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Differential effects of childhood trauma and cannabis use disorders in patients suffering from schizophrenia

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ABSTRACT

Background: Childhood trauma (CT) and cannabis use are both environmental and modifier risk factors for schizophrenia. However, little is known about how they interact in schizophrenia. We examined the main effect of each of these two environmental factors on the clinical expression of the disease using a large set of variables, and we tested whether and how cannabis and CT interact to influence the course and the presentation of the illness.

Methods: A sample of 366 patients who met the DSM-IV-TR criteria for schizophrenia was recruited through the FACE-SCZ (Fondamental Advanced Centre of Expertise – Schizophrenia) network. Patients completed a large standardized clinical evaluation including Structured Clinical Interview for DSM Disorders-I (SCID-I), Positive and Negative Symptoms Scale (PANSS), Columbia-Suicide Severity Rating Scale (C-SSRS), Global Assessment of Functioning (GAF), Short-Quality of Life-18 (S-QoL-18), and Medication Adherence Rating Scale (MARS). We assessed CT with the Childhood Trauma Questionnaire and cannabis status with SCID-I.

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Results: CT significantly predicted the number of hospitalizations, GAF, and S-QoL-18 scores, as well as the PANSS total, positive, excitement, and emotional distress scores. Cannabis use disorders significantly predicted age of onset, and MARS. There was no significant interaction between CT and cannabis use disorders. However, we found evidence of a correlation between these two risk factors.

Conclusions: CT and cannabis both have differential deleterious effects on clinical and functional outcomes in patients with schizophrenia. Our results highlight the need to systematically assess the presence of these risk factors and adopt suitable therapeutic interventions.

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1. Introduction

Childhood trauma (CT) and cannabis consumption are among the most studied environmental risk factors for schizophrenia and are also considered to be risk-modifying factors. A recent meta-analysis (Varese et al., 2012) found that CT was associated with an increased risk for psychosis (overall OR = 2.78). Moreover, some studies suggest a robust link between CT and the levels of schizophrenic symptoms (Janssen et al., 2004; Morgan and Fisher 2007; Read et al., 2005). Individuals who are victims of CT have higher global symptomatology (Read et al., 2004), positive symptoms (McCabe et al., 2012), particularly auditory-verbal hallucinations (Bentall et al., 2014; Read et al., 2005; Whitfield et al., 2005), and affective symptoms (Matheson et al., 2013; Norman et al., 2012). Some authors even found a dose response relationship between CT and severity of psychotic symptoms (Cohen et al., 2012; Holowka et al., 2003; Lysaker and LaRocco 2008; Shevlin et al., 2007).

Previous studies also reported an association between CT and an earlier age of disease onset (Álvarez et al., 2011), poorer quality of life (Lysaker and LaRocco 2009), impaired general functioning (Amr et al., 2010; Gil et al., 2009; Lysaker and Salyers 2007), a higher risk of attempted suicide (Álvarez et al., 2011; Conus et al., 2010) and an elevated number of hospitalizations (Rosenberg et al., 2007).

Cannabis consumption is also a well-known risk factor for psychosis (Drewe et al., 2004; Matheson et al., 2014; Moore et al., 2007; van Os et al., 2010) and impacts dramatically on the course of schizophrenia (Konings et al., 2008). Schizophrenic subjects who have used cannabis during adolescence tend to have more frequent and longer hospitalizations (Manrique-Garcia et al., 2014; van Dijk et al., 2012). A dose-effect relationship between cannabis consumption and severity of psychotic symptoms has also been reported (Moore et al., 2007). Focusing on specific dimensions of schizophrenia, two meta-analyses found higher levels of positive symptoms in cannabis users (Large et al., 2014; Talamo et al., 2006). Cannabis use is also associated with worse functional outcomes (Schimmelmann et al., 2012), with first episode psychosis patients who decrease or stop their cannabis consumption improving their global functioning (Faber et al., 2012; Stone et al., 2014). In addition, Large et al., (2011) found in their meta-analysis that cannabis-users had an earlier age of onset of psychotic disorder, especially schizophrenia (Large et al., 2011). One study found a linear association between the age of initiation of cannabis use and the age of psychosis onset (Stefanis et al., 2013). The relationship between cannabis consumption and suicidal behavior in patients with psychotic disorders has been systematically reported in most studies. However, the authors suggest that this link is mediated by other risk factors, including CT (Serafini et al., 2012).

The relationships between CT and cannabis consumption have, to date, been insufficiently addressed. Some studies show that children victims of adversities are more likely to use cannabis (Fergusson et al., 2008; Hayatbakhsh et al., 2009; Oshri et al., 2011; Rogosch et al., 2010), suggesting an environment × environment correlation where CT influences the risk to be exposed to cannabis consumption. Other studies found an interaction between CT and cannabis use, where CT makes individuals more sensitive to the psychotomimetic effects of cannabis (Houston et al., 2011, 2007; Morgan et al., 2014; Murphy et al.,

2013; Shevlin et al., 2009). Finally, several studies indicate that CT and cannabis use in adolescence additively increase the risk of psychosis (Harley et al., 2010; Konings et al., 2012; Morgan et al., 2014).

In the present study, in order to disentangle the complex relationship between CT and cannabis use in schizophrenia, we examined: (1) the main effect of each of the two environmental factors on the clinical expression of the disease using a large set of variables; and (2) whether and how cannabis and CT interact to influence the course of the illness.

2. Materials and methods

2.1. Recruitment and population

Patients who met the DSM-IV-TR (APA, 2000) criteria for schizophrenia or schizo-affective disorder were recruited through the FACE-SCZ (Fondamental Advanced Centre of Expertise – Schizophrenia) network. FACE SCZ is a French national multicenter network of ten schizophrenia expert centers of the FondaMental foundation (Schürhoff et al., 2015), which assesses patients referred by their general practitioner or psychiatrist and then provide a detailed evaluation report along with suggestions for therapeutic interventions. A web application, e-schizo© is used to record data in a common computerized medical file. Anonymized data was entered into a shared national database for use in multi-center audit and research. The assessment protocol was approved by the ethical review board (CPP-Ile de France IX, January 18th, 2010). The ethical board requested that each patient received an information letter. In this case, seeking permission from patients was a prerequisite to any analysis of the clinical data. Access to the system was carefully regulated and approval was obtained from the committee in charge of the safety of computerized databases (CNIL) (DR-2011-069).

2.2. Data collection

A large standardized clinical evaluation with structured clinical interview providing DSM-IV-TR diagnoses was used to determine diagnosis of schizophrenia or schizo-affective disorder as well as comorbid psychiatric conditions, especially alcohol and cannabis addictions. Socio-demographic factors (age, educational level, marital status), age of onset of schizophrenia or schizo-affective disorder, age at first hospitalization, number and total duration of hospitalizations were collected with the Structured Clinical Interview for DSM Disorders-I (SCID-I). Current psychotic symptoms were assessed with the Positive and Negative Symptoms Scale (PANSS); suicide risk with the Columbia-Suicide Severity Rating Scale (C-SSRS); global functioning with the Global Assessment of Functioning Scale (GAF); adherence to treatment with the Medication Adherence Rating Scale (MARS); and quality of life with a shortened quality of life questionnaire (S-QoL-18). These latter three variables are thereafter named psychosocial variables.

All these variables have been previously described elsewhere (Schürhoff et al., 2015).

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