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Predictors and longitudinal course of cognitive functioning in schizophrenia spectrum disorders, 10 years after baseline: The OPUS study

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ABSTRACT

Background: Identifying baseline predictors of the long-term course of cognitive functioning in schizophrenia spectrum disorders is important because of associations between cognitive functioning (CF) and functional outcome. Determining whether CF remains stable or change during the course of illness is another matter of interest.
Methods: Participants from The Danish OPUS Trial, aged 18–45 years, with a baseline ICD-10 schizophrenia spectrum diagnosis, were assessed on psychopathology, social and vocational functioning at baseline, and cognitive functioning 5 (N = 298) and 10 years (N = 322) after baseline. Uni- and multi-variable regression analyses of potential baseline predictors of 10-year CF were performed. Also, changes in CF and symptomatology between 5 and 10 years of follow-up were assessed.
Findings: Baseline predictors of impaired CF after 10 years included male gender, unemployment, poor premorbid achievement and later age of onset. Having finished high school and receiving early intervention treatment was associated with better CF. Age, growing up with both parents, number of family and friends, primary caregivers education, premorbid social function, negative symptoms, GAF (symptoms, function) and substance abuse, were associated with CF in univariable analyses. Non-participants generally suffered from more severe dysfunction. Longitudinally, amelioration in negative symptoms was associated with improved speed of processing and executive functions. Symptom scores generally improved with time, while scores for all cognitive tests remained stable.
Conclusion: The current study identifies several robust associations between baseline characteristics and 10-year cognitive outcome. Several other variables were univariably associated with 10-year cognitive outcome. Also, we found evidence for stability of CF over time.

1. Introduction

Cognitive deficits are cardinal features in schizophrenia (Galderisi et al., 2009). They are strongly related to poor social, and functional outcome, and little influenced by antipsychotic treatment. Studying cognitive functioning (CF), throughout the course of schizophrenia, may help in elucidating whether CF continues to decline after onset of the disorder (Kahn and Keefe, 2013). Schizophrenia is likely to be a neurodevelopmental disorder, or a collection of neurodevelopmental disorders, involving alterations in brain circuits (Insel, 2010). The Kraepelinian view of a deteriorating disease; with a course leading to severe cognitive decline, is only poorly supported by evidence (Zipursky et al., 2013). If substantial neurodegeneration and progressive brain tissue loss occurred over the course of illness, one would expect a concurrent progressive deterioration in CF. Although studies report a decline in certain CF's over time (Kobayashi et al., 2014; Meier et al., 2014), robust evidence suggest that CF remains stable, or improve, rather than deteriorate following a first episode of psychosis (Szöke et al., 2008).

Studies on the longitudinal course of cognition in schizophrenia spectrum disorders, enable investigation of correlates of change in CF. Associations have been found between improved CF and reduced negative symptoms (Censits et al., 1997; Gold et al., 1999; Rodríguez-Sánchez et al., 2013), and with global symptomatology (Irani et al., 2012), but there are also studies reporting no association (Hoff et al., 2005). CF plays a key role in everyday life; whether it concerns planning for dinner

Abbreviations: (SPD), Schizotypal personality disorder; (CF), Cognitive functioning; (GCF), Global cognitive functioning; (VLM), Verbal learning and memory; (SP), Speed of processing; (RPS), Reasoning and problem solving; (DUP), Duration of untreated psychosis.

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or remembering which groceries to purchase. Also, CF predicts functional outcome, including quality of life, in patients with schizophrenia spectrum disorders (Green et al., 2004). Investigation of associations between baseline factors and long-term CF (i.e. after 10 years) can be useful in the prediction of future functional outcome, and the prospects of patients living an independent life after their first contact with mental health services. For schizophrenia, suggested predictors of CF include educational level (Galderisi et al., 2009); young age of onset (Rajji et al., 2009), male gender (Goldstein et al., 1998), negative or disorganised symptoms (Dominguez et al., 2009; Ventura et al., 2010), and poor premorbid adjustment (González-Blanch et al., 2008; Rund et al., 2004). The role of duration of untreated psychosis (DUP) appears uncertain (Norman et al., 2001) as does the potential impact of comorbid substance abuse (Dickerson et al., 2014).

The Danish OPUS Trial (Petersen et al., 2005) has followed participants with first-episode schizophrenia spectrum disorders over a decade. From these data, we aim to investigate whether a range of factors, previously found to be associated with CF in schizophrenia, are predictive of 10-year CF. Also, we aim to explore whether changes in CF correlate with changes in symptom severity. Lastly, we investigate whether CF remain stable during the later course of illness.

