

Publication

Distinct effects of {delta}9-tetrahydrocannabinol and cannabidiol on neural activation during emotional processing

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CONTEXT: Cannabis use can both increase and reduce anxiety in humans. The neurophysiological substrates of these effects are unknown. OBJECTIVE: To investigate the effects of 2 main psychoactive constituents of Cannabis sativa (Delta9-tetrahydrocannabinol [Delta9-THC] and cannabidiol [CBD]) on regional brain function during emotional processing. DESIGN: Subjects were studied on 3 separate occasions using an event-related functional magnetic resonance imaging paradigm while viewing faces that implicitly elicited different levels of anxiety. Each scanning session was preceded by the ingestion of either 10 mg of Delta9-THC, 600 mg of CBD, or a placebo in a double-blind, randomized, placebocontrolled design. PARTICIPANTS: Fifteen healthy, English-native, right-handed men who had used cannabis 15 times or less in their life. MAIN OUTCOME MEASURES: Regional brain activation (blood oxygenation level-dependent response), electrodermal activity (skin conductance response [SCR]), and objective and subjective ratings of anxiety. RESULTS: Delta9-Tetrahydrocannabinol increased anxiety, as well as levels of intoxication, sedation, and psychotic symptoms, whereas there was a trend for a reduction in anxiety following administration of CBD. The number of SCR fluctuations during the processing of intensely fearful faces increased following administration of Delta9-THC but decreased following administration of CBD. Cannabidiol attenuated the blood oxygenation level-dependent signal in the amygdala and the anterior and posterior cingulate cortex while subjects were processing intensely fearful faces, and its suppression of the amygdalar and anterior cingulate responses was correlated with the concurrent reduction in SCR fluctuations. Delta9-Tetrahydrocannabinol mainly modulated activation in frontal and parietal areas. CONCLUSIONS: Delta9-Tetrahydrocannabinol and CBD had clearly distinct effects on the neural, electrodermal, and symptomatic response to fearful faces. The effects of CBD on activation in limbic and paralimbic regions may contribute to its ability to reduce autonomic arousal and subjective anxiety, whereas the anxiogenic effects of Delta9-THC may be related to effects in other brain regions.

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