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OPPOSITE NEURAL EFFECTS OF THE MAIN PSYCHOACTIVE INGREDIENTS OF CANNABIS- NEURAL BASIS FOR POTENTIAL THERAPEUTIC EFFECTS OF CANNABIDIOL

S. Bhattacharyya, P. Fusar-Poli, S. Borgwardt, R. Martin-Santos, C. Carroll, M. Seal, J. Crippa, Z. Atakan, P. McGuire

Section of Neuroimaging, Division of Psychological Medicine & Psychiatry, Institute of Psychiatry, KCL, London, UK

There is considerable interest in the therapeutic potential of Cannabidiol (CBD), the second most abundant component of Cannabis. While delta-9-THC, the main psychoactive ingredient of cannabis, impairs memory and induces anxiety and psychotic symptoms acutely and increases the risk of psychotic disorders in regular cannabis users, CBD does not impair memory, may have anxiolytic and possibly antipsychotic effects. Hence, we compared directly the acute neural effects of these two active ingredients of cannabis, by combining pharmacological challenge with fMRI. Using a double-blind, repeated measures design and oral challenge with 10mg of delta-9-THC, 600mg of CBD or placebo in 15 healthy volunteers, we examined whether delta-9-THC and CBD have opposing effects on the neural substrates of verbal memory and fear processing and whether they also have opposing effects on the neural substrates of anxiety and psychotic symptoms induced by delta-9-THC. Delta-9-THC induced anxiety and psychotic symptoms acutely while there was a trend for a reduction in anxiety but no change in psychotic symptoms with CBD. During the memory task, delta-9-THC attenuated and CBD increased activation in the striatum bilaterally. Effect of delta-9-THC on striatal activation was inversely correlated with the psychotic symptoms induced by it concomitantly. During the processing of fearful faces, delta-9-THC increased and CBD attenuated activation in the amygdala and these effects correlated with their anxiogenic and anxiolytic effects respectively. These opposing effects of CBD on the key neural substrates for psychotic symptoms and anxiety induced by delta-9-THC may suggest its possible therapeutic role in countering these conditions.