

Article Title: The Impact of THC and CBD in Schizophrenia: A Systemic Review

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Overview: This article is a systematic review evaluating the impact of tetrahydrocannabinol (THC) and cannabidiol (CBD) in individuals with schizophrenia, specifically assessing their effects on psychotic symptoms and cognition.

Background: Schizophrenia is defined as a chronic neurodevelopmental disorder that affects approximately 0.5 to 1.0% of the global population, typically emerging in late adolescence or early adulthood. It is associated with positive symptoms (hallucinations and delusions), negative symptoms (flat affect, avolition, social withdrawal), and cognitive deficits (impaired attention, working memory, and executive function). Cannabis is the most common illicit drug used by those with schizophrenia, with up to 43% developing a cannabis use disorder compared to only 6.3% of the general population. Both THC and CBD are found in cannabis. THC is the psychoactive component associated with intoxication and psychosis risk, while CBD is non-intoxicating and has been hypothesized to have antipsychotic properties. Despite increasing legalization and interest in cannabis-derived treatments, the therapeutic role of THC and CBD in schizophrenia remains unclear.

Method: A systematic literature search across multiple databases (PubMed/MEDLINE, PsycINFO, EMBASE, Cochrane, CINAHL, Scopus, and others) identified controlled human studies using defined doses of THC and/or CBD in schizophrenia-spectrum disorders. Inclusion criteria focused on randomized controlled trials (RCTs), placebo-controlled studies, and prospective interventional designs evaluating symptom severity, cognition, or neuroimaging outcomes.

Findings:

THC studies

- Consistently associated with worsening of psychotic symptoms in controlled settings (especially IV THC in patients without CUD)
- Produces acute cognitive impairment, particularly in verbal learning and working memory
- Effects on symptoms are less consistent in patients with comorbid CUD

CBD studies

- Generally does not worsen psychosis and is well tolerated across studies
- Evidence for antipsychotic benefit is mixed:
 - One RCT showed CBD (800 mg) had similar efficacy to amisulpride (atypical antipsychotic) in reducing psychotic symptoms
 - Other RCTs showed no significant difference vs placebo in symptom reduction
 - Some studies suggest improvement in positive symptoms, especially at higher doses.
- Mechanism unknown but proposed MOA suggests that CBD increases hippocampal glutamate signaling which is inversely correlated with symptom severity

Safety

- THC: Associated with transient psychosis exacerbation, tachycardia, and cognitive disruption
- CBD: Generally safe; mild adverse effects include sedation and GI symptoms

Limitations:

- Sample size – small sizes across THC studies
- Study duration – many studies were single dose or <4-6 weeks, limiting conclusions about long-term efficacy and safety
- High heterogenous study design
- Few direct comparisons to standard antipsychotics
- Risk of bias – unclear randomization or blinding in several studies