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The impact of cannabis use on age of onset and clinical characteristics in first-episode psychotic patients. Data from the Psychosis Incident Cohort Outcome Study (PICOS)

Sarah Tosato [a,*], Antonio Lasalvia [a], Chiara Bonetto [a], Rodolfo Mazzoncini [a], Doriana Cristofalo [a], Katia De Santi [a], Mariaelena Bertani [a], Sarah Bissoli [a], Lorenza Lazzarotto [a], Giovanna Marrella [a], Dario Lamonaca [b], Rosanna Riolo [c], Francesco Gardellin [d], Anna Urbani [e], Michele Tansella [a], Mirella Ruggeri [a], the PICOS-VENETO GROUP

[a] Department of Public Health and Community Medicine, Section of Psychiatry, University of Verona, 37134 Verona, Italy
[b] Department of Mental Health, NHS Local Health Authority, Legnago (VR), Italy
[c] Department of Mental Health, NHS Local Health Authority, Camposampiero (PD), Italy
[d] Department of Mental Health, NHS Local Health Authority, Vicenza, Italy
[e] Department of Mental Health, NHS Local Health Authority, Dolo-Mirano (VE), Italy

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ABSTRACT

Cannabis use is frequent among first-episode psychosis (FEP) patients and has been associated with several clinical features. This study aimed in an FEP sample to determine whether cannabis use is associated with 1) a higher level of positive symptoms, a lower level of depression and a better premorbid adjustment, 2) an earlier age of onset, and a better premorbid IQ.

The study was conducted within the framework of the *Psychosis Incident Cohort Outcome Study (PICOS)*, a multisite collaborative research on FEP patients who attended the psychiatric services in Veneto Region, Italy. Standardized instruments were used to collect sociodemographic, clinical, and drug use data.

A total of 555 FEP patients met the inclusion criteria, 517 of whom received an ICD-10 diagnosis of psychosis; 397 (55% males; mean age: 32yrs ± 9.5) were assessed. Out of these, 311 patients agreed to be interviewed on drug and alcohol misuse; 20.3% was positive for drug misuse: cannabis (19.0%), cocaine (3.9%), and hallucinogens (3.9%). Cannabis use was not associated with a higher level of positive symptoms, but correlated with less severe depressive symptoms. No relationship was observed between premorbid adjustment or IQ and cannabis use. FEP patients who used cannabis had an earlier age of onset than abstinent patients, even after adjusting for gender and diagnosis.

Our results suggest a possible causal role of cannabis in triggering psychosis in certain vulnerable subjects. Particular attention must be paid to this behaviour, because reducing cannabis use can delay or prevent some cases of psychosis.

1. Introduction

Cannabis use is frequent among first-episode psychosis (FEP) patients and has a significant impact on the onset, course, and treatment of this disease. Cannabis users are more likely to be male (Kavanagh et al., 2004) and younger (Mueser et al., 1992; Barnes et al., 2006). Moreover, lower educational level (Mueser et al., 1992; Kavanagh et al., 2004; Barnes et al., 2006), higher rates of unemployment, less desirable living conditions (Kavanagh et al., 2004), and unstable relationship status are common in these patients.

Cannabis use has been linked to a shorter duration of untreated psychosis (DUP) (Morgan et al., 2006), more severe positive symptoms (Wade et al., 2007), and less severe negative symptoms (Pencer and Addington, 2003). Yet, the effects of regular cannabis use on mood vary: whereas one study reported less depressed mood in cannabis users than in nonusers (Denson and Earleywine, 2006), another observed that cannabis use is associated with depression (Degenhardt et al., 2003).

* Corresponding author. Tel.: +39 045 8124441; fax: +39 045 8027498.
E-mail address: sarah.tosato@univr.it (S. Tosato).

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Among the clinical variables that characterize psychotic disorders (Nasrallah et al., 2011), age of onset is widely accepted as bearing strong clinical and prognostic significance. Some studies (Compton et al., 2009; De Hert et al., 2011; Galvez-Buccolini et al., 2012) have suggested that cannabis use decreases the age of onset of psychotic disorders, and a recent meta-analysis (Large et al., 2011) reported that cannabis users have an earlier onset of psychosis than nonusers, even if the association between cannabis use and age of onset should be considered spurious as FEP users patients tend to be younger than nonusers (Wade et al., 2007). Earlier age at onset is associated with poorer outcomes in schizophrenia and seems to reflect the severity of the underlying neuropathological process (DeLisi, 1992).

In contrast, some authors (Sevy et al., 2001) have reported higher IQ levels and a better premorbid adjustment in those cannabis users who have developed schizophrenia, which also have greater cognitive reserve and lower severity of illness (Barnett et al., 2006). Taken together, these two observations suggest that cannabis might trigger psychosis earlier in individuals who otherwise have good prognostic features and that the age at onset may be due to the action of cannabis rather than reflect a more severe illness.

