

## PSYCHOSIS ONSET: USE OF CANNABIS X COMT GENOTYPE INTERACTION. A CASE-ONLY DESIGN ANALYSIS IN A FIRST-EPISODE PSYCHOSIS SAMPLE

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**Background:** Cannabis consumption is associated with approximately doubling of the risk of subsequent schizophrenia. There is evidence that a functional val158met polymorphism in the catechol-O-methyltransferase gene (COMT) and use of cannabis interact to increase risk. This gene by environment (G x E) interaction is not accounted by a correlation between cannabis use and the COMT genotype (1).

**Hypothesis:** We predicted a significant difference in the frequency of the COMT Val158 allele between cases consuming and not consuming cannabis, consistent with those homozygous for the Val158 allele being at highest risk of developing schizophrenia if cannabis users.

**Methods:** We collected demographic, clinical, cannabis use data and DNA in a sample of 278 first-episode psychosis patients, recruited as part of the Genetic And Psychosis (GAP) study. DNA was extracted by standard methods from blood samples (82.4%) or cheek swabs (17.6%) for those patients unwilling to undergo phlebotomy. The COMT val158met polymorphism was genotyped by standard procedures and a case-only design (2) conducted.

**Results:** 137 (55,7%) smoked cannabis, 63.4% of them began their use before age 16 with a mean length of cannabis use was 9,5 years. There was no significant difference in cannabis consumption between ethnic groups. As in case-only studies of gene-environment interaction, we calculated an odds ratio (OR) from cross-classification of cannabis use and COMT genotype in the patients. Logistic regression was used to control for the effect of potential confounders.

**Conclusions:** In our first episode psychosis sample we did not find a COMT by cannabis interaction,  $COR < 1$ . Nevertheless COMT Genotype seems to moderate the effect of cannabis use on age of onset of Psychosis. Subjects carrying the Val allele and smoking cannabis have an earlier age of onset of psychosis than the other groups ( $p = 0.02$ ).

**Keywords:** cannabis, COMT, case-only design.

### References:

- (1) Caspi A., Moffitt T.E., Cannon M., McClay J., Murray R., Harrington H., Taylor A., Arseneault L., Williams B., Braithwaite A., Poulton R., Craig I.W. (2005) *Biol Psychiatry* 15;57(10):1117-27.
- (2) Kohury MJ, Flanders D, (1996) *American J. of Epidemiology* 144 (3): 207-213.