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Genetic modulation of the long-term effects of cannabis on brain structure, function and symptomatology

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Abstract

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Genetic modulation of the long-term effects of cannabis on brain structure, function and symptomatology

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Background: Long-term heavy cannabis use has been shown to result in changes to the structure and function of the brain and is thought to be a component cause of triggering schizophrenia in vulnerable individuals. Little is known about what constitutes vulnerability to psychosis in the context of cannabis use or indeed vulnerability toward other adverse effects to the brain. This study aimed to investigate potential genetic vulnerability to such adverse effects in long-term cannabis users.

Methods: A range of structural and functional magnetic resonance imaging data, electrophysiological, cognitive, neuropsychological and clinical symptomatic measures were investigated from two separate studies of long-term heavy cannabis users (combined sample n=130) and matched non-user controls. Modulation of effects of cannabis use on these measures by single nucleotide polymorphisms (SNPs) from a range of candidate genes implicated in schizophrenia or involved in cognition and brain cellular and functional integrity was examined.

Results: Variation in several genes was found to be associated with functional and brain structural outcomes. In particular, gene x group interactions were observed involving variations in the COMT gene in association with greater reduction of hippocampal and amygdala volumes and in modulating reduction of the mismatch negativity (MMN) event-related potential. There was also evidence of epistasis between several of the candidate genes investigated, and evidence of genetic modulation of some of the cognitive and symptomatic measures.

Discussion: The results of this investigation implicate several genes in modulating the long-term effects of cannabis on brain structure and function. The implications of these findings may guide our understanding of vulnerability toward the adverse effects of cannabis on the brain, including the propensity for cannabis to trigger psychosis.