Research Paper

Poor premorbid school performance, but not severity of illness, predicts cognitive decline in schizophrenia in midlife

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ABSTRACT

Neurocognitive dysfunction is common in schizophrenia but its course and determinants remain uncertain. Our aim was to analyse if premorbid school performance and the severity of illness and functioning predict change in cognition in schizophrenia in a general population sample.

The sample included cases with schizophrenia spectrum disorder from the Northern Finland Birth Cohort 1966. Data on school marks at the age of 16 years, educational level at the age of 34 years, severity of symptoms and occupational functioning around first episode and after years of illness were gained from national registers, hospital notes and interviews. Change of verbal and visual learning and memory and executive functioning were examined between ages 34 and 43 years. The number of cases varied in analyses from 29 to 41, depending on missing data in particular cognitive tests.

Lower school marks at age 16 years and lower education at age 34 years predicted more decline of cognition. Measures of severity of illness or functioning were not associated statistically significantly with change of cognition. Premorbid school performance, but not later course of schizophrenia, related to change of cognition in midlife. Poor premorbid scholastic performance and post-onset cognitive decline may represent related processes as part of an endophenotype of schizophrenia.

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1. Introduction

Neurocognitive deficits in schizophrenia are associated with functional impairments (Ekerholm et al., 2012; Hedman et al., 2013, Mesholam-Gately et al., 2009, Touloupoulou and Murray, 2004). Understanding more about the predictors of neurocognitive function in schizophrenia is of theoretical and potential practical importance. However, the longitudinal course of cognitive functioning and its predictors in schizophrenia remain unclear (Bora and Murray, 2014; Bozikas and Andreou, 2011; Irani et al., 2010). Longitudinally, in one study, 10-years follow-up duration of untreated psychosis (DUP) and

change of IQ did not relate, but a subgroup with long duration of active psychosis after the start of treatment demonstrated a significant cognitive decline (Barder et al., 2014). Low education, instead, has been associated with decline in selective attention over 4.5 years follow-up (Ekerholm et al., 2012) and decline in other cognitive scores (e. g., immediate memory, language, delayed memory) (Han et al., 2012); these results, combined with prior studies suggesting that scholastic performance may predict schizophrenia risk (Jones et al., 1994; MacCabe et al., 2008) and illness severity (Lauronen et al., 2007; Mäkinen et al., 2010), encouraged us to further investigate whether premorbid scholastic performance is associated with subsequent course of cognition in schizophrenia within the population based setting of the Northern Finland Birth Cohort 1966. Given previous evidence that higher amount of relapses associated with poorer cognition measured repeatedly at 5-years follow-up (Barder et al., 2013),

we also investigated whether illness severity predicts subsequent cognitive decline.

Here, our aim was to analyse premorbid school performance, educational level and severity of illness and occupational functioning as predictors of cognitive change in schizophrenia. We hypothesized that both poor school performance and lower educational level, and more severe illness during the first episode and later course of illness, would associate with more decline in cognition.

2. Methods

2.1. Participants

The Northern Finland Birth Cohort 1966 (NFBC 1966) is an unselected general population birth cohort ascertained during mid-pregnancy, consisting 12,058 live-born children in the provinces of Lapland and Oulu with an expected delivery date during 1966. There were 11,017 eligible individuals in Finland at the age of 16 years. Of them, 83 individuals did not consent to the use of their data and have been excluded. The Ethical Committee of the Northern Ostrobothnia Hospital District has approved the study design of the NFBC 1966. The current study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

A baseline study of this sample was conducted in 1999–2001 (around the age of 34 years), with follow-up in 2008–2010 (around the age of 43 years). Participants were given a complete description of the study and had an opportunity to refuse to participate. All participants provided written informed consent (Husa et al., 2014, Kobayashi et al., 2014, Rannikko et al., 2015, Veijola et al., 2014).

2.2. Case identification

All cohort members over 16 years appearing on the nationwide Finnish Hospital Discharge Register (FHDR) until the end of 1997 for any mental disorder (i.e. ICD-8 diagnoses 290–309, ICD-9 290–316, and ICD-10 F00–F69, F99) were identified. All case records were scrutinized and diagnoses were validated for the DSM-III-R criteria. The reliability of researchers assessing schizophrenia diagnoses was good (kappa = 0.85) (Moilanen et al., 2003).

