Cannabis use in patients with schizophrenia: motivation for use and relation to clinical variables
Dekker, N.

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CHAPTER 2.2

Substance use in a large sample of patients with schizophrenia or related disorders and co-morbid obsessive-compulsive symptoms


Submitted for publication.
Abstract

This study examined relationships between obsessive compulsive symptoms (OCS) and substance use in patients with a non-affective psychotic disorder. We found no significant differences in substance use between patients without OCS (n=777), patients with mild OCS (n=143), and patients with more severe OCS (n=85). There was a trend for patients with mild OCS to be more likely to use alcohol heavily and to have a lifetime diagnosis of cannabis use disorder.
Introduction

Obsessive compulsive symptoms (OCS) and obsessive compulsive disorder (OCD) are common in patients with schizophrenia and related disorders, with prevalence rates ranging from 7.8 to 55% for OCS (Berman et al. 1998), and a mean prevalence rate of 12.1% for OCD (Achim et al. 2009). This is considerably higher than the prevalence of OCS and OCD in the general population in the Netherlands, which is estimated at 5.8% and 0.9% respectively (De Bruijn et al. 2010). The higher prevalence of OCS/OCD in schizophrenia suggests a relation between the two disorders.

Prevalence rates of substance use disorders (including nicotine use) are higher in patients with schizophrenia compared to the general population (Mueser et al. 1990, Dixon et al. 1991, Buckley 1998, De Leon et al. 2002, McCreaddie 2002, Zammit et al. 2003, Roick et al. 2007). A co-morbid prevalence rate of 47.0% for abuse or dependence of substances has been found in schizophrenia patients in the Epidemiologic Catchment Area Study (Regier et al. 1990). In contrast, studies showed that the prevalence of substance use disorders is lower in OCD patients compared to the general population. For example, Denys et al. (2004) found a current prevalence of 4.3% of substance use disorders in 420 Dutch OCD patients, compared to 5.8% in the Dutch general population (Bijl et al. 1998). Further, Bejerot and Humble (1999) found that smoking rates were lower in OCD patients, compared to smoking rates in the general population (14.5% vs. 25.4%). In contrast, one study found that lifetime prevalence of substance use disorders was higher in patients with OCD (40.1%), compared to people without OCS (17.8%; De Bruijn et al. 2010). Overall, prevalence of substance use disorders in OCD seems to be lower than in schizophrenia. In sum, OCS occur relatively frequent in schizophrenia, schizophrenia patients show elevated rates of substance use as compared to the general population, but most studies in OCD patients show lower rates of nicotine and substance use compared to the general population. It would be interesting to know whether schizophrenia patients with OCS might have lower substance use rates than schizophrenia patients without OCS. So far, studies that compared smoking rates between schizophrenia patients with and without co-morbid OCS found no significant differences (Dome et al. 2006, Fawzi et al. 2007). Additionally, Poyurovsky and colleagues (Poyurovsky et al. 1999, Poyurovsky et al. 2008) found that substance abuse rates did not differ between schizophrenia patients with and without OCD. In comparison with OCD patients without co-morbid psychotic illness, prevalence of illicit substance use in patients with OCD and co-morbid psychotic illness was found to be higher (3.8% vs 15.4%; De Haan et al. 2009).

The aim of this study was to explore the relationship between OCS and substance use in patients with schizophrenia or related disorders, in a large cohort study of schizophrenia patients. We hypothesized that patients suffering from schizophrenia and co-morbid OCS had lower substance use rates than schizophrenia patients without OCS. Bejerot and Humble (1999) suggested that symptoms linked to OCD (e.g. fear of bodily harm and diseases) may keep subjects from using substances, and substance use may deteriorate OC symptoms by further overactivating the frontal cortex, thus withholding patients of substance use. Therefore, having OCS might be a protective factor for substance use in schizophrenia.
**Methods**

**Participants**
Patients took part in the Genetic Risk and Outcome of Psychosis (GROUP) study, a multi-site longitudinal cohort study in The Netherlands that focuses on vulnerability and resilience factors for variation in expression and course of non-affective psychotic disorders (for details, see Korver and Quee et al submitted for publication). All participants gave written informed consent after complete description of the study. The study was approved by the human subject review boards of all four Academic Centres.

