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Associations between cognition and internalizing problems in young adults with early-onset schizophrenia: A 13-year follow-up study

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ABSTRACT

The present follow-up study examines the associations between cognition and parent-rated internalizing problems among adolescents with early-onset schizophrenia (EOS) at baseline (T1) and self-rated internalizing problems 13 years later (T2). Twelve individuals (8 male/4 female) with EOS and 30 healthy controls (16 male/14 female) were included in the study. All were between 12 and 18 years of age at T1. Internalizing problems were measured with the Achenbach System of Empirically Based Assessment Internalizing Scale. Cognition was examined with a neuropsychological test battery measuring auditory attention/working memory, visuomotor processing, cognitive flexibility and verbal memory. Compared to healthy controls, the EOS group had significant cognitive deficits and more internalizing problems both at T1 and T2. There was no correlation between parent-rated internalizing problems at T1 and self-rated internalizing problems at T2. A focus on improving the treatment of cognitive impairments may be important in preventing the development of internalizing problems in young patients with schizophrenia. The small sample size of the study is a limitation and further research is recommended.

1. Introduction

Depressive symptoms are common among patients with first-episode psychosis (Coentre et al., 2017). Results indicate that depressive symptoms in schizophrenia are a discrete symptom domain with only partial overlap with positive or negative symptoms (Schennach et al., 2015). There are only few studies examining the course and development of depressive symptoms in patients with a first episode psychosis. In one 12-month follow-up study it was found that depression early in the emergence of a psychosis was fundamental to the development of future depression and suicidal thinking (Upthegrove et al., 2010). Another study found that poor childhood social functioning, long duration of untreated psychosis and depressive symptoms at baseline predicted depression at 12-month follow-up in patients with first episode psychosis (Sönmez et al., 2013). In a ten-year follow-up study of firstepisode psychosis patients, it was found that patients with poor social functioning in childhood and alcohol use at baseline were more prone to have depressive symptoms at 10-year follow-up (Sönmez et al., 2016). Longitudinal studies on depressive symptoms in adult first episode patients have consistently found that the depressive symptoms decreased during the follow-up period (Sönmez et al., 2013).

Research indicates that between 30% and 62% of patients with schizophrenia present with co-morbid anxiety disorders (Howells et al., 2017), with the most frequent co-morbid anxiety disorder being social phobia (Achim et al., 2011). Pallanti et al. (2004) showed that social phobia was not related to the positive or negative symptoms of schizophrenia. According to Birchwood et al. (2007), comorbid social phobia can develop from the expectation of a devastating loss of social status in patients with schizophrenia. There is a close relationship between anxiety and depression and increased suicidality in people with a psychotic disorder (Bertelsen et al., 2007; Diaz-Caneja et al., 2015; Fenton, 2000; Jarbin and Von Knorring, 2004). Thus, knowledge about variables associated with development of depressive and anxiety symptoms in people with a psychotic disorder may facilitate earlier identification of patients who are prone to develop a severe course.

Most of the research on depression and anxiety in schizophrenia has been on adults, and the affective dimension has scarcely been studied in early-onset schizophrenia (EOS) (Sanchez-Gistau et al., 2015). EOS is defined as an occurrence of schizophrenia before the age of 18 (Frangou, 2006). Partly because neurobiological and psychosocial development is not yet complete at this age, 50–60% of individuals with EOS have a poor prognosis (Clemmensen et al., 2012). It is therefore

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important to acquire more insight into the causes of internalizing problems in this particularly vulnerable group of young individuals for prevention and treatment purposes.

A child or adolescent who has depressive symptoms and anxiety frequently experiences other internalizing symptoms such as social withdrawal and physical concerns (Merrell, 2008). Thus, it makes sense to examine internalizing problems as a group of symptoms in research on adolescents with EOS, as opposed to only focusing on depression or anxiety. In this regard, the Children Behavior Check List (CBCL) provides a reliable and valid measurement with high stability over time in children with ADHD (Biederman et al., 2001; Mattison and Spitznagel, 1999; Bingham et al., 2003). Petty et al. (2008) showed that the CBCL Internalizing Scale predicted anxiety disorders in a 5-year follow-up study of 2-17-year-old children of parents with a panic disorder or major depression. In a longitudinal study by Roza et al. (2003) of children and adolescents from the general population, both the CBCL Internalizing and Externalizing Scales proved to be significant independent predictors of mood disorders (Roza et al., 2003). One study found that internalizing problems, as measured by the CBCL, are common among children who later develop EOS (Muratori et al., 2005). Øie et al. (2011) reported that individuals with EOS between 12-18 years of age had a considerably higher level of internalizing problems measured by the CBCL than healthy controls. The level of internalizing problems was still elevated relative to controls after 13 years. However, Øie et al. (2011) did not examine possible baseline factors that may be associated with later internalizing problems. Therefore, in this study, we intend to gain more knowledge about early predictors (i.e., internalizing problems or cognitive deficits during adolescence) of later internalizing problems during young adulthood among individuals with EOS.