2. Material and methods

2.1. Participants and study design

This study is part of a large prospective cohort study. All participants originate from the OPUS I trial (Petersen et al., 2005) evaluating the effects of specialised early intervention (OPUS treatment) versus treatment as usual. A small group of severely ill participants received hospital based intensive long-term treatment (Ohlenschlaeger et al., 2007). There were originally 578 participants aged 18–45 years with a diagnosis within the schizophrenia spectrum (ICD-10, F20-29), recruited between the years of 1998 and 2000 in the catchment areas of the two largest cities in Denmark, Copenhagen and Aarhus (Fig. 1). None of the participants had received more than 12 weeks of antipsychotic medication before inclusion. After two years, participants receiving OPUS treatment were transferred to treatment as usual, and all participants were invited to participate in 5 and 10-year follow-up. A wide range of data was collected at all time-points. At the 5-year follow-up, 314 subjects participated, whereof 298 completed a small cognitive test battery. At the 10-year follow-up, 322 participants completed a comprehensive cognitive assessment, whereof 273 had a complete record of data on socio-demographic, premorbid and clinical characteristics for inclusion in the analyses. We included participants with a full record of baseline variables, exclusively. Analyses of change in psychopathology and CF from 5 to 10 years were based on 171 participants who took part in cognitive testing at both time points, and presented a complete record of symptoms. The trial was approved by the local ethics committee.

2.2. Measures

Psychopathologic assessments were carried out using face-to-face semi-structured interviews performed by trained staff that maintained a moderate to high degree of inter-rater reliability (Petersen et al., 2005). Psychiatric diagnosis and comorbidity were assessed using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Wing et al., 1990). Chapters 11 and 12 of SCAN were used for evaluation of substance abuse. Symptoms were assessed using Scales for Assessment

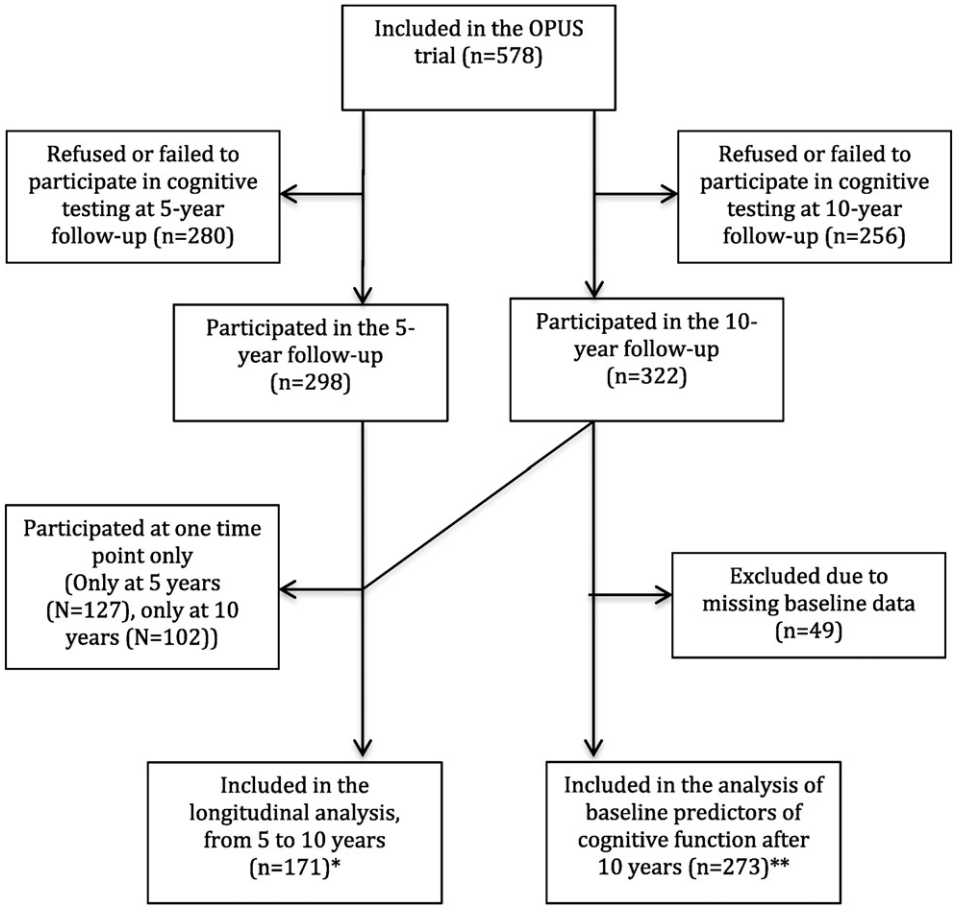

Fig. 1. Flow chart of participants from the OPUS cohort included in the study, based on participation in cognitive testing at 5 and 10-year follow-up *Out of the 322 participants who took part in the 10-year follow-up, 171 had also participated at the 5-year follow-up. The longitudinal analyses are based on this