2.2.1. Baseline study

During 1999–2001 around the age of 34 years all 146 living cases with diagnosis of psychosis (62 females, 42%) were invited to participate in the baseline study. Altogether 92 (63%) cases (72 (79%) with schizophrenia spectrum disorders) participated. The Structured Clinical Interview for DSM-III-R (SCID I; Spitzer et al., 1989) was used for diagnostic assessment, together with all available information on illness history including individual medical records. The examination also included cognitive tests described below. After diagnostic interviews a total of 61 cases with a lifetime diagnosis of schizophrenia and 12 cases with other schizophrenia spectrum disorder were detected. Mean duration of illness of all these cases was 10.2 years (standard deviation, SD 4.3) at the baseline. The baseline study in 1999–2001 is presented in detail in Haapea et al. (2007).

2.2.2. Follow-up study

The follow-up study took place in 2008–2010 when the participants were around age 43 years. All the participants of the baseline study were invited to participate in the follow-up, and 44 (61%) individuals with schizophrenia spectrum disorder participated. The follow-up study included diagnostic interview (SCID-I, First et al., 2002) and the same cognitive tests as done at baseline. The original diagnoses were validated at follow-up for all subjects based on the SCID interview and by review of medical records. The mean duration

of illness until the follow-up study was 20.0 (SD 4.1) (Husa et al., 2014, Kobayashi et al., 2014, Rannikko et al., 2015, Veijola et al., 2014).

2.2.3. Final sample

The present study is based on those 41 individuals with a schizophrenia spectrum disorder for whom data on cognition was available at both baseline and follow-up. The schizophrenia spectrum group included the following DSM-III-R diagnoses: schizophrenia 295.1 (n = 9); 295.3 (n = 8); 295.6 (n = 1); 295.9 (n = 16); schizophreniform psychosis 295.4 (n = 1), schizoaffective disorder 295.7 (n = 5) and delusional disorder 297.1 (n = 1). Hereafter in this paper the term "schizophrenia" is used for schizophrenia and other schizophrenia spectrum disorders. The mean follow-up time between baseline and follow-up study was 9.1 years (SD 0.6) years.

2.3. Analysis of attrition

The final sample (n = 41) did not differ from those who participated in the baseline study but not the follow-up in gender, in a summary measure of the CVLT (correct responses in trials 1–5) at baseline, in PANSS total symptoms, onset age or number of psychiatric hospital treatment days. Compared to non-participants, participants had statistically significantly lower educational level at age of 31 years (based on national register data) (p = 0.038). The only five cases with tertiary education did not participate in the follow-up study.

The final sample (n = 41) did not differ from all the other schizophrenia spectrum cases of the whole NFBC 1966 regarding educational level at the age of 31 years, being or not being on disability pension, or cumulative number of psychiatric hospital treatment days.

2.4. Outcomes – neuropsychological assessments and change of cognition

A neuropsychological battery included the CVLT (California Verbal Learning Test; Delis et al., 1987), the VOLT (Visual Object Learning Test; Glahn et al., 1997) and the AIM (Abstraction, Inhibition, Memory; Glahn et al., 2000). These tests were administered at both baseline and follow-up (Juola et al., under revision, Kobayashi et al., 2014, Rannikko et al., 2015).

2.4.1. Verbal learning and memory

The CVLT was administered and scored by trained examiners in a fixed order in exactly the same way at baseline and follow-up. The CVLT was the only word-list memory task administered in a given neuropsychological test session to minimize possible interference effects between tests. The CVLT provides a brief, individually administered assessment of multiple strategies, processes, and errors involved in learning and remembering verbal material (Delis et al., 1987).

The following variables describing different domains of verbal learning and memory were analysed in this study: 1. *Immediate free recall* – performance (correct responses) on List A provides a sum of trials 1 through 5. 2. *Long delay free recall* – the number of correct responses on List A in any order and by category after 15–20 min interval, reflects the examinee´s ability to retain verbal information over time. 3. *All intrusions* – the type of recall errors, which are responses not on the target list on short and long delay.

2.4.2. Visual learning and memory

The VOLT, a measure of visual-spatial learning and memory, was developed to examine aspects of visual-spatial learning and memory in a manner analogous to available verbal tests (e.g., CVLT). Like the CVLT, the VOLT has multiple learning trials, although the VOLT consists of four rather than five, followed by an interference list, as well as short delay and long delay trials (Glahn et al., 1997).