

Differential effects of sex on substance use between first episode psychosis patients and healthy people

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Abstract

Background: Substance use in psychosis is an important field of study given that it can be a risk factor for the development of psychosis and can give rise to psychotic symptoms. Studies of substance use in first episode psychosis patients do not frequently assess non-pathological substance consumption among patients, but rather the prevalence of substance abuse or dependence disorders. Moreover, most of these studies do not address the effects of sex in sufficient depth, and the consumption of caffeine or tobacco, which are two of the most frequently used substances, is often not assessed.

Objectives: The aim of this study was to compare patterns and quantities of substance use between first episode psychosis patients and healthy controls and between men and women, and explore the potential interactive effects between group (patients or controls) and sex.

Methods: A total of 158 participants (82 first episode psychosis patients and 76 healthy controls) were included in the study. Both adults and adolescents were included in the study. Frequency and amount of use of caffeine, tobacco, alcohol, cannabis, cocaine, hallucinogens, stimulants, and opiates were gathered.

Results: A significant main effect of sex was found for the frequency of use of tobacco ($p = .050$). Main effects of group were found for the quantity of tobacco ($p < .001$) and cannabis ($p < .001$) consumed, as well as main effects of sex for the quantity of alcohol ($p = .003$) and cannabis ($p = .017$) consumed. There were also interaction effects between group and sex for the frequency of use of tobacco ($p = .005$) and cannabis ($p = .009$), and for the amount of cannabis consumed ($p = .049$). Qualitative differences between males and females regarding combined substance use are also reported.

Conclusions: Among patients, men used tobacco more frequently than women, but this sex difference was not the same for the control group, in which women smoked more often than men. Regarding cannabis, men smoked cannabis more frequently and in larger amounts than women, but only in the patients group, whereas no sex differences for cannabis were found for the controls. Main effects of group and sex for tobacco and alcohol, as well as the lack of differences for the frequency and amount of use of caffeine, are also commented. This is the first study to assess the different effects of sex on substance use in first episode psychosis patients and healthy controls.

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1. Introduction

Patients with a psychotic disorder are more prone to use substances, and in larger quantities, than healthy people. This has been well studied in patients with chronic schizophrenia [1–4]. Although the studies in first episode psychosis are less frequent, the available data seem to indicate that greater substance use than in the healthy population is already present before disease onset [5–10], and decreases during the first year of the disease [11–14].

The study of substance consumption in the context of a first episode of psychosis is important for various reasons. First of all, some studies have reported an association between tobacco [15]

and cannabis [16,17] consumption and risk of psychosis; also, caffeine [18,19], alcohol [20], and cocaine [21] can give rise to psychotic symptoms. Second, tobacco and cannabis consumption is also associated to an earlier onset of psychosis [15,16,22,23]. Third, some studies have associated substance use to an exacerbation of positive symptomatology in psychotic patients [24–26].

Most of the first episode psychosis studies on substance consumption analyze the prevalence of diagnosed substance abuse or dependence disorders [5,6,10–14,27–34]. According to these studies, the most abused illicit drug is cannabis, with up to a 66% of participants having had a cannabis use disorder at some time in their lives [33], followed by alcohol, with a lifetime alcohol use disorder prevalence of up to 43% [10]. Cocaine, hallucinogen, and amphetamine use disorders are much less prevalent, ranging from less than 1% to 5% in the studies that considered these substances [5,12,28–31].

Only a few studies have reported analyses of non-pathological substance use. The most widely consumed substances throughout the lives of participants were alcohol (ranging from 86% to 99% [10,35]), cannabis (from 60% to 80% [8–10,35]), MDMA (from 33% to 46% [8,10]), amphetamines (from 6% to 40% [9,10]), hallucinogens (from 29% to 42% [8–10]), cocaine (from 20% to 40% [9,10]), and opiates (from 12% to 16% [8,10]). Other studies have assessed substance use during the last year or half year [36–38], reporting lower prevalence rates compared to lifetime studies.

Despite the relevance of caffeine consumption and smoking, as noted above, there are no studies available reporting caffeine use in first episode psychosis patients. Regarding smoking, information about tobacco use is often not included. A meta-analysis of studies addressing tobacco use, by Myles et al. [39], concluded that 58.9% of first psychotic patients were smokers at the time of presenting for treatment, a rate significantly higher than that found in the general population [39]. Lifetime studies of tobacco smoking reported prevalences ranging from 60% to 77% [8,11,35].

The available information about sex and substance use in first episode psychosis patients is scarce, as most studies do not address this question or, at least, not in sufficient depth. The general conclusion is that, among first episode psychosis patients, men are more likely to consume substances than women [10,12,14,27–30,32,34], just as happens in the general population [40,41]. Sex is an important variable to consider in substance use studies for biological and psychosocial reasons [42]. Substance metabolism is different between men and women, as men have, in general, faster clearance rates [43]. The release of dopamine in the ventral striatum, implicated in substance reward and addiction [44,45], differs between men and women, with dopamine release being greater in men after amphetamine [44] and alcohol [45] intake. Both faster clearance rates and greater dopamine release in the ventral striatum suggest that men are more vulnerable than women to use or abuse substances. In spite of this, women seem to be more affected from substance use than men; they are more vulnerable to morphological brain changes induced by cannabis [46], and,

among patients with schizophrenia, those women that abuse substances have a more severe course of the illness than their non-abusing counterparts, including an earlier age of onset of the disease, more hospitalizations, and more severe symptoms [47]. In addition, the subjective experience derived from substance consumption can vary in function of sex, as has been reported for caffeine [48], nicotine [49,50], cannabis [51], alcohol [52], cocaine [53], and amphetamines [44]. While caffeine increased state anxiety in men but not in women [48], abstinence from nicotine seemed to increase anxiety and irritability more in women than in men [49], although women are supposed to be less sensitive to nicotine reward [50]. Moreover, nicotine administration appears to increase alcohol consumption in men and to decrease it in women [50]. With respect to cannabis, men are more sensitive to the effects of Δ^9 -tetrahydrocannabinol, but women report more dizziness when consuming it [51]. Women consuming alcohol seem to be more cognitively impaired than men; in addition, men appear to develop some tolerance to these negative effects, while women do not [52]. In people with cocaine dependence, women experienced more stress and nervousness than men when performing a stressing task [53]. Finally, men were more sensitive to the subjective effects of amphetamines, especially for those effects perceived as positive, while there were no differences between men and women regarding the perceived negative effects [44]. An important question that has not been addressed in previous studies of substance use is whether sex differences are different in patients and controls.

Investigating the differences in substance use that may exist between first episode psychosis patients and the general population, as well as between men and women, will allow us to increase the current knowledge regarding substance use and risk of psychosis, and whether there are sexual differences that may have an influence. Therefore, the aim of the present study is to compare patterns and quantities of substance use between patients and controls and between men and women. First, we will describe the pattern and amount of substance use of a sample of first episode psychosis patients and another sample of healthy controls. Next, we will study the effects of group (patient or control) and sex on frequency and amount of substance use; we will also explore the potential interactions between group and sex. Based on previous literature, we expect to find group and sex differences in, at least, the most commonly used substances, such as caffeine, tobacco, alcohol, and cannabis. In particular, we expect both first episode psychosis patients and men to use these substances more frequently and in larger quantities than controls and women, respectively. The analysis of the interaction effects between sex and patients or controls is mainly exploratory.

2. Methods

2.1. Participants

A total of 158 participants, 82 patients with a first episode of psychosis, and 76 healthy controls, were included in the study.

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