Cognitive deficits have been well documented in both adult onset schizophrenia and in EOS. In a review of cognitive function in individuals with EOS, Frangou (2010) found that EOS patients showed impairments with medium to large effect sizes in IO, attention, memory and executive functions (Frangou, 2010). Both in first episode schizophrenia and in chronic schizophrenia, cognitive deficits are strongly related to poorer functional outcome (Fett et al., 2011; Stouten et al., 2014). In a study of youth with EOS, Øie et al. (2011) found that poorer cognition at baseline was correlated with worse social functioning and vocational/educational functioning at 13-year follow-up. Cognitive deficits occur early in the course of psychosis and generally tend to improve marginally or remain stable over time in adult onset schizophrenia (Szöke et al., 2008). In contrast, Øie et al. (2011) found a decline in verbal memory, attention and processing speed in EOS patients when reassessed after 13 years. Given that chronic and first-episode samples and EOS samples vary in the longitudinal course of cognitive functions, research documenting associations between cognition and outcomes in adult onset samples cannot be generalized to patients with EOS. Further, compared to older patients with schizophrenia, individuals with EOS are about to enter adulthood, attending school, deciding on further education, and establishing important social networks. If cognitive impairments in individuals with EOS halt their development in social and academic areas (Øie et al., 2011), they may also mediate the development of internalizing symptoms.

The current study is part of a larger 13-year follow-up study of 19 adolescents with EOS between 12–18 years of age, 20 adolescents with Attention Deficit Hyperactivity Disorder (ADHD) and 30 healthy controls (Øie et al., 2010, 2011). The aim of the present study was to investigate possible 13-year longitudinal predictors of self-rated internalizing symptoms in the EOS patient sample. Cognition and parent-rated internalizing symptoms were the outcome measure assessed at follow-up. By identifying early predictors of later internalizing problems, treatment can start early and possibly influence the course, morbidity and mortality.

individuals whether a) baseline parent-rated internalizing symptoms and b) baseline cognitive deficits, could predict self-rated internalizing symptoms at 13-year follow-up.

2. Methods

2.1. Participants

Participants in the study were 12 subjects from a baseline (T1) sample of 19 adolescents with a Diagnostics and Statistical Manual, Fourth Edition (DSM-IV)-based diagnosis of schizophrenia and 30 healthy control individuals. At T2, two of the subjects in the schizophrenia group were deceased (one by suicide and one by overdose, in combination with an underlying medical disorder) and two declined to participate in the study. Furthermore, data from the Internalizing scale at T2 were missing for three individuals in the EOS group. All 30 healthy control individuals were available for reassessment after 13 years. At follow-up, there were eight male and four female patients in the EOS group, whereas in the healthy control group there were 16 male and 14 female participants. The level of intellectual ability in the EOS group at T2 was within the normal range; 93.2 (\pm 15.1). We used the expanded Brief Psychiatric Rating Scale (BPRS) (Lukoff et al., 1986) to assess symptoms of psychosis at T2. The BPRS covers a 2-week period and intends to indicate general severity of psychotic symptoms. It consists of 24 items that rate severity of psychiatric symptoms on a scale from 1 (not present) to 7 (extremely severe). A positive and a negative symptoms score were based on a factor analysis conducted by Ventura et al. (1995), with seven and three items, respectively. The total psychosis symptoms score was 42.8 (\pm 16.0), the positive symptoms score was 12.1 (\pm 7.5) and the negative symptoms score was 6.5 (\pm 3.4). Ten of the patients in the EOS group had been hospitalized during the follow-up period. Five of the individuals had been continuously in the hospital or in sheltered housing, and five for only a short period of time. At T2, two of the individuals in the EOS group had recovered. They were living independently, had a partner and were employed. Among the group that was still symptomatic, half were living on their own, all were unemployed and only one of the patients had a partner. Eleven of the individuals in the EOS group had not yet started neuroleptic treatment at the time of testing at T1 and one was still drug naive at T2. Healthy controls were volunteers attending regular schools. They were screened for mental problems using the CBCL, and individuals were excluded if they had a raw score higher than 45 (Øie and Rund, 1999). The healthy comparison group had significantly more education and significantly higher IQ scores at T2 than the EOS group. Øie et al. (2011) have previously shown that the current EOS sample group had a lower social functioning score and more internalizing problems than the healthy control group at T2. Characteristics of the EOS group compared to the healthy controls at T2 are presented in Table 1.

2.2. Procedure

The schizophrenia diagnosis was determined at T1 using semistructured clinical interviews by senior clinicians and information from the patient case records. After 13 years, the schizophrenia diagnosis at T2 was based on the Structured Clinical Interview for DSM-IV and information from parents, psychiatrists, nurses or social workers. One psychologist and one psychiatrist reviewed the diagnosis, and agreed on it in 94% of the cases. Disagreements in diagnosis at T2 were discussed between the two, to arrive at a consensus diagnosis. The patients were tested when they were judged by the examiner or by their clinician to be clinically stable.

2.3. Internalizing problems measure

With this background, we wished to test in a sample of EOS

The Child Behavior Checklist (CBCL) Internalizing scale was used as

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