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Cannabis use and dimensions of psychosis in a nonclinical population of female subjects

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Abstract

Objective: The aim of the present study was to explore the pattern of associations between cannabis use and dimensions of psychosis in a nonclinical population of female subjects. *Method*: The Community Assessment of Psychic Experiences (CAPE), a 42-item self-report questionnaire that evolved from the Peters et al. Delusions Inventory [Schizophr. Bull. 25 (1999) 553], was used to measure dimensions of psychosis in a sample of undergraduate female students ($n = 571$). The participants were also asked to complete a self-report questionnaire collecting information on substance use. *Results*: Three correlated dimensions of positive, negative and depressive experiences were identified using principal components factor analysis. Frequency of cannabis use was independently associated with the intensity of both positive and negative psychotic experiences. No significant association was found between cannabis use and the depressive dimension, or between alcohol use and any of the three positive, negative and depressive dimensions. *Conclusion*: This cross-sectional study supports the hypothesis that exposure to cannabis may induce the emergence of positive psychotic symptoms in subjects without clinical psychosis, and additionally suggests that cannabis users exhibit greater levels of negative symptoms. Prospective studies are required to explore the direction of causality and the impact of cannabis on the course of psychotic experiences in subjects from the general population.

Keywords: Psychosis proneness; Positive dimension; Negative dimension; Cannabis

1. Introduction

The existence of an experiential continuum between subjects from the general population and clinical cases of psychosis is suggested by epidemiological findings showing that delusions and hallucinations are experienced by a relatively large percentage of subjects without clinical psychosis (Eaton et al., 1991; Tien, 1991; Verdoux et al., 1998a; van Os et al., 2000; Poulton et al., 2000). Further evidence supporting the continuum hypothesis is drawn from studies reporting that the risk factors associated with nonclinical delusional or hallucinatory experiences are similar to those associated with clinical cases of psychotic disorders. For example, positive psychotic experiences are more frequent in nonclinical subjects of lower age (Venables

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and Bailes, 1994; Verdoux et al., 1998b; Peters et al., 1999), with single marital status, lower level of education, lower quality of life (van Os et al., 2000) and in urban populations (van Os et al., 2001).

The approach based upon the exploration of risk factors for psychosis in nonclinical settings has also been applied to the study of schizotypal signs or attenuated psychotic symptoms. Although the number of factors best describing the structure of schizotypal signs in nonclinical samples is still a matter of debate, virtually all studies agree on the existence of separate positive and negative dimensions of schizotypy (Raine et al., 1994; Venables and Rector, 2000; Vollema and van den Bosch, 1995). Some studies have investigated the links between these two dimensions of schizotypy and risk factors for psychosis, such as gender (Kremen et al., 1998; Raine, 1992; Venables and Bailes, 1994), developmental abnormalities (Rosa et al., 2000) and cognitive functioning (Diforio et al., 2000). These studies have also shown that the patterns of associations between these risk factors and dimensions of schizotypy parallel those observed in clinical samples.

It has recently been reported that current cannabis use may be associated with positive schizotypal signs in nonclinical subjects, but not with negative ones (Skosnik et al., 2001). This issue is of clinical importance, since the nature of the link between cannabis use and psychosis remains to be clarified (Hall and Solowij, 1998; Johns, 2001; McGuire et al., 1994). Findings from retrospective (Linszen et al., 1994; Hambrecht and Hafner, 1996; Hambrecht and Hafner, 2000) and prospective (Andreasson et al., 1987) studies examining the temporal relationship between cannabis use and psychosis suggest that cannabis use may be a risk factor for the onset of psychosis. Indirect evidence supporting this hypothesis is also drawn from studies showing that subjects with a dual diagnosis have an earlier age at onset of psychosis than subjects with no history of substance use (DeLisi et al., 1991; Gearon and Bellack, 2000; Salyers and Mueser, 2001). However, no association between age at onset and psychosis was found in other studies (Cantor-Graae et al., 2001), and a recent prospective study carried out in subjects identified as being at risk of developing psychosis did not confirm that cannabis use was associated with an increased risk of transition to psychosis (Phillips et al., 2001).

