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## Smoking does not impact social and non-social cognition in patients with first episode psychosis

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### ABSTRACT

**Background:** Many studies having shown significant improvements in non-social and social cognitive performance in smoking FEP patients compared to non-smoking FEP patients. The findings are controversial. This study analyzed the effects of tobacco use on non-social and social cognitive function in a large group of FEP patients and a matched healthy control group.

**Methods:** A sample of 335 patients with FEP and 253 healthy controls was divided into four subgroups: control tobacco users (CTU), control non-tobacco users (CNTU), patient tobacco users (PTU) and patient non-tobacco users (PNTU). Demographic variables, tobacco use variables (presence or absence, frequency and duration of tobacco use), neurocognitive (non-social) performance and social cognition were assessed.

**Results:** Comparison of 4 subgroups in non-social cognitive function revealed significant differences after controlling for covariables in executive functions ( $F = 13.45$ ;  $p \leq 0.001$ ) and working memory domains ( $F = 4.30$ ;  $p = 0.005$ ). CTU and CNTU subgroups scored higher in all the domains compared to the PTU and the PNTU subgroups respectively. Social cognitive function was also significantly different within the four subgroups, with control subgroups showing better social cognition than patient subgroups. Significant differences in the executive functions domain were observed when comparing PTU and CTU groups ( $F = 19.60$ ;  $p \leq 0.001$ ). No significant differences were revealed in the comparison between the patient groups.

**Conclusions:** This large study suggests that tobacco use in FEP patients is not related to better non-social or social cognitive performance.

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### 1. Introduction

It is well established that tobacco smoking is more prevalent in patients with schizophrenia (60–90%) than in the general population (25–30%) (Batra, 2000; Chapman et al., 2009; De León and Díaz, 2005; Dervaux and Laqueille, 2008; Tidey and Miller, 2015; Wehring et al.,

2012) and smoking cessation rates are much lower (de Leon et al., 2005; Gonzalez-Pinto et al., 2012). The number of daily cigarettes consumed correlates positively with the dose of antipsychotic drug intake (Ruther et al., 2014) and patients with lower levels of general functioning smoke more heavily (Kotov et al., 2010).

Compared to the healthy population, both adult and adolescent patients with psychosis have lower general and specific non-social and social cognitive function, according to numerous studies (Allott et al., 2011; Bombin et al., 2013; Kahn and Keefe, 2013; Mayoral et al., 2008; Mesholam-Gately et al., 2009; Zabala et al., 2009; Zabala et al., 2010). However, attempts to clarify how substances of abuse affect the brain under these circumstances (mental illness) have not shown conclusive results. Specifically, the cognitive approach to the self-medication hypothesis suggests that patients smoke to improve their cognitive functioning, as previous studies suggested that nicotine improves attention, working memory and executive functions in patients with psychosis (Ahlers et al., 2014; Dome et al., 2010; Hahn et al., 2012; Heishman et al., 2010; Jubelt et al., 2008; Ochoa and Lasalde-Dominicci, 2007; Rabin et al., 2009; Sacco et al., 2005; Segarra et al., 2011; Wing et al., 2011). For example, a longitudinal study with 26 smoker FEP patients and 15 non-smoker FEP patients, aged 15–65 years, suggested that attention and working memory improved in the smoker group to an extent similar to that of atypical antipsychotics, thus reflecting an effort to ameliorate the cognitive dysfunctions previous to treatment instauration (Segarra et al., 2011). Furthermore, nicotine may improve deficits in social cognition in patients with schizophrenia by activating the cortico-limbic circuits (Drusch et al., 2013; Mansvelder et al., 2009) involved in arousing and reinforcing behaviors related to social interactions.

On the contrary, several studies found no significant differences in the general neurocognitive (non-social) functioning between nicotine user and non-user patients with psychosis (Boggs et al., 2017; Hickling et al., 2018; Levander et al., 2007). A recent study with a sample of 304 tobacco-smoker and non-smoker FEP patients and 156 tobacco-smoker and non-smoker controls found no significance difference between smoker FEP patients and the non-smoker FEP group, suggesting that chronic exposure to tobacco is not associated with non-social cognitive performance in patients or in controls (Hickling et al., 2018). Another study suggested that, the attentional enhancement enjoyed by smoker patients with schizophrenia was not significantly different from the improvement on attentional tasks in a smoker control group (Hahn et al., 2013). Regarding social cognition, while one study did not find nicotine effects on social cognitive tasks (facial affect recognition) or on social competence (Drusch et al., 2013), another study found an improvement on social decision-making in non-smoker patients (Quisenarts et al., 2013). Additionally, it is suggested that

smoking is associated with cognitive decline and loss of gray matter tissue in the brain over time (Almeida et al., 2011), specifically in the hippocampus and dorsolateral prefrontal cortex (Schneider et al., 2014).

