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Impact of substance use on the onset and course of early psychosis

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Abstract

The strong comorbidity between psychosis and substance use is already identifiable in early psychosis, raising the question of the direction of the association between substance use and psychosis onset. It has long been considered that this association was explained by the self-medication hypothesis. This hypothesis has been recently challenged by several prospective studies carried out in population-based samples, showing a dose–response relationship between cannabis exposure and risk of psychosis. This association was independent from potential confounding factors such as exposure to other drugs and pre-existence of psychotic symptoms. As a large percentage of subjects from the general population is now exposed to this drug, even a small increase in the risk of adverse effects may have significant deleterious consequences for the health of the population. Hence, reducing exposure to cannabis may contribute to prevention of some incident cases of psychosis. Regarding prognosis, persistent substance misuse after the onset of psychosis has a deleterious impact on clinical outcome. Therapeutic programs for subjects with dual diagnosis should be implemented early in the course of psychosis to maximise their impact on the course of illness.

Keywords: Cannabis; Psychosis; Risk factor; Prognostic factor

1. Introduction

The nature of the link between psychosis and substance use in general, and cannabis in particular, has been questioned for decades and even centuries, generating a huge body of literature. However, few answers were available until recently regarding the actual mechanisms underlying the comorbid association between psychosis and substance use identified in epidemiological or clinical samples (Regier et al., 1990; Boutros and Bowers, 1996; Degenhardt and Hall, 2001; Bühler et al., 2002). Cross-sectional or retrospective studies have provided relevant information on the characteristics associated with substance use in subjects with psychosis. In particular these studies have shown that this comorbid association is already present at illness onset (Hambrecht and Hafner, 1996; Rabinowitz et al., 1999; Verdoux

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et al., 1999; Bühler et al., 2002). They have also revealed that compared to subjects with no history of substance use, subjects with dual diagnosis have an earlier age at onset of psychosis (DeLisi et al., 1991; Addington and Addington, 1998; Van Mastrigt et al., 2004), present with fewer negative symptoms (Peralta and Cuesta, 1992; Addington and Addington, 1998) and have a better premorbid adjustment and a less severe form of illness (Dixon et al., 1991; Arndt et al., 1992; Salyers and Mueser, 2001). These cross-sectional or retrospective studies, however, were unable to clarify the direction of the association between substance use and psychosis, i.e. whether subjects with psychosis use psychoactive substances in general, and cannabis in particular, to self-medicate psychotic symptoms, or whether (vulnerable) substance users are at increased risk of psychosis. This state of uncertainty has considerably changed over the past years, in particular regarding the association between cannabis use and psychosis, because of the new light shed on this issue by prospective epidemiological studies.

2. Is cannabis a risk factor for psychosis?

The first answer to that question was provided by a prospective study carried out on a cohort of Swedish conscripts, which showed that young men with cannabis use at conscription were at increased risk of being admitted for schizophrenia over the subsequent 15-year period (Andreasson et al., 1987). This precursor study provided strong arguments supporting the hypothesis of a causal relationship, in particular the existence of a dose–response relationship between number of self-reported episodes of cannabis use and risk of schizophrenia. However, no firm conclusion could be drawn from these findings, as they were not replicated in another population-based sample, and as their interpretation was hampered by the lack of information on persisting substance use over the follow-up period and the case definition of incident psychosis restricted to individuals requiring hospital admission. These initial findings have been recently confirmed in an extension of this study on the same cohort with assessment of outcome at 27 years (Zammit et al., 2002), which further showed that the association between cannabis use and risk of schizophrenia was independent from use of other substances.

The last few doubts regarding the validity of the Swedish findings can now be considered as groundless, since these findings have been replicated by two independent prospective studies. First, a study conducted on a cohort of subjects from the Netherlands general population followed-up over three years showed that among subjects with no psychotic disorder at inclusion, cannabis users were at increased risk of presenting at the end of the follow-up with clinically significant psychotic symptoms, or with a psychotic disorder with need for care (van Os et al., 2002). These associations were found after adjustment for a range of potential confounding factors, including presence of a non-psychotic psychiatric disorder at inclusion, and use of other substances. Second, a study carried out in a New Zealand birth cohort reported that cannabis users at age 15 and 18 were at increased risk of presenting with psychotic symptoms or with schizophreniform disorder at 26 years (Arseneault et al., 2002). The main strength of this study was that presence of psychotic symptoms was measured at age 11, allowing the authors to demonstrate that the association between cannabis use and increased risk of psychosis was independent from pre-existing psychotic symptoms. Hence, these results provide strong arguments against the self-medication hypothesis, which is based upon the postulate that cannabis use is a consequence of the emergence of psychotic symptoms. As in the other cohort studies, the association between cannabis use and risk of psychosis was independent from use of other substances, such as psychostimulants. These findings support the hypothesis that the association is not explained by the fact that some cannabis users are polysubstance users, and hence that the association may be confounded by use of other psychoactive substances inducing psychosis.

Another prospective study on Israeli male conscripts showed that self-reported substance use at adolescence was associated with an increased risk of hospitalization for schizophrenia or non-affective psychotic disorder over the 5–11 follow-up period (Weiser et al., 2003). However, no information was available in this study on the type of drugs and in particular on the prevalence of cannabis use among subjects with self-reported drug use. Moreover, the