Most studies conducted in clinical settings reported that subjects with psychosis using cannabis are more likely to present with prominent positive symptoms and fewer negative symptoms than nonusers (Allebeck et al., 1993; Kirkpatrick et al., 1996; Mathers and Ghodse, 1992; Peralta and Cuesta, 1992; Salyers and Mueser, 2001). However, these findings were not replicated by other studies (McGuire et al., 1994). The possible lower severity of negative symptoms in cannabis users has been interpreted as supporting the hypothesis that subjects with psychosis may use cannabis to self-medicate negative symptoms (Peralta and Cuesta, 1992; Skosnik et al., 2001). However, the interpretation of such findings is not straightforward, since subjects with a dual diagnosis may also be characterised by a better premorbid adjustment and a less severe form of illness (Arndt et al., 1992; Dixon et al., 1991; Mueser et al., 1990; Salyers and Mueser, 2001). The association between fewer negative symptoms and cannabis use found in clinical settings may be explained at least in part by the fact that the level of social competence required to obtain illicit drugs is impaired in subjects with prominent negative symptoms. Thus, the lower frequency of cannabis use in those subjects might be a consequence of negative symptoms and poor premorbid adjustment. It is therefore of interest to explore this association in a nonclinical setting, where causal associations between risk factors and symptoms are not obscured by a number of uncontrolled confounding factors linked to the clinical status of the subjects.

The findings by Skosnik et al. (2001) were obtained in a small sample of subjects, and the associations with dimensions of psychosis were explored by comparing scores on each of the nine subscales of the Schizotypal Personality Questionnaire (SPQ) (Raine, 1991). These findings thus remain to be replicated in a larger sample using more stringent measures of psychosis dimensions. Using the Community Assessment of Psychic Experiences (CAPE), a self-rating questionnaire measuring a broad range of psychotic experiences derived from the Peters et al. Delusions Inventory (PDI-21) (Peters et al., 1999), we recently demonstrated the existence of a three-factor model of separate depressive, positive and negative dimensions of psychosis in a nonclinical sample of 932 young males conscripts (Stefanis et al., in press).

The aim of the present study was to explore the pattern of associations between cannabis use and dimensions of psychosis measured with the CAPE in a nonclinical population.

2. Methods

2.1. Assessment of substance use and psychopathology

Undergraduate university students from the University of Bordeaux were invited to participate in a study on daily life behaviour and experiences. All subjects gave written informed consent to participate in the investigation. A standardized self-report questionnaire was used to collect information on demographic characteristics, substance use and psychotic experiences. The questionnaire included questions exploring use of alcohol and of illicit substances (cannabis, ecstasy, amphetamines, heroine, cocaine, LSD, solvents, poppers), with a list of the most frequently used slang expressions for each illicit substance. The subjects were asked to specify the frequency of use of each substance over the last month ranging from 1 (never in the past 30 days) to 7 (several times a day).

The Community Assessment of Psychic Experiences (CAPE) (Stefanis et al., in press), a 42-item (final version) self-report questionnaire derived from the Peters et al. Delusions Inventory (PDI-21) (Peters et al., 1999), was used to measure dimensions of psychosis. In view of our previous studies using the PDI-21 in nonclinical populations (Verdoux et al., 1998a, 1999; van Os et al., 1999), we excluded or reformulated ambiguous items and added others exploring hallucinations. A total of 20 items of positive psychotic experiences was used, to which were added 14 items exploring negative experiences derived from the SENS (Selten et al., 1998), and 8 cognitive depressive experiences discriminating between depressive and negative symptoms (Kibel et al., 1993). Each item explores the frequency of the experience on a four-point scale of ''never'', ''sometimes'', ''often'' and ''nearly always''.

2.2. Statistical analyses

Statistical analyses were conducted using STATA software, version seven (StataCorp, 2001). Dimensions of psychosis were identified using principal components factor analysis on the correlation matrix of the 42 items of the CAPE. Since previous studies have demonstrated that psychotic symptom dimensions are correlated in subjects with psychosis (Peralta and Cuesta, 1998) as well as in nonclinical populations (Stefanis et al., in press), we used non-orthogonal (promax) rotation to define correlated dimensions of psychosis. The number of factors retained for rotation was a priori limited to three factors, in accordance with a previous study showing that a three-factor model of separate depressive, positive and negative dimensions was the best model to describe psychosis dimensions measured using the CAPE (Stefanis et al., in press). Regression factor scores were obtained for each subject. Correlations between factor scores were assessed using Pearson's correlation. We also explored correlations between age and psychosis dimensions since previous studies have reported associations between age and psychosis proneness (Peters et al., 1999; Venables and Bailes, 1994; Verdoux et al., 1998b). Multiple regression analyses, yielding regression coefficients (β) and 95% confidence intervals (95% CI), were subsequently computed to examine and adjust associations between factor scores and substance use. Cannabis use was categorized according to the frequency of use as ''no use over the last month'', ''once a month to once a week'' and ''more than once a week''. For each psychosis dimension, we tested the hypothesis that there would be a linear trend in the association between cannabis use and psychosis dimension score, i.e., the more frequent the use of cannabis, the higher the score on that dimension. To take into account the correlations between the dimensions, we tested whether there were independent effects of cannabis use on the three dimensions of psychosis by estimating the effect of cannabis on each dimension while adjusting for the two other dimensions.

