The Clinical Impact of Substance Use in Schizophrenia: A Study in an Irish Population.

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Clinical Points:

- Substance use is common among people with schizophrenia. 48% of participants in this study reported a history of substance use and/or alcohol misuse.
- Cannabis and alcohol were the most commonly used substances among schizophrenics.
- This study found no difference in the symptom profile between substance users and non-users.
- Cannabis use is associated with an earlier age at onset of illness and has an association to schizophrenia which is stronger than that of other substances. Cannabis use may, therefore, be a risk factor for the onset of schizophrenia.

ABSTRACT

Background: Substance use may be a risk factor for the onset of schizophrenia. However to date the impact of substance use in schizophrenia has not been fully explored in an Irish population. In this study we examine the clinical impact of substance use in schizophrenia within an Irish population.

Methods: The study sample consisted of 159 participants with a diagnosis of schizophrenia who were recruited to the ongoing Resource for Psychoses Genomics Ireland Study. All participants were interviewed with the Structured Clinical Interview for Diagnostic Statistical Manual IV to confirm diagnosis. Information on age at onset, illness course and substance use was collected at this interview and from case note review.

Results: In total, 48% of the participants reported lifetime substance use (including alcohol misuse). Cannabis was the most commonly used substance (82% of all users). Cannabis had an independent effect on the age at onset of psychosis, after adjusting for gender and use of substances other than cannabis. There was a trend towards more positive psychotic symptoms in substance users but it was not statistically significant.

Conclusions: Our results confirm the high lifetime prevalence of substance use in schizophrenia. In addition, results show an earlier age at onset of illness in cannabis users. This provides further evidence for the association between cannabis use and onset of schizophrenia, although causality cannot be assumed.

INTRODUCTION

Substance use in people with schizophrenia is up to five times more common than in the general population and is associated with a poorer clinical outcome (1,2). Substance use has also been implicated as a risk factor for the onset of schizophrenia (3). In a 2006 meta-analysis Talamo et al. showed that those with co-morbid substance use in schizophrenia have greater severity of positive symptoms and fewer "negative" symptoms than those without substance use (4). Previous studies in an urban, Irish population have estimated the prevalence of substance use among in-patients with schizophrenia and assessed its influence on depressive symptoms and suicidal ideation (5).

The aims of this study are to: 1) assess the lifetime prevalence of substance use among people with schizophrenia, 2) examine the association between substance use and the age at onset of schizophrenia, 3) examine the relationship between substance use and the severity of positive and "negative" symptoms of schizophrenia and 4) assess the association between substance use and global severity of illness.

METHODS

Recruitment of Participants

Participants were recruited to the ongoing Resource for Psychoses Genomics Ireland (RPGI) study. RPGI is a collaborative study between Trinity College Dublin; National University of Ireland, Dublin; National University of Ireland, Cork; Queen's University, Belfast; and The Royal College of Surgeons, Ireland. Participants were recruited through psychiatric services in the region of each university's research team, through lay support organisations and through self-referral from information provided in local and national media. The RPGI inclusion criteria required that participants i) be over 16 years of age, ii) have Irish born grandparents, iii) have a Diagnostic Statistical Manual IV (DSM-IV) diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder or bipolar affective disorder with psychosis and iv) be able to provide written informed consent. The RPGI exclusion criteria required that participants not have i) a substance-induced psychosis or medical disorder responsible for their psychosis or, ii) have a learning disability. All participants were assessed using the Structured Clinical Interview for DSM-IV (SCID). Those participants with a diagnosis of schizophrenia and who were entered onto the centralised electronic database (BCClin) before the arbitrary cut-off date July 20th, 2007,

were included in this study. This was in order to facilitate timely data analysis.

Assessment of Participants

Basic demographic data were collected directly from participants and from their case notes. SCID was used to elicit information on lifetime substance use and age at onset of illness. Mental state was assessed using the Scale for Assessment of Positive Symptoms (SAPS) and the Scale for Assessment of "Negative Symptoms" (SANS) (6). Scores for three symptom-derived syndromes of schizophrenia were calculated for each participant by adding together the global sub-scale scores pertaining to each factor and dividing by the maximum possible score to give a value between 0 and 1 for each factor. The syndromes were categorised as follows: positive syndrome (SAPS hallucinations and delusions), disorganisation syndrome (SAPS bizarre behaviour and positive formal thought disorder) and negative syndrome (all SANS sub-scales). Global severity of illness was assessed using the Global Assessment of Functioning Scale (GAF) (7). The GAF is a numeric scale (0 to 100) which rates the combined social, occupational and psychological functioning of an adult.

