



## Letters

### Remission of severe, treatment-resistant schizophrenia following adjunctive cannabidiol

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To the Editor

Cannabidiol (CBD), a major non-psychoactive constituent of *Cannabis sativa*, showed beneficial effects in the treatment of schizophrenia (McGuire et al., 2018), however not in treatment-resistant patients (Zuardi et al., 2006). We report a patient with treatment-resistant schizophrenia remitting following adjunctive CBD.

A 57-year-old woman with a 21-year history of schizophrenia was admitted after a suicide attempt. Leading symptoms, constantly persisting since age 48, were continuous, acoustic hallucinations in the form of loud voices commanding her to commit suicide ('Come on! Do it!') and severe negative symptoms. She already has had eight suicide attempts due to these constant voices. Prior treatments included atypical (clozapine, olanzapine, risperidone, aripiprazole) and typical (haloperidol, flupenthixol) antipsychotics and two series of 12

treatments of electroconvulsive therapy (ECT).

On admission, the patient, having been hospitalized for 13 months in the last 2 years, was severely ill. Total score on the Positive and Negative Syndrome Scale (PANSS) was 117, and the score on the negative scale was 41. We increased pre-existing clozapine to 275 mg/day (mean plasma level: 635 µg/L, therapeutic range: 350–600 µg/L) and continued lamotrigine 225 mg/day. However, symptoms remained unchanged. We then additionally applied 12 ECTs, again, without any effect. We therefore added oral CBD 500 mg twice daily for 7 weeks (blood level 12 hours after intake: 90–107 ng/mL), resulting in markedly softened, but still continuous acoustic hallucinations and reduced negative symptoms. After increasing CBD to 750 mg twice daily (121–144 ng/mL), voices gradually ceased within 2.5 weeks, now for 8 months. Also, negative symptoms further improved. On discharge, the PANSS total score was decreased to 68 and the patient fulfilled remission criteria with only mild negative symptoms (PANSS negative scale: 21). CBD did not affect clozapine levels and was well tolerated apart from a mild transient hand tremor.

CBD acts both independently of and dependently on cannabinoid CB1/CB2 receptor signalling, despite only low affinity. Not blocking dopaminergic d2 receptors, its antipsychotic properties are differently transmitted than in antipsychotics (Gururajan and Malone, 2016). The striking improvement was related to both the dose, causing comparatively (Gururajan and Malone, 2016) high blood levels, and

the treatment duration, possibly explaining differences to a report showing no effect in treatment-resistant patients (Zuardi et al., 2006). Our case report contradicts the assumption 'that CBD is not likely to be any superior than existing antipsychotics' (Gururajan and Malone, 2016). In fact, CBD might be particularly suitable for those patients being resistant to antipsychotics due to its different mode of action.

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#### Patient consent

The patient provided written informed consent.

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