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### Current smoking in real world schizophrenia: Relationship to psychopathology and clinical characteristics. Results from the FACE dataset

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**Background** Tobacco smoking is common in schizophrenia. Some characteristics are usually associated to tobacco smoking in schizophrenia, such as younger age, earlier onset of the disease, number of hospitalizations or higher treatment doses. However, little is known about positive symptoms or aggressiveness, as well as trauma history.

**Objectives** to study the relationship between smoking status and clinical characteristics in patients with schizophrenia.

**Method** A total of 474 patients with were consecutively included in the network of FondaMental Expert Center (FACE) for schizophrenia and assessed with the structural clinical interview for DSM-IV axis 1 disorders (SCID), validated scales for psychotic symptomatology and childhood trauma questionnaire. Tobacco abuse or dependence was defined according to the SCID. Ongoing antipsychotic treatment was recorded. Aggressiveness was measured with Buss-Perry Aggression Questionnaire (BPAQ).

**Results** A sample of 474 patients with schizophrenia was included in this study (non-smokers,  $n=215$ ; non-smokers,  $n=259$ ). Mean age at tobacco onset was 17.19 years old ( $SD=3.93$ ). In multivariate analysis, smoking was associated with SGA use ( $P=0.028$ ), with higher scores of physical aggressiveness ( $P=0.042$ ), with current alcohol-dependence ( $P=0.002$ ). However, no association was observed with sex, age of onset, trauma history, global functioning, observance or psychotic symptomatology.

**Conclusions** Tobacco smoking was associated with physical aggressiveness, but not with earlier onset of the disease nor traumas or psychotic symptomatology. Besides, the results of the present study are in favor of a superior efficacy of second-generation antipsychotics in the treatment of comorbid tobacco use. These results need further investigation in longitudinal studies.

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### How could affect stress, PEP and sex in working memory?

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**Background** The first episode of psychosis is a crucial period when early intervention can alter the trajectory of the young person’s ongoing mental health and general functioning. Cognitive abilities are nuclear for the social recovery. Stress impairs

higher cognitive processes, dependent on the prefrontal cortex (PFC) and that involve maintenance and integration of information over extended periods, including working memory and attention. Different mechanism are involved such as HPA-Axis hyperactivity, affecting PFC. Recently, investigations show the different evolution of cognitive abilities between different sex in WM.

**Methods** A sample of 41 FEPs and 39 healthy subjects were evaluated. The variables assessed were verbal and visual memory, attention, working memory, processing speed, mental flexibility, verbal fluency, motor coordination, planning ability and intelligence.

**Results** We found an interaction between age (<16 years and >16 years) and group (psychosis vs. controls) in working memory ( $P=0.04$ ). There were no difference in men <16 years old control group and men with same age plus psychosis ( $5.87 \pm 1.57$  vs.  $5.83 \pm 1$ ;  $P=0.1$ ) in WM. However, this work was found to be significantly different in the univariate analysis of working memory in the group <16 years old women control ( $7.30 \pm 1.56$ ) and women psychosis group ( $5.61 \pm 1.91$ ).

**Conclusion** Social cognition and stress seem to be directly relation. Some studies show that stress enhance cognition performance in men while impairing it in women. Stress affect a variety of cognitive processes such attention and working memory. Deficit in social cognition are present in the prodromal phases of psychosis.

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### Identification of novel genes associated to major mental disease by whole exome sequencing in families with high prevalence

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**Introduction** The identification of new genetic variants underlying psychosis is crucial to improve its molecular diagnosis and to determine the disease etiology, which is necessary to develop new therapeutic targets.

**Aim** To identify novel rare genetic variants associated to mental disorders, using whole exome sequencing (WES).

**Methods** Two families with high prevalence of mental disease were genotyped using WES. The first family has 5 members affected, the mother with a bipolar disorder, three sons, two with schizophrenia and one with schizoaffective disorder, and a cousin with major depression and psychotic symptoms. The second family is constituted by 38 members affected by major mental diseases in three generations. Key affected members of each family were genotyped by WES. Shared rare variants, with allelic frequencies below 0.5% in general population, were identified among the affected members of the family. The segregation of those variants was confirmed by Sanger sequencing.

**Results** In family 1, thirty-seven genetic variants related to neurodevelopment were identified. Two of those variants in the genes *TRIP12* and *RNF25* segregated with psychosis. In family 2, seven rare genetic variants contained in genes related to neurodevelopment were identified. A mutation in the gene *ARHGAP19* segregated with psychosis.