Statistical Analysis

The data were analysed using the Statistical Package for the Social Sciences, version 14 for Windows. In a comparison of participants with and without a history of substance use, the t-test was employed for continuous data and the x^2 test was used for categorical data. Age at onset of psychosis was used as the outcome variable in a linear regression model, and potentially influential variables (relating to gender and substance use) were entered as independent variables.

RESULTS

The Prevalence of Substance Use Among People with Schizophrenia

Of the 159 participants with schizophrenia 16.4% of participants reported substance use within the month previous to the interview and 47.8% reported substance use at some point during their lifetime. This lifetime figure of substance use is similar to previous estimates in an Irish population (5). From a list of substances including alcohol, ectasy, cocaine and heroin, cannabis was the most commonly used drug (39%) while aerosols was the least commonly used drug (0.6%). The 159 participant sample was divided into two sub-groups, one group reporting a history of substance use (and/or alcohol misuse) (N=76), and another group made up of those with no such history (N=83). Thirty four percent of the group reporting a history of substance use (and/or alcohol misuse) had abused a substance in the month previous to the interview.

Poly-substance use was a significant characteristic in the user group. Fifty nine percent of all substance users did so in tandem with at least one other substance while 35.5% of users used three or more substances (see Fig. 1.). Two thirds of cannabis users also used at least one other substance (data not shown).

	Total sample (N=159)	Substance users (N=76)
Time period		
In previous month	16.4	34.2
Lifetime	47.8	100
Substance used		
Cannabis	39.0	81.6
Alcohol	21.4	44.7
Ecstasy	13.8	28.9
Cocaine	11.9	25.0
Lysergic acid diethylamide	11.3	23.7
Amphetamine	6.9	14.5
Mushrooms	5.7	11.8
Heroin	2.5	5.3
Benzodiazepines	1.3	2.6
Ketamine	1.3	2.6
Aerosols	0.6	1.3

Table 1. Characterisation of substance use in schizophrenia. This table summarises the different substances used by this population of people with schizophrenia. The use of each substance is expressed, both as a percentage of the total sample (N=159), and of the subgroup of substance users (N=76). values presented arein percentages

The Association Between Substance Use and the Age at Onset of Illness

The demographic characteristics and GAF scores of the participants with or without a history of substance use are shown in Table 2. A younger age at interview and a younger age at onset of illness were both associated with a history of substance use.

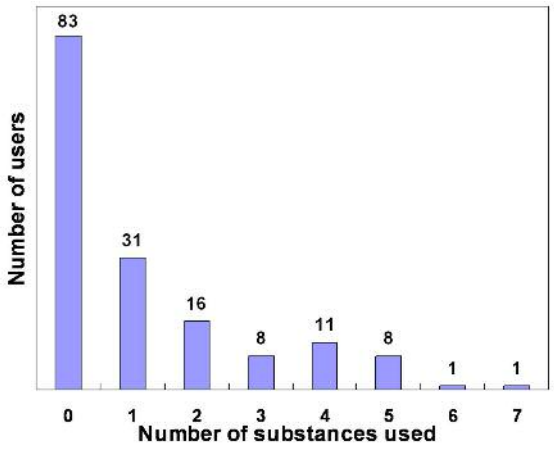

Fig. 1. Polysubstance use by a population of people with schizophrenia . This figure looks at the number of substances each of the 159 participants of this trial were using.

Characteristics	No lifetime history of substance use (N=83)	Any lifetime history of substance use (N=76)	Statistical Analysis t	x^2	p
Gender					
Male	61	84			
Female	39	16		9.16	0.002
Age at interview, years	45.9 ± 12.1	36.4 ± 11.7	-4.95		<0.001
Age at onset, years	25.0± 8.7	22.6 ± 7.6	-1.85		0.066
G.A.F. scores	58.0 ± 18.4	62.2 ± 13.9	1.59		0.114

Table 2. Clinical characteristics of people with schizophrenia, both with and without a lifetime history of substance use. This table summarises certain characteristics such as gender, age at interview, age at onset of illness, and G.A.F scores that existed in the two groups; i.e. those with any lifetime history of substance use and those with no lifetime history of substance use. The mean ± SD values are given for age, age at onset and G.A.F while the gender is expressed as a percentage.

	Mean difference in age at onset of illness (years)	Confidence intervals (years)		p
Female	-2.1	-0.81	- 3.4	0.156
Use of substances other than cannabis	+3.9	-0.63	- 7.2	0.091
Cannabis use	-4.3	-2.0	- 6.7	0.001

Table 3. Mean age difference at onset of illness by gender, non-cannabis-drug-use, and cannabis use. Gender, non-cannabis-drug-use, and cannabis use were entered as independent variables in a linear regression analysis, with age at onset of illness as the outcome variable. Only cannabis use proved significant after the variances of the other independent variables were controlled for.

