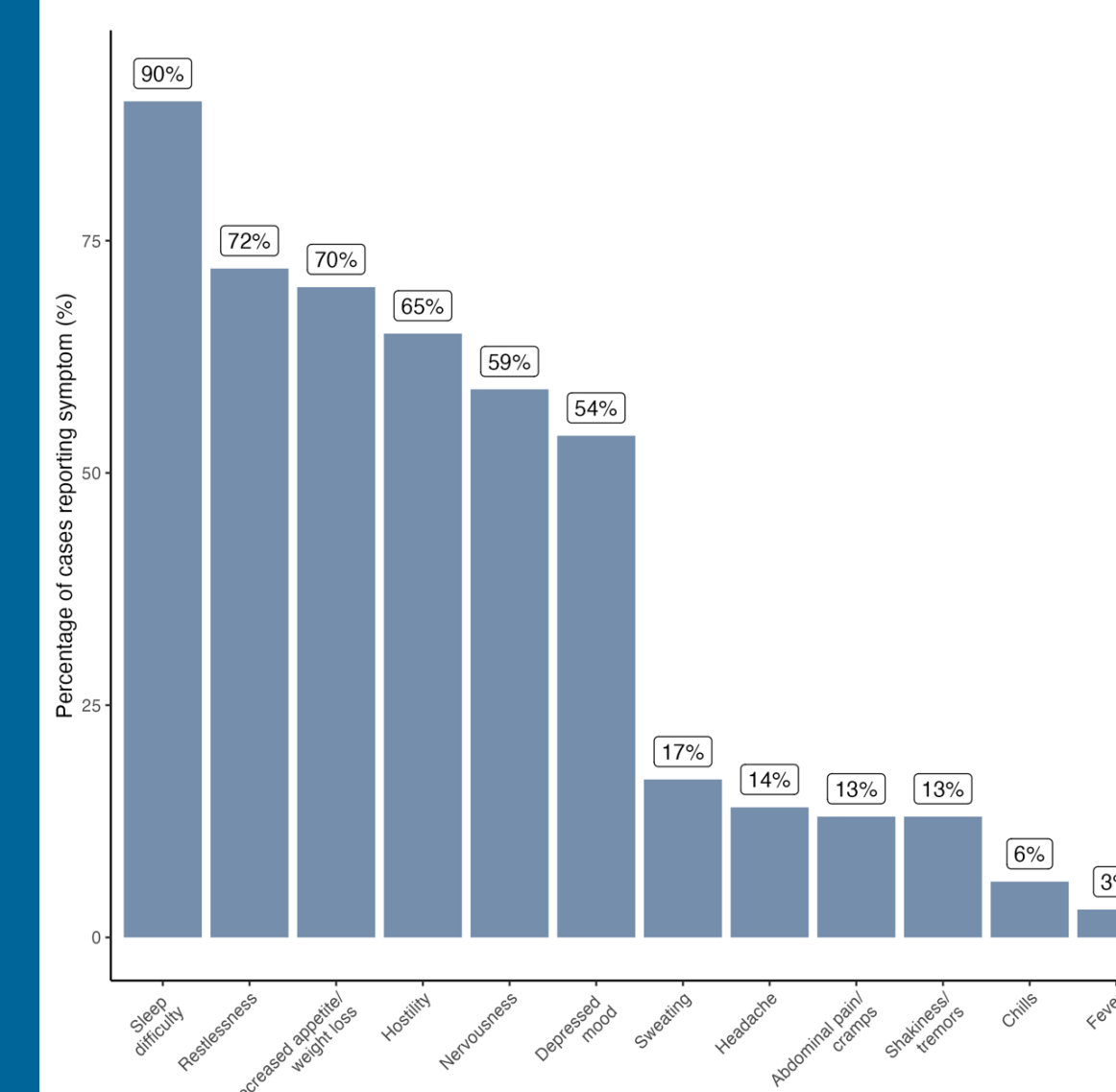


Figure 1: proportions of cases reporting individual cannabis withdrawal symptoms

The prevalence of symptoms from the OPCRIT criteria is shown in **Figure 2** (right). The symptoms with the highest prevalence were sleep disturbance (89.9%), persecutory delusions (76.8%) and poor appetite (71.0%).

Most (62.3%) continued to use cannabis, and most of this subgroup (81.6%) experienced a relapse of psychosis. The risk of relapse in those who continued to use cannabis was much higher than in those who abstained (Odds ratio = 14.7 [95% CI: 4.3 to 60.0]).