**Measures**

**Clinical measures**
The Y-BOCS (Goodman et al 1989a, Goodman et al 1989b) was used to measure the severity of OCS over the previous week. For more details on the Y-BOCS and its reliability as used in schizophrenia patients, see Boyette et al (2010). Patients were categorized into three groups according to their level of OCS: one group without obsessions or compulsions, one group with OCS but Y-BOCS total scores between 1 and 15, and one group with total Y-BOCS scores that equaled or exceeded 16. The threshold of 16 was also used by two other studies on the relation between smoking and OCS in schizophrenia (Dome et al 2006, Fawzi et al 2007). Furthermore, this threshold is typically used for inclusion in drug trials, and typical scores for patients with OCD are in the 16 to 30 range (Blacker 2009).

**Substance use measures**
Use of nicotine, alcohol, cannabis and hard drugs (stimulants, opiates, hallucinogens, cocaine, and ecstasy) was assessed with the Composite International Diagnostic Interview (CIDI) (WHO 1994) section B, J and L. Nicotine use was defined as daily use of cigarettes for at least one month in the past 12 months. Alcohol use in the past year was defined as having consumed more than 12 alcoholic drinks in the past 12 months. Heavy alcohol use in the past year was defined as having consumed more than 21 alcoholic units per week. Diagnosis of cannabis- or hard drug abuse or dependency at present state (= in the past year) and lifetime was made according to DSM-IV (APA 1994). In order to have objective knowledge about recent use of cannabis, urinalysis for the presence of the tetrahydrocannabinol (THC), amphetamines and cocaine was carried out using immunoassays with a cut off of resp. 50 ng/ml, 1000 ng/ml, and 300 ng/ml. The total score of Obsessive Compulsive Drug Use Scale (OCDUS) was used as a measure for cannabis craving in the past week (Dekker et al, in press).

**Statistical Analysis**
The chi-square test for independence was used to determine whether two categorical variables were related to each other. A one-way between-groups analysis of variance (ANOVA) was conducted to explore differences between the three groups in one dependent variable. The Kruskal-Wallis test was conducted to explore differences between the three groups in one dependent variable, in case data were not normally distributed.
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Results

Of 1005 patients in whom the Y-BOCS was assessed, 777 patients did not have OCS, 143 patients had OCS with a total Y-BOCS score between 1 and 15 (mean 11.0, SD 2.5), and 85 patients had a total Y-BOCS score that equaled or exceeded 16 (mean 19.4, SD 3.6). DSM-IV diagnoses were: schizophrenia (66.2%), schizoaffective disorder (11.1%), schizophreniform disorder (5.5%), psychotic disorder NOS (10.2%), and other psychotic disorders (7.0%).

There were no significant differences between the three patients groups on substance use variables (table 1), except for a statistically different score for cannabis craving in the past week (Kruskal-Wallis test: $\chi^2 = 6.2$, $p = 0.045$), however post hoc comparisons with Mann–Whitney Tests did not survive Bonferroni correction. Further, there was a trend for the mild OCS group to be more likely to have a lifetime diagnosis of a cannabis use disorder use ($p = 0.08$) and to use alcohol heavily ($p = 0.07$), compared to the other groups (no OCS, or Y-BOCS $\geq 16$).

Table 1. Substance use variables in patients with a total Y-BOCS score 1-15, $\geq$ 16, and patients without OCS

