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Adolescent vs. adult onset of a first episode psychosis: Impact on remission of positive and negative symptoms

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ABSTRACT

Objective: Adolescent-onset psychosis has traditionally been characterized as a more severe form of psychosis with a poorer prognosis. However, it is still unclear if patients with an adolescent-onset have worse symptom remission outcomes. Symptom remission is the principal clinical outcome known to predict quality of life and social functioning in the long term. The goal of this study is to clarify the influence of age of onset of psychosis on symptom remission in a sample of first-episode psychosis patients.
Method: A total of 246 first-episode psychosis patients were recruited from a specialized early intervention program serving a defined epidemiological catchment area. Age of onset of psychosis (adolescence vs. adulthood) was used as the main predictor, and duration of untreated psychosis (DUP), baseline symptoms, baseline functioning, substance abuse diagnosis, medication adherence and gender were used as covariates in hierarchical regression models predicting the following positive and negative symptom remission outcomes: maximum continuous months in remission and early remission (i.e., occurring in the first three months of follow-up).
Results: After controlling for other variables, onset of psychosis in adulthood and shorter DUP predicted early remission of positive symptoms. This effect was stronger in patients with a diagnosis of a schizophrenia-spectrum disorder. Remission of negative symptoms did not depend on age of onset, and was only predicted by baseline negative symptoms.
Conclusion: Patients with onset of psychosis during adulthood are more likely to achieve early positive symptom remission than those with adolescent onset. This effect might be stronger in patients with a diagnosis of a schizophrenia-spectrum disorder.

1. Introduction

An important clinical characteristic associated with the course of psychotic disorders is the age at onset of psychosis. Earlier ages of onset of psychosis are associated with more psychopathology (Langeveld et al., 2012), greater cognitive impairment (Rajji et al., 2009), more early conduct problems (Vinokur et al., 2014), premorbid personality changes (Skokou et al., 2012), and structural brain changes (Burke et al., 2008). Furthermore, adolescent-onset patients often exhibit unfavorable risk factors such as longer duration of untreated psychosis (DUP) (Ballageer et al., 2005), poorer premorbid adjustment (Larsen et al., 2004), and higher rates of substance abuse (Pencer et al., 2005). Thus, adolescent-onset patients are expected to have worse clinical and functional outcomes than those with an adult onset.

Symptom remission is a fundamental clinical outcome by itself (Iyer et al., 2015), that also has prognostic value for social and occupational functioning (Cassidy et al., 2010a; Jordan et al., 2014), higher levels of life satisfaction (Bodén et al., 2009) and paid or voluntary employment (Üçok et al., 2011), better quality of life (Emsley et al., 2007), and better long-term functional and vocational recovery (Alvarez-Jimenez et al., 2012). Thus, assessing the influence of having an adolescent versus an adult onset of psychosis on symptom remission might provide insight on the natural history, clinical evolution, and functional prognosis of a first-episode of psychosis in these two different groups of patients.

Previous studies have examined the influence of age at onset of psychosis as a continuous variable on symptom remission, yielding equivocal findings (Addington and Addington, 2008; Ballageer et al., 2005; Chang et al., 2012; Crumlish et al., 2009; Langeveld et al., 2012; Verma et al., 2012). Only one previous study has compared adolescent versus adult-

Abbreviations: CORS, Circumstances of Onset and Relapse Schedule; DUP, duration of untreated psychosis; LOCF, last observation carried forward; OR, odds ratio; PAS, Premorbid Adjustment Scale; PEPP, Prevention and Early Intervention Program for Psychosis Montreal; RSWG, Remission in Schizophrenia Working Group; SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms; SCID-IV, Structured Clinical Interview for DSM-IV Axis I Disorders; SOFAS, Social and Occupational Functioning Assessment Scale; β, Standardized Beta Coefficient; VIF, variance inflation factor.

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onset patients without finding any differences (Schimmelmann et al., 2007). However, to our knowledge, no study has assessed the influence of having an adolescent versus an adult onset of psychosis (as a grouping variable) on symptom remission using a widely accepted definition, or studied related aspects such as length or remission of negative symptoms, while accounting for other established predictors of symptom remission. Separating adolescents and adults may have an additional value considering these groups have different roles, living situations, legal statuses, and are offered services in different parts of the system.

The main goal of this study is to determine the influence of having an adolescent versus an adult onset of psychosis on various aspects of symptom remission while controlling for other known predictive variables. We hypothesized that patients with adolescent-onset psychosis would have poorer symptom remission outcomes — early remission (i.e., occurring in the first three months after initiation of treatment), and number of continuous months in remission — when compared to their adult-onset counterparts. As a secondary objective, we sought to explore the impact of age of onset on symptom remission outcomes separately among individuals with non-affective psychotic disorders, given the known differences in clinical outcomes (Jarbin et al., 2003) and neurobiological changes (Walterfang et al., 2009) between these and individuals with an affective psychotic disorder.