Cases from Systematic Review

The systematic review identified a total of 36 cases from 17 studies. The findings were consistent with those from our health record study, with similar demographic and clinical features, and histories of abrupt discontinuation and frequent emergence of insomnia.

OPCRIT Symptom Information

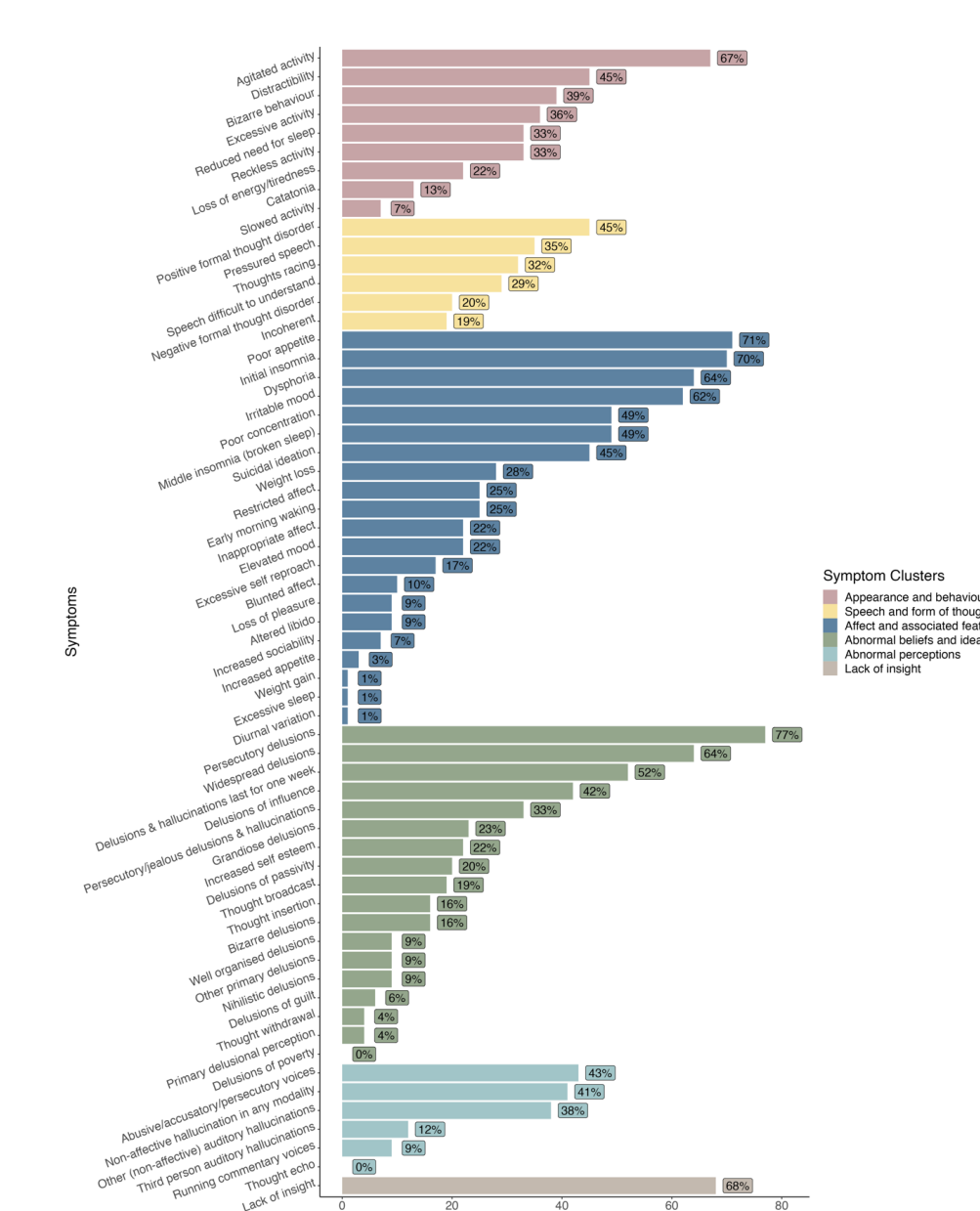


Figure 2: proportion of cases with OPCRIT symptoms recorded in health records

Conclusions

We identified 69 cases of psychosis associated with cannabis withdrawal from retrospective health record review and 36 cases from 17 studies in a systematic review, comprising the largest set of episodes of psychosis precipitated by cannabis withdrawal (n=105).

It is important clinicians are aware of psychosis associated with cannabis withdrawal as a clinical entity.

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