<table>
<thead>
<tr>
<th></th>
<th>Without OCS</th>
<th>Y-BOCS 1-15 (n=143)</th>
<th>Y-BOCS $\geq$ 16 (n=85)</th>
<th>$x^2$ or $F$</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (S.D.)</td>
<td>28.0 (8.3)</td>
<td>27.4 (7.3)</td>
<td>25.8 (7.8)</td>
<td>2.9</td>
<td>2</td>
<td>0.053</td>
</tr>
<tr>
<td>Gender, male (%)</td>
<td>597 (76.8)</td>
<td>109 (76.2)</td>
<td>64 (75.3)</td>
<td>0.01</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>Nicotine use in past year, yes (%)</td>
<td>500 (65.6)</td>
<td>97 (68.8)</td>
<td>58 (69.0)</td>
<td>0.8</td>
<td>2</td>
<td>0.7</td>
</tr>
<tr>
<td>Cigarettes per day, mean (SD)</td>
<td>17.4 (8.6)</td>
<td>17.8 (8.7)</td>
<td>18.3 (10.0)</td>
<td>0.2</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>Alcohol use in past year, yes (%)</td>
<td>568 (74.8)</td>
<td>105 (73.9)</td>
<td>53 (63.1)</td>
<td>5.4</td>
<td>2</td>
<td>0.07</td>
</tr>
<tr>
<td>Heavy alcohol use past year, yes (%)</td>
<td>56 (7.2)</td>
<td>18 (12.6)</td>
<td>5 (5.9)</td>
<td>5.3</td>
<td>2</td>
<td>0.07</td>
</tr>
<tr>
<td>Alcoholic drinks per week, mean (S.D.)</td>
<td>8.8 (11.5)</td>
<td>11.1 (13.8)</td>
<td>9.9 (16.5)</td>
<td>3.4</td>
<td>2</td>
<td>0.2</td>
</tr>
<tr>
<td>DSM-IV cannabis use disorder present state, yes (%)</td>
<td>152 (19.9)</td>
<td>31 (21.7)</td>
<td>16 (19.0)</td>
<td>0.3</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>DSM-IV cannabis use disorder lifetime, yes (%)</td>
<td>292 (38.3)</td>
<td>69 (48.3)</td>
<td>32 (38.1)</td>
<td>5.1</td>
<td>2</td>
<td>0.08</td>
</tr>
<tr>
<td>DSM-IV hard drug use disorder present state, yes (%)</td>
<td>44 (5.8)</td>
<td>13 (9.1)</td>
<td>4 (4.8)</td>
<td>2.6</td>
<td>2</td>
<td>0.3</td>
</tr>
<tr>
<td>DSM-IV hard drug use disorder lifetime, yes (%)</td>
<td>136 (17.8)</td>
<td>32 (22.4)</td>
<td>16 (19.0)</td>
<td>1.7</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>Urine test for THC, positive (%)</td>
<td>116 (16.9)</td>
<td>26 (19.9)</td>
<td>8 (11.8)</td>
<td>2.1</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>Urine test for cocaine, positive (%)</td>
<td>9 (1.3)</td>
<td>4 (3.0)</td>
<td>0 (0)</td>
<td>3.4</td>
<td>2</td>
<td>0.2</td>
</tr>
<tr>
<td>Urine test for amphetamines, positive (%)</td>
<td>6 (0.9)</td>
<td>2 (1.6)</td>
<td>0 (0)</td>
<td>1.2</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>Craving for cannabis (OCDUS-CAN score), mean (SD)</td>
<td>1.56 (0.66)</td>
<td>1.73 (0.77)</td>
<td>1.68 (0.74)</td>
<td>6.2</td>
<td>2</td>
<td>0.045*</td>
</tr>
</tbody>
</table>

* $p < 0.05$

Percent in the columns and means are sometimes based on less than n presented in the top row, because of missing data; CIDI data of 19 patients (1.9%) were missing, urine data of 118 patients (11.7%) were missing. Craving for cannabis data were available for 439 patients from the group without OCS, 78 patients from the Y-BOCS 1-15 group, and 48 patients from the Y-BOCS $\geq 16$ group.
Discussion

We found no differences in substance use between patients with mild OCS (Y-BOCS score 1-15), patients with more severe OCS (Y-BOCS score ≥ 16) and patients without OCS. Patients with more severe OCS were less likely to use alcohol in the last 12 months. However, this difference was small and non-significant. Taken together, our results suggest co-morbid OCS is not a protective factor against the use of nicotine and other substances in patients suffering from non-affective psychotic illness.

There was a trend for patients with mild OCS to be more likely to use alcohol heavily and to have a lifetime diagnosis of cannabis use disorder. Because of the small differences, it is questionable whether this non-significant finding is clinically relevant. However, speculative explanations for our findings might be the possibility of mild OCS mediating the tendency to use cannabis and alcohol as self-medication (relaxation), or cannabis and alcohol use mediating mild OCS.

In concordance with our results, previous studies did not find differences in prevalence rates of nicotine and substance use in schizophrenia patients with or without OCS (Poyurovsky et al 1999, Dome et al 2006, Fawzi et al 2007, Puyorovsky et al 2008). Our large study sample and more detailed comparison of substance use rates strongly adds to the evidence that schizophrenia patients with OCS do not differ in prevalence of substance use compared to patients without OCS.

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References


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Korver N, Quee PJ (Korver and Quee are combined first authors), Boos H, Simons C, G.R.O.U.P. authors: Genetic Risk and Outcome of Psychosis (GROUP), a multi site longitudinal cohort study focused on gene-environment interaction: Objectives, Sample Characteristics, Recruitment, Assessment Methods and validity of diagnostic categories. Submitted for publication.