To assess the specificity of any association between cannabis use and psychosis dimensions, we also used the same method to explore the associations between psychosis dimensions and alcohol use. Since very few subjects have reported other substance use (ecstasy: $n=7$; amphetamine: $n=6$; cocaine: $n=2$; heroine: $n=1$; LDS: $n=1$; solvents: $n=2$), we could not explore their effect.

3. Results

3.1. Subjects

Of the 685 subjects included in the survey, 632 (92.3%) fully completed the self-report screening questionnaire. There were no large or significant differences with regard to demographic variables between the subjects with complete and incomplete self-report questionnaires. Owing to the skewed gender distribution in the sample (61 males, 571 females), only female subjects were considered in the present study to increase sample homogeneity. The subjects had a mean age of 19.8 years (SD = 2.9; range = 18–51) and most (n = 549, 96.5%) were single.

Table 1
Factorial analysis of the CAPE-42 items

Variance explained	Depressive factor 20.1%	Positive factor 7.1%	Negative factor 4.1%
Sad	**0.70**	−0.01	0.05
Double meaning	0.33	0.33	−0.01
Lack of enthusiasm	**0.43**	−0.18	0.38
Not talkative	0.23	−0.09	**0.43**
Messages TV	−0.02	**0.44**	0.08
False appearance	0.28	0.27	−0.04
Being persecuted	0.31	**0.43**	−0.21
No emotion	−0.10	0.16	**0.53**
Pessimism	**0.72**	−0.06	−0.05
Conspiracy	0.23	**0.43**	0.05
Being important	−0.26	0.31	0.38
No future	**0.57**	−0.03	0.18
Being special	−0.20	**0.48**	0.29
Not worth living	**0.53**	0.12	0.14
Telepathy	−0.15	**0.50**	0.04
No interest in others	0.11	0.12	**0.46**
Influence by devices	0.07	0.36	−0.17
No motivation	**0.42**	−0.09	**0.41**
Frequently cry	**0.50**	0.11	0.05
Voodoo	−0.06	0.50	0.13
No energy	**0.46**	−0.12	0.33
Odd looks	0.23	0.31	0.18
Empty mind	0.30	0.10	0.23
Thought withdrawal	0.16	0.39	−0.09
Lack of activity	0.17	0.05	**0.46**
Thought insertion	0.20	**0.50**	−0.12
Blunted feelings	−0.03	−0.02	**0.51**
Thought broadcasting	0.03	**0.57**	−0.02
Lack of spontaneity	0.13	−0.08	**0.53**
Thought echo	−0.05	**0.55**	0.04
External control	0.13	**0.49**	0.01
Blunted emotions	0.28	0.21	0.15
Verbal hallucinations	−0.05	**0.58**	−0.02
Voices conversing	−0.11	**0.42**	0.01
Lack of hygiene	0.05	−0.02	**0.49**
Unable to terminate	0.28	0.06	**0.40**
Lack of hobby	0.19	−0.01	**0.53**
Guilty	**0.56**	0.19	−0.06
Failure	**0.72**	−0.05	0.01
Feeling tense	**0.61**	0.07	0.01
Capgras	−0.24	**0.41**	0.14
Visual hallucinations	−0.04	**0.59**	0.01

Table 2
Pattern of psychoactive substance use

Substance use over the last month	N (%)
Cannabis	
No	400 (70.1%)
Once a month	44 (7.7%)
Two to three times a month	42 (7.4%)
Once a week	25 (4.4%)
Two to three times a week	27 (4.7%)
Once a day	17 (3%)
Several times a day	16 (2.8%)
Alcohol	
No	59 (10.3%)
Once a month	135 (23.6%)
Two to three times a month	181 (31.7%)
Once a week	123 (21.5%)
Two to three times a week	54 (9.5%)
Once a day	16 (2.8%)
Several times a day	3 (0.5%)

3.2. Psychosis dimensions

Items exploring depressive experiences were loaded especially (>0.4) on the first factor, while those exploring delusional ideas and hallucinations were loaded on the second and items exploring negative symptoms on the third (Table 1). These three factors are hereafter referred to as "depressive, "positive" and "negative" dimensions, respectively. Significant positive correlations were found between the three dimensions (positive and negative $r = 0.27$, $p = 0.0001$; positive and depressive $r = 0.34$, $p = 0.001$; negative and depressive $r = 0.38$, $p = 0.001$), and a weak negative correlation was found between age and the positive dimension ($r = -0.11$, $p = 0.01$).

