Article: EPA-1227
Topic: FC02 - Free Communications Session 02: Neurobiology of schizophrenia

INTERACTION BETWEEN GENETIC FACTORS AND CANNABIS USE IN SCHIZOPHRENIA: PHENOTYPIC, ENVIRONMENTAL AND GENETIC APPROACH

J. Mallet[1], N. Ramoz[2], P. Gorwood[2], C. Dubertret[1]

[1]Service de Psychiatrie et Addictologie, Assistance Publique-Hôpitaux de Paris (AP-HP) Hôpital Louis Mourier, Colombes, France ; [2]Centre Psychiatrie et Neurosciences, INSERM U894, Paris, France

Introduction
Identifying schizophrenia vulnerability factors requires testing specific hypotheses concerning etiopathogenic models, candidate genes, and environmental factors involved. We hypothesized that patients developing schizophrenia after using regularly cannabis represent an homogenous phenotypic entity which could result from a specific interaction between genetic polymorphisms (SNPs) of *CNR1*, *CNR2* and *COMT* genes and cannabis use (an environmental factor intervening lately in the neurodevelopment).

Objectives
The main objective was to confirm that patients using cannabis before the onset of schizophrenia had fewer markers of early-neurodevelopmental impairment. The secondary objective was to identify a gene environment interaction in this subset of patients.

Methods
Patients were prospectively included and underwent a standardized interview and an evaluation of cognitive functions and neurological soft signs. Blood and saliva samples were collected. For the case-case genetic study, those patients were pooled with patients included in a cannabis-dependent schizophrenic-patients cohort. Eight *CNR1*, *CNR2* and *COMT* SNPs were analyzed.

Results
We included 61 patients in the clinical part. Regular cannabis users before the onset of the disorder had fewer neurological soft signs, less cognitive impairment and a different clinical symptomatology. For the genetic part 26 patients were added to the 57 patients from the clinical part (4 non Caucasian patients excluded). Results were in favor of a gene environment interaction for rs1049353 of *CNR1*.

Conclusions
We found that regular cannabis users before the onset of schizophrenia had less neurodevelopmental impairment. In this subset of patients, cannabis could play a causal role in a gene environment interaction leading to schizophrenia.

https://doi.org/10.1016/S0924-9338(14)78470-6 Published online by Cambridge University Press