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A risk gene for cannabis psychosis

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The ability of cannabis to produce psychosis has long been an important public health concern. This concern is growing in importance as there is emerging data that cannabis exposure during adolescence may increase the risk of developing schizophrenia, a serious psychotic disorder. Further, with the advent of medical marijuana, a new group of people with uncertain psychosis risk may be exposed to cannabis.

For these reasons, it would be valuable if a biological test could be developed that predicted the risk for developing cannabis psychosis. This test could be used to advise people who abuse cannabis or to inform marijuana-prescribing decisions by physicians.

Recent research has implicated a variation in the gene that codes for a protein called RAC-alpha serine/threonine-protein kinase (Akt1) in the risk for cannabis psychosis. However, independent verification of these findings is critical for genetic associations with complex genetic traits, like cannabis-related psychosis, because these findings are notoriously difficult to replicate.

Led by first author Dr. Marta Di Forti at King's College London's Institute of Psychiatry, genetic researchers carried out a case control study to investigate variation in the AKT1 gene and cannabis use in increasing the risk of psychosis.

Di Forti said, "We studied the AKT1 gene as this is involved in dopamine signaling which is known to be abnormal in psychosis. Our sample comprised 489 patients with their first episode of psychosis and

278 healthy controls."

They performed genotyping on all volunteers, and assessed their use of cannabis. They found that AKT1 genotype influences the risk of psychotic disorders in cannabis users, which confirmed the prior report.

"We found that cannabis users who carry a particular variant in the AKT1 gene had a two-fold increased probability of a psychotic disorder and this increased up to seven-fold if they used cannabis daily," explained the authors. "Our findings help to explain why one cannabis user develops psychosis while his friends continue smoking without problems."

"While the AKT1 genotype does not rise to the level of a clinically useful test of the risk for cannabis psychosis, it does show that this source of psychosis risk has a genetic underpinning," commented Dr. John Krystal, Editor of *Biological Psychiatry*. "This advance also points to cellular signaling mechanisms mediated by Akt1 as being relevant to the biology of cannabis psychosis. This may suggest research directions for novel therapeutics for cannabis psychosis."

Di Forti agreed, adding that "such findings could also help to design health educational campaigns tailored to reach those young people at particular risk."

More information: The article is "Confirmation that the AKT1 (rs2494732) Genotype Influences the Risk of Psychosis in Cannabis Users" by Marta Di Forti, Conrad Iyegbe, Hannah Sallis, Anna Kolliakou, M. Aurora Falcone, Alessandra Paparelli, Miriam Sirianni, Caterina La Cascia, Simona A. Stilo, Tiago Reis Marques, Rowena Handley, Valeria Mondelli, Paola Dazzan, Carmine Pariante, Anthony S. David, Craig Morgan, John Powell, and Robin M. Murray (doi: 10.1016/j.biopsych.2012.06.020). The article appears in *Biological*

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