Linear regression analysis was performed with age at onset of illness as the outcome variable and the following independent variables: gender, cannabis use and use of substances other than cannabis (see Table 3.). When the variances of all the independent variables were controlled for, the use of substances other than cannabis and gender were not significant in relation to age at onset of illness. Cannabis use was significantly associated with a younger age at onset of illness after adjusting for gender and substance use other than cannabis. A comparison of the means revealed that cannabis users had a younger age at onset of illness by a mean value of 4.3 years (95% CI 2.0 to 6.7, p<0.001) (see Table 3).

The Association Between Substance Use and the Type of Symptoms

The clinical assessments that were administered to the participants with and without a history of substance use are summarised in Table 4. No significant differences were found between the two groups with regard to positive and "negative" syndromes. A separate analysis comparing those with a history of cannabis use to those without revealed that those who reported cannabis use experienced more types of positive symptoms than those who did not (mean difference 1.7, t=3.5, p=0.001).

The Relationship of Substance Use with Global Severity of Illness

GAF scores are listed in Table 2. No significant difference was found between those with a history of substance use and those without such a history.

DISCUSSION

The association between substance use and schizophrenia is well documented (1,2). The aims of this study were to assess the association between substance use and the nature and severity of symptoms in schizophrenia, the age at onset of illness and the global severity of illness in an Irish population.

A significant result in this study was that a younger age at onset of psychosis was found in those participants who had reported a history of substance use. The most commonly used drug was cannabis. Participants with a history of cannabis use had a significantly younger age at onset after controlling for other possible confounding factors. This means that those participants with a history of cannabis use had an earlier age at onset of psychosis than other participants who had not used cannabis but who shared the same profile with regard to the other variables. A possible explanation for this pattern is that substance use precipitates the illness, although it remains unclear whether or not this effect is confined to those with a predisposition to psychosis (8). Another possible explanation could be that the symptoms of schizophrenia lead to a tendency towards substance use (9).

Previous studies have addressed the temporal relationship between substance use and onset of psychosis but not the relationship between substance use and the schizophrenia prodrome (10). The data did not allow us to determine whether or not the substance use preceded the onset of illness. Also, the amount of multiple-substance-use limited the analysis of the unique contribution of any particular substance. However, the results of the linear regression analysis suggest that cannabis is more closely linked with

Syndromes assessed	No lifetime history of substance use (N=83)		Any lifetime history of substance use (N=76)		t	p
Positive syndrome:	0.41	± 0.26	0.44	± 0.26	0.59	0.56
Disorganisation syndrome:	0.36	± 0.17	0.31	± 0.15	-1.94	0.054
Negative syndrome:	0.56	± 0.22	0.53	± 0.18	-0.1	0.32
Total variety of lifetime positive symptoms (number of different symptoms)	5.16	± 3.53	6.51	± 2.97	2.61	0.01

Table 4. Clinical assessments for participants with and without a history of substance use. This table summarises the difference in syndrome scores between the two groups. The three syndromes were: positive syndrome, disorganisation syndrome and negative syndrome. The total variety of lifetime positive symptoms is also presented for both groups. The syndromes were measured using the symptom-based syndrome score (0-1). The mean ± SD are given for each score.

earlier onset of illness than other drugs. This finding is in line with the results of other studies (11).

There were no significant differences in symptom scores between substance users and non-users. This correlates with a previous study in an Irish population which did not find an association between substance use and depressive symptoms (5). It has been reported elsewhere that substance use is associated with more positive symptoms (12). A weakness of this study is that the positive symptoms were only graded for their severity during the previous month, and not over the duration of the illness. However, the total variety of lifetime positive symptoms was increased in substance users, with cannabis users in particular experiencing almost two more types of symptom than non cannabis-users.

No association was found between global rating of functioning and substance use. It has been reported elsewhere that people with schizophrenia and co-morbid substance use have a more severe form of illness (4).

CONCLUSIONS

In conclusion this study demonstrates the earlier age at onset of illness in substance users and in cannabis users in particular. The results confirm the high lifetime prevalence of substance use in schizophrenia. Although cannabis and alcohol were the most commonly used substances, most of the participants reported using multiple substances. Substance use tends to predict a poorer clinical outcome and therefore it is important to ask patients about their substance use and consider appropriate psychosocial intervention in people with schizophrenia. Also, clinicians should advocate abstinence from substance use (including cannabis) as it may be a risk factor for the onset of schizophrenia.

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