# P-698 - ANALYSIS OF SMARCA2 AND GENES ENCODING INTERACTORS OF SWI/SNF SMARCA2/BRM PROTEIN IN SCHIZOPHRENIA PATIENTS FROM AN ALGERIAN TRIO COHORT

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The genetic architecture of schizophrenia (SZ) is based on common variants identified by Genome Wide Association Studies (GWIS) and on rare variants. We found that the SZ-GWIS genes are part of an interacting network centered on SMARCA2 (Loe-Mie et al., HMG, 2010). Both rare and common variants have been identified in SMARCA2 gene (Koga et al., HMG, 2009; Walsh et al., Science, 2008).
Taking advantage of an Algerian trio cohort of one hundred SZ patients (Benmessaoud et al., BMC Psychiatry, 2008), we replicated the association of SNP rs2296212 localized in exon 33, resulting in D1546E amino acid change. We found that exon 33 displays a signature of positive evolution in the primate lineage, with an excess of rare variants in SZ-patients compared to their parents (p=0.038, Fisher test) and a higher proportion of rare variants in the primate-accelerated exons compared with the non-evolutionary exon in SZ-patients (p=0.032, Fisher test).
As SMARCA2/BRM protein is part of a large SWI/SNF protein complex involved in epigenetics regulation of synaptic plasticity (Lepagnol-Bestel et al., in preparation), this raises the question of possible rare variants in SMARCA2 gene and in genes encoding SMARCA2/BRM interactors, in particular for those displaying a signature of primate-accelerated evolution. A total of 17 genes have been selected: MEECP2, SMARCA2, DNMT1, SMARCA4, SMARCE1, EHMT2, SMARCC1, HDAC2, SIN3A, RCOR2, CSF2RA, TCF4, PGBD1, RBM9, UTP11L, DDX5, EWRS1. The sequencing data obtained from Roche 454 device will be presented.
Altogether, these results are expected to give new insights into the genetic architecture of SZ.



https://doi.org/10.1016/S0924-9338(12)74865-4 Published online by Cambridge University Press