

## Publication

### Modulation of mediotemporal and ventrostriatal function in humans by Delta9-tetrahydrocannabinol : a neural basis for the effects of Cannabis sativa on learning and psychosis

#### **JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**

**ID** 1193637

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**Year** 2009

**Title** Modulation of mediotemporal and ventrostriatal function in humans by Delta9-tetrahydrocannabinol : a neural basis for the effects of Cannabis sativa on learning and psychosis

**Journal** Archives of general psychiatry

**Volume** 66

**Number** 4

**Pages / Article-Number** 442-51

CONTEXT: Cannabis sativa use can impair verbal learning, provoke acute psychosis, and increase the risk of schizophrenia. It is unclear where C. sativa acts in the human brain to modulate verbal learning and to induce psychotic symptoms. OBJECTIVES: To investigate the effects of 2 main psychoactive constituents of C. sativa, Delta9-tetrahydrocannabinol (Delta9-THC) and cannabidiol, on regional brain function during verbal paired associate learning. DESIGN: Subjects were studied on 3 separate occasions using a block design functional magnetic resonance imaging paradigm while performing a verbal paired associate learning task. Each imaging session was preceded by the ingestion of Delta9-THC (10 mg), cannabidiol (600 mg), or placebo in a double-blind, randomized, placebo-controlled, repeated-measures, within-subject design. SETTING: University research center. PARTICIPANTS: Fifteen healthy, native English-speaking, right-handed men of white race/ethnicity who had used C. sativa 15 times or less and had minimal exposure to other illicit drugs in their lifetime. MAIN OUTCOME MEASURES: Regional brain activation (blood oxygen level-dependent response), performance in a verbal learning task, and objective and subjective ratings of psychotic symptoms, anxiety, intoxication, and sedation. RESULTS: Delta9-Tetrahydrocannabinol increased psychotic symptoms and levels of anxiety, intoxication, and sedation, whereas no significant effect was noted on these parameters following administration of cannabidiol. Performance in the verbal learning task was not significantly modulated by either drug. Administration of Delta9-THC augmented activation in the parahippocampal gyrus during blocks 2 and 3 such that the normal linear decrement in activation across repeated encoding blocks was no longer evident. Delta9-Tetrahydrocannabinol also attenuated the normal time-dependent change in ventrostriatal activation during retrieval of word pairs, which was directly correlated with concurrently induced psychotic symptoms. In contrast, administration of cannabidiol had no such effect. CONCLUSION: The modulation of mediotemporal and ventrostriatal function by Delta9-THC may underlie the effects of C. sativa on verbal learning and psychotic symptoms, respectively.

**Publisher** American Medical Association

**ISSN/ISBN** 0003-990X

**edoc-URL** <http://edoc.unibas.ch/dok/A6003876>

**Full Text on edoc** No;

**Digital Object Identifier DOI** 10.1001/archgenpsychiatry.2009.17

**PubMed ID** <http://www.ncbi.nlm.nih.gov/pubmed/19349314>

**ISI-Number** WOS:000264924400011

**Document type (ISI)** Journal Article, Randomized Controlled Trial