3.3. Associations between substance use and dimensions of psychosis

The pattern of cannabis and alcohol use is presented in Table 2. Significant associations were found

Table 3
Associations between CAPE-42 factor scores and substance use

	Depressive factor	Positive factor	Negative factor
Cannabis use[a]		β (95% CI) adjusted for age	
Once a month to once a week	0.21 (0; 0.42) $p=0.05$	0.30 (−0.09; 0.51) $p=0.005$	0.24 (0.03; 0.45) $p=0.02$
More than once a week	0.11 (−0.16; 0.38) $p=0.43$	0.28 (0.01; 0.54) $p=0.04$	0.56 (0.29; 0.83) $p=0.0001$
Linear trend[b]	*0.09 (−0.02; 0.22) p= 0.13*	*0.18 (0.06; 0.3) p= 0.004*	*0.27 (0.15; 0.39) p= 0.0001*
Alcohol use[a]		β (95% CI) adjusted for age	
Once a month to once a week	0.07 (−0.20; 0.34) $p=0.61$	−0.11 (−0.38; 0.15) $p=0.41$	−0.07 (−0.34; 0.20) $p=0.59$
More than once a week	0.21 (−0.13; 0.56) $p=0.22$	0.23 (−0.11; 0.57) $p=0.19$	0.22 (−0.12; 0.57) $p=0.20$
Linear trend[b]	*0.11 (−0.06; 0.28) p= 0.21*	*0.13 (−0.04; 0.30) p= 0.13*	*0.13 (−0.5; 0.30) p= 0.15*

[a] The baseline condition is "no use over the last month".
[b] β linear trend: summary increase in dependent variable with one unit change in cannabis frequency.

between cannabis use and positive and negative dimension scores, i.e., increased levels of cannabis use were associated with higher positive and negative dimension scores (Table 3). There was no association between cannabis use and depressive experiences, and there was no significant linear trend in any of the associations between alcohol use and psychosis dimension scores. Accordingly, the effect sizes of the associations between psychosis dimension scores and cannabis use changed by only a tiny amount after further adjustment for alcohol use (positive dimension and cannabis use: β linear trend = 0.17, 95% CI 0.04; 0.29, $p=0.01$; negative dimension and cannabis use: β linear trend = 0.27, 95% CI 0.14; 0.39, $p=0.0001$).

The effect sizes of the associations between cannabis use and positive and negative dimensions were slightly reduced after adjustment for the other two dimension scores, but significant linear trends were still found between frequency of cannabis use and higher positive (β linear trend = 0.11, 95% CI 0; 0.22, $p=0.05$) and higher negative (β linear trend = 0.21, 95% CI 0.10; 0.32, $p=0.0001$) dimension scores. These findings indicate that positive and negative dimensions were independently associated with cannabis use.

4. Discussion

In this study carried out in a sample of female students, frequency of cannabis use was independently associated with intensity of positive and negative psychotic experiences. No significant association was found between cannabis use and the depressive dimension, or between alcohol use and the three positive, negative and depressive dimensions.

4.1. Methodological limitations

Information on psychotic experiences and substance use was collected using self-report data. Thus, we cannot exclude overreporting due to misinterpretation of some items exploring psychotic experiences (Eaton et al., 1991; Jablensky, 1995; Verdoux et al., 1998a), or underreporting due to stigmatisation of illicit substance use. Using data collected in a subgroup of subjects, we previously showed that there was a good agreement between high frequency of cannabis use (more than once a week) identified by the self-report questionnaire and the diagnosis of cannabis abuse or dependence identified by a structured diagnostic interview, as well as between high CAPE positive scores and level of psychotic symptoms identified by a structured diagnostic interview (Verdoux et al., submitted for publication). Furthermore, misclassification, if random with regard to exposure and outcome, would have attenuated rather than increased the strength of the associations between cannabis and dimensions of psychosis.

Although students may differ with regard to several characteristics from subjects in the general population, such as the prevalence of substance use disorders, it is unlikely that these differences in themselves modified the direction and the strength of the associations between cannabis use and dimensions of psychosis. However, since these associations were obtained in a

sample of female subjects, they may not necessarily extrapolate to men.

The dimensional solution of psychosis found in the present sample of female subjects is similar to that previously reported in an independent sample of male subjects (Stefanis et al., in press), giving further support to the existence of three independent and correlated dimensions of positive, negative and depressive experiences in the general population, irrespective of gender. The CAPE questionnaire used in these two studies does not include self-report assessment of other dimensions of psychosis identified in previous studies based upon schizotypal questionnaires, such as the disorganisation dimension (Raine et al., 1994; Venables and Rector, 2000; Vollema and van den Bosch, 1995). Thus, we cannot comment on possible associations between cannabis use and other dimensions of psychosis in the general population.

4.2. Interpretation of findings

In accordance with the findings by Skosnik et al. (2001), we found that frequent cannabis use was associated with increased propensity to present with positive psychotic experiences. However, unlike the findings by Skosnik et al. (2001), we also found a similar and independent association between cannabis use and negative psychotic experiences. These discrepancies may be due to the methodological differences between the two studies. For example, in the study by Skosnik et al. (2001), associations between cannabis and psychotic experiences were assessed using SPQ subscale scores in a small sample of subjects, which may have limited the statistical power of the study. Moreover, there was no assessment of the independence of the associations between cannabis and positive and negative dimensions. It is nevertheless interesting to notice that both studies report that cannabis users recruited in nonclinical samples present with an increased propensity to experience psychosis-like symptoms.

Few studies to date have systematically investigated the associations between cannabis use and psychotic experiences in nonclinical samples. Higher total schizotypal scores were reported in subjects who used cannabis as compared to never-users (Williams et al., 1996), but that study did not explore the links between cannabis use and dimensions of schizotypy. Anecdotal experimental evidence suggests that the administration of tetrahydrocannabinol or cannabis to volunteers may induce positive psychotic symptoms in a limited number of subjects (Thornicroft, 1990). A systematic review of randomised controlled trials comparing the antiemetic effects of cannabis with placebo or other antiemetics showed that 6% of patients receiving cannabis were presented with hallucinations and 5% with "paranoia", while no patient treated with control drugs presented with such side effects (Tramèr et al., 2001). These findings, including those obtained in the present study, support the hypothesis that exposure to cannabis may induce the emergence of positive psychotic symptoms in subjects without clinical psychosis.

It has been suggested that heavy cannabis use may induce a persisting "amotivational syndrome", characterised by loss of motivation and interests and impaired occupational achievement (Tennant and Groesbeck, 1972). The validity of this nosological entity has been questioned, and it is currently considered that these symptoms are related to the subacute encephalopathy linked to chronic cannabis intoxication (Castle and Ames, 1996; Hall and Solowij, 1997; Johns, 2001). Regardless of this nosological debate, few studies have systematically investigated the occurrence of such symptoms in cannabis users. There is a striking phenomenological similarity between the so-called "amotivational syndrome" and the negative dimension of psychosis. It is thus of interest that the present study demonstrates the existence of a dose–response relationship between the frequency of cannabis use and the intensity of the negative symptoms, independent from the intensity of the depressive and positive symptomatology. Our findings provide direct evidence that cannabis users present with greater negative symptoms. If we extrapolate these findings to clinical populations of subjects with psychosis, they do not support the hypothesis that the lower severity of negative symptoms in cannabis users is explained by the "therapeutic" effects of cannabis on such symptoms (Peralta and Cuesta, 1992; Skosnik et al., 2001).

Since our study was cross-sectional, the direction of causality, if any, between cannabis use and dimensions of psychosis cannot be definitely established. We cannot rule out the possibility that frequent cannabis use is a consequence rather than a cause of more intense negative and positive symptoms. However, the

specificity of the findings to cannabis use, as demonstrated by the lack of association between alcohol use and dimensions of psychosis, does not support the self-medication hypothesis. If cannabis were used to alleviate the anxiety or distress induced by psychotic experiences, one would expect similar associations with alcohol, which is a licit and more easily available psychoactive substance. Nevertheless, we cannot exclude a third hypothesis, i.e., that similar risk factors such as personality characteristics (Liraud and Verdoux, 2000) may favor both the occurrence of psychotic experiences and frequent cannabis use. Thus, our findings have to be interpreted with caution in terms of causality. Prospective studies are required to explore the impact of cannabis on the course of psychotic symptoms in subjects from the general population.

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