The purpose of this study is to examine the differences in the effect of tobacco use on non-social and social cognition in a large sample of patients with FEP and matched healthy controls. We hypothesized that tobacco using patients with FEP will have better non-social and social cognitive performance than non-tobacco using FEP patients. Also, we expected that the tobacco-smoker patient group would present worse non-social and social cognitive performance than the tobacco-smoker and non-smoker control groups.

## 2. Methods and materials

### 2.1. Participants

A sample of 335 patients with FEP (84.8% Caucasian, age =  $23.58 \pm 6$ , range 9–36) and 253 healthy controls (90.1% Caucasian, age =  $24.23 \pm 6.4$ , range 12–45) was enrolled in a multicenter, naturalistic, prospective and longitudinal study designed to evaluate clinical, neuropsychological, neuroimaging, biochemical, environmental and genetic variables in patients with FEP and healthy controls (The Phenotype-Genotype and Environmental Interaction. Application of a Predictive Model in First Episodes: PEPs study). The present report is based on clinical and cognitive data. Inclusion and exclusion criteria and further methodological aspects of this study were described elsewhere (Bernardo et al., 2013). Of 588 participants, 85 were excluded. Fig. 1 shows the sample flow chart and the tobacco group distribution.

The study was approved by the Board of Research and Ethics Committee of all participant centers and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Study groups were divided into 4 subgroups according to their pattern of tobacco use: 1) patients with FEP who use tobacco (PTU), 2) patients with FEP who do not use tobacco (PNTU), 3) healthy controls who use tobacco (CTU) and 4) healthy controls who do not use tobacco (CNTU).

### 2.2. Instruments

#### 2.2.1. Clinical assessments

Sociodemographic data such as age, sex, race, employment, marital status, years of education and parental socioeconomic status (SES), measured with the Hollingshead-Redlich Index of Social Position (Hollingshead and Redlich, 1958) was obtained from patients and controls.

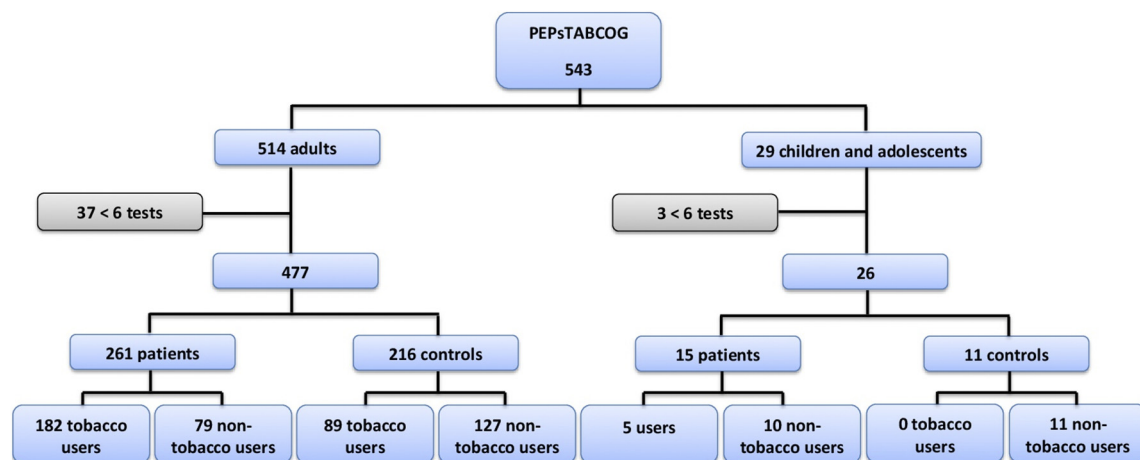


Fig. 1. Sample flow chart and tobacco group distribution.

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