2. Materials and methods

2.1. Participants and setting

Participants were recruited from the Prevention and Early Intervention Program for Psychosis (PEPP), the *only* specialized early intervention service for patients experiencing a first episode of psychosis in a predominantly urban catchment-area of 400,000 inhabitants in Montreal, Canada. PEPP treats nearly all potential cases of FEP in this catchment area (Anderson et al., 2013), increasing the generalizability of our findings. Further, due to strong linkages with all local health care and community partners, participants who disengage from PEPP and later seek services elsewhere are almost always referred back. PEPP's admission criteria include: a DSM-IV diagnosis of non-affective or affective psychosis not due to an organic brain disorder (e.g. epilepsy); age 14 to 35 years old; IQ of 70 or greater; and no more than one month of prior treatment with antipsychotics. Patients are offered low-dose antipsychotic medication, assertive case-management and psychosocial interventions for two years (Iyer et al., 2015). This study was approved by the appropriate ethics board. All participants granted informed consent.

2.2. Remission definitions

Remission was defined using the Remission in Schizophrenia Working Group (RSWG) criteria, which are based on symptom severity and duration, and are widely accepted (Andreasen et al., 2005). This definition has demonstrated prognostic validity for functional outcome (Jordan et al., 2014) and quality of life (Brissos et al., 2011). Using RSWG severity criteria for every month of follow-up, patients were considered in positive symptom remission if they scored ≤2 on all Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984) global subscales (i.e., hallucinations, delusions, bizarre behavior and formal thought disorder). Patients were considered in negative symptom remission if they scored ≤2 on all Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) global items except 'attention' (i.e., affective flattening, alogia, avolition-apathy, anhedonia-asociality). Symptom evaluations were conducted nine times during the two-year treatment period (at entry and months 1, 2, 3, 6, 9, 12, 18, and 24). For the months without an evaluation, information on positive remission was coded from clinical notes. If clinical notes were insufficient, the last observation carried forward (LOCF) technique was used. For negative symptom remission, only the LOCF technique was applied for months without symptom evaluations due to the lower accuracy when scoring negative symptoms from clinical notes. Data were considered valid for analysis if baseline and last month (month 24) evaluations were conducted, and there was no gap of six or more consecutive months of evaluations (thus hindering the application of LOCF). Our previous work has shown these estimates to be 82.9% accurate (Jordan et al., 2014). No significant differences in the percentage of patients with early remission or the number of total or continuous months in remission (positive or negative) were found between cases with complete observations and those for which LOCF was needed (Supplementary Table 1).

Two aspects of remission were considered. The first consisted of the maximum number of continuous months in which the RSWG severity criterion for symptom remission was present. The second reflected the achievement of early remission, defined as attaining the RSWG severity criterion at any month within the first three months after admission. The number of continuous months of symptom remission is arguably a more ecologically valid metric of remission than a categorical metric of whether or not persons were in remission for a specified duration. Early remission has shown stronger predictive value for lower positive symptoms, better global functioning, and better employment stability after five years (Norman et al., 2014). Both variables were independently established for remission of positive and negative symptoms, as the latter represent different psychopathological dimensions (Kumar and Khess, 2012), have different neuroanatomical substrates (Nenadic et al., 2010), and prognostic implications (Milev et al., 2005; Rosen and Garety, 2005).

2.3. Predictors of remission

Age at onset of psychosis was defined as the age at which the severity and duration of psychotic symptoms met threshold criteria for psychosis using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-IV) (First et al., 2002). It was determined using the Circumstances of Onset and Relapse Schedule (CORS) (Norman et al., 2004), a semi-structured interview administered to patients by a trained evaluator with collateral information from families and medical records. Onset between 14 and 17 years of age was considered 'adolescent-onset' psychosis and onset occurring at or after age 18 was considered 'adult-onset'.

The following ancillary factors that predict symptom remission were included in the analyses: DUP, premorbid adjustment, severity of psychopathology and functional levels upon entry, substance use/abuse diagnosis, medication adherence, and gender (Lambert et al., 2010). DUP was defined as the time (in weeks) from onset of psychosis to the beginning of antipsychotic medication taken either continuously for 30 days or until symptom remission, whichever came earlier. Premorbid functioning was assessed with the Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982), using a composite score of social and academic dimensions during childhood and early adolescence. Late adolescence and adulthood information was omitted due to the temporal overlap with the period of onset of psychosis. Baseline psychotic symptoms were determined using the SAPS and the SANS. Baseline functioning was determined with the Social and Occupational Functioning Assessment Scale (SOFAS) (Goldman et al., 1992). Modal medication adherence was defined using a validated method (Cassidy et al., 2010b) and dichotomously coded as either good (75–100% compliance) or not (0–74% compliance). Monthly assessments were conducted using several sources, including patients, families and clinical notes. Diagnoses (including baseline substance abuse or dependence) were established using the SCID-IV, administered by a trained interviewer and corroborated by two psychiatrist-researchers. Diagnoses were further clustered into diagnostic categories: Schizophrenia Spectrum Disorders (i.e., schizophrenia, schizophreniform disorder, schizoaffective disorder, psychosis NOS), and affective psychoses (i.e., bipolar or depressive disorders with psychotic features).

2.4. Statistical analyses

Preliminary analyses comprised: 1) comparing participants and non-participants in terms of diagnosis, predictors of remission and

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