Based on this evidence, this study examined the clinical features and the age of onset of FEP patients who reported cannabis use versus nonusers. Specifically, we hypothesized that in a cohort of Italian FEP patients cannabis use is associated with:

1. higher level of positive symptoms, lower level of depressive symptoms, and better premorbid adjustment at onset;
2. earlier age of onset and better premorbid IQ.

2. Material and methods

2.1. Design of the study

Data were collected within the framework of Psychosis Incident Cohort Outcome Study (PICOS), a multisite collaborative research that examined incident cases of psychosis in contact with public mental health services in the Veneto Region, northeastern Italy (Lasalvia et al., 2007; Bertani et al., 2012). Overall, 25 collaborating sites participated in PICOS, encompassing a catchment area of nearly 3.3 million inhabitants, one of the largest cohorts ever examined. Detailed information on the study design, sample recruitment, sample representativeness, and clinical assessment has been reported elsewhere (Lasalvia et al., 2012).

2.2. Study settings

The participating PICOS sites were routine public community-based mental health services, operating within the Italian National Health Service (NHS). Psychiatric care in Veneto is delivered by the NHS through its Departments of Mental Health (DMHs), each of which has a geographically defined catchment area. Multidisciplinary teams that operate the DMHs provide a wide range of comprehensive and integrated programs for the local adult population, including inpatient care, day care, rehabilitation, outpatient care, home visits, 24-h emergency services, and residential facilities for long-term patients.

In Veneto, the majority of psychotic patients is treated within the public sector: a negligible fraction of psychotic patients in treated in private hospitals or in private practice alone, and it is standard practice for general practitioners to refer all psychosis cases to public mental health services (Lasalvia et al., 2012). Standard care for FEP patients generally comprises personalized outpatient psychopharmacological treatment, combined with nonspecific supportive clinical management at the Community Mental Health Center level or, when required, at the patient's home (Lasalvia et al., 2007).

2.3. Participants

Based on the screening method (Jablensky et al., 1992), the initial target group for the study comprised people aged 15–54 years who were residents in the Veneto Region and had had first contact with any mental health service in the PICOS area during the index period (Jan 1, 2005–Dec 31, 2007), with evidence of the following: delusions, hallucinations, thought disorder, or negative symptoms of schizophrenia, irrespective of cause. The primary exclusion criterion was any previous presentation or treatment for psychotic illness, other than initiation of treatment for the current episode at an earlier stage—for example, initiation of antipsychotic therapy by a health professional before referral to a participating mental health service provider, usually within the past 3 months. Patients who refused to participate in the study were contacted an additional 3 times at monthly intervals.

Written informed consent, including permission to contact their relatives, was obtained by participant after receiving a complete description of the study.

2.4. Measures

Information on drug and alcohol use in the year prior to the first contact with the service for psychosis was collected using the CDAUS (*Clinical Drug and Alcohol Use Scale*, Mueser et al., 1995) (information was gathered from the subject and his relatives). A set of standardized instruments was used to collect other clinical information: an *ad hoc* schedule to collect patients' sociodemographic characteristics; the PANSS (*Positive and Negative Symptoms Scale*, Kay et al., 1987) for symptoms; the HAM-D (*Hamilton Rating Scale for Depression*, Hamilton, 1960) for depressive symptoms; the GAF (*Global Assessment of Functioning*, APA, 1994) for global functioning; the DAS-II (*Disability Assessment Schedule-II*, WHO, 1988) for disability in the social roles; the TIB (*Test d'Intelligenza Breve*, Sartori et al., 1997) (the Italian version of the NART, Nelson, 1982) for premorbid IQ; and the PSA (*Premorbid Social Adjustment Scale*, Foerster et al., 1991) for premorbid adjustment.

Duration of untreated psychosis (DUP) was defined as the interval (in months) between the onset of the first psychotic symptoms and the initiation of adequate psychopharmacological treatment (Norman and Malla, 2001) (information of psychosis onset was obtained from interviews with the patient or a close relative and from clinical notes).

The diagnosis was confirmed 6 months after inclusion into the study using the IGC (*Item Group Checklist)* of SCAN (*Schedule for Clinical Assessment in Neuropsychiatry*, WHO, 1992), which allows one to rate information from case records, integrated with interviews with the patient case manager if needed.

All investigators underwent specific training on the use of the standardized instruments, and an interrater reliability session was organized to determine the consistency of evaluations between investigators. The interrater reliability for PANSS was 0.902 (Cronbach's alpha).

2.5. Statistical analysis

Categorical variables were compared by chi-square test or Fisher's exact test if cell frequencies <5. Continuous variables were compared between independent groups by Mann–Whitney (2 groups) or Kruskal–Wallis (>2 groups) test. All tests were bilateral at $p < 0.05$.