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Risk factors for increased duration of untreated psychosis. Results from the FACE-SZ dataset

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ABSTRACT

Objectives: Reducing the duration of untreated psychosis (DUP) may improve the prognosis of schizophrenia. This study investigated the prevalence, and associated risk factors, of long DUP in a large, non-selected sample of community-dwelling schizophrenia patients (SZ).
Method: 478 community-dwelling stable SZ participants (122 women and 356 men; mean age 32.37 ± 9.86 years) were recruited between 2010 and 2016. The mean retrospective DUP was evaluated from both patient and family reports, as well as hospital/psychiatrists records. Long DUP was defined as >2 years.
Results: The mean DUP was 1.5 years. 80 participants (16.7%) had a DUP > 2 years. In multivariate analyses, after adjustment for sex, education level, history of childhood trauma and history of maternal schizophrenia or bipolar disorder, long DUP was associated with a younger age of illness onset (19.3 ± 6.67 years vs. 22.0 ± 6.51 years, adjusted odd ratio aOR = 0.91, 95%CI [0.86; 0.97], p = 0.003) and cannabis use disorder (20.0% vs. 10.3%, aOR = 2.41, 95%CI [1.14–5.09], p = 0.02).
Conclusion: A high proportion of SZ patients still have a long DUP. The present results suggest that illness onset before age 19 years and cannabis use are associated with long DUP in schizophrenia patients. Early psychosis detection programs should prioritize the targeting of these populations.

1. Introduction

For most affected individuals, schizophrenia (SZ) is a chronic and disabling disorder. Although SZ vulnerability is associated with genetic and environmental factors that influence early brain development, the disorder does not typically emerge until adolescence or young adulthood. Despite historical pessimism regarding prognosis, more recent studies suggest that early intervention can improve outcome (Lieberman et al., 2001). These findings have stimulated great interest and enthusiasm regarding intervention at, or even prior to, the onset of the first episode, with consequent improvements in antipsychotic treatment response and better long-term outcome. Numerous "early psychosis" or "prodromal" clinics have been developed, with the intention to facilitate early interventions (Johannessen et al., 2001; Linszen et al., 1998; Malla et al., 2002; McGorry et al., 1996). According to staging models (McGorry et al., 2006), the development of SZ may have at least three stages; the prodrome, the first episode, and the chronic phase. The early detection of the prodromal phase, with a resultant reduced duration of untreated psychosis, predicts better long-term outcome (Penttilä et al., 2014). Efforts at early identification and treatment are based, in part, on the assumption that through still to be clarified processes, illness duration causally influences treatment response and outcome (Lieberman et al., 1998). A recent meta-analysis has shown that only 13.5% of SZ patients achieve recovery, an outcome that has not improved despite intensive investigation (Jääskeläinen et al., 2013). This is primarily due to the few potentially modifiable predictors of outcomes that have been identified. The duration of untreated psychosis (DUP) has been one of the most commonly studied outcome predictors (Marshall et al., 2005; Perkins et al., 2005). DUP is defined in most studies by the time between first psychotic symptoms to antipsychotic treatment, which is to be distinguished from the duration of untreated illness (Marshall et al., 2005). Untreated psychosis is postulated to have a toxic effect, through unknown pathophysiological processes, leading to a long DUP having a poorer prognosis (Sheitman and Lieberman, 1998). Data comparing long vs. short DUP show an association between long DUP and poorer outcomes at 6 months, including total symptoms, overall functioning, positive symptoms, and quality of life (Marshall et al., 2005). A systematic review indicates long DUP to be associated with significantly lower remission rates (Marshall et al., 2005).

While most studies have focused on the comparative effects of short vs. long DUP on patient outcomes, the risk factors for increased DUP await clarification. Several studies carried out in different countries have suggested that onset during adolescence (<18 years) is associated with increased DUP (Ballageer et al., 2005; Dominguez et al., 2013; Schimmelmann et al., 2007). A recent meta-analysis found no association between cannabis use and increased DUP (Burns, 2012). However one recent large study ($N = 940$) found that a history of cannabis use disorder may be associated with increased DUP (Dominguez et al., 2013). This discrepancy may be explained by the age at onset of cannabis use disorder, which has not been explored to date. A recent meta-analysis indicated no influence of gender on DUP (Cascio et al., 2012). One study indicates that childhood trauma positively correlates with increased DUP (Broussard et al., 2013). However, it still awaits clarification as to whether other commonly investigated factors, such as the presence of a psychiatric disorder in one parent, associate with increased DUP. Although urban birth has been suggested as an environmental risk factor for SZ (Szöke et al., 2014), its impact on DUP has never been explored. Hypothetically, urban birth may be associated with better health care access and therefore shorter DUP, or urbanicity may be a proxy for some underlying, as yet unidentified, risk factor. Place of birth, perhaps especially the environment where fetal development occurred, associates with SZ disease risk. As to whether such factors are relevant to an increased DUP is unknown. Likewise, it is unknown as to whether lower premorbid intellectual functioning increases DUP, perhaps by diminishing help seeking.

The objective of the present study was therefore to determine relevant risk factors associated with increased DUP. Our hypothesis was that increased DUP was associated with a lower age of SZ onset, lower premorbid intellectual functioning, childhood trauma and a positive parental history of severe psychiatric disorder, but not with gender or the use of cannabis or alcohol. We also hypothesized that higher education level and urban birth would be associated with a shorter DUP.

2. Materials and methods

2.1. Study population

The FACE-SZ (FondaMental Academic Centers of Expertise for Schizophrenia) cohort is based on a French national network of 10 Schizophrenia Expert Centers (Bordeaux, Clermont-Ferrand, Colombes, Créteil, Grenoble, Lyon, Marseille, Montpellier, Strasbourg, Versailles), set up by a French scientific cooperation foundation, FondaMental Foundation (www.fondation-fondamental.org) and created by the French Ministry of Research in order to build a platform that links systematic clinical assessment to research (Schürhoff et al., 2015). In the present study, patients were recruited between 2010 and 2016.

Inclusion criteria: consecutive, clinically stable patients, as defined by no hospitalization and no treatment changes during the 4 weeks before evaluation, aged 16 years or older, with a DSM-IV-TR diagnosis of SZ or schizoaffective disorder. Diagnosis was confirmed by two trained psychiatrists of the Schizophrenia Expert Centres network. All participants were referred by their general practitioner or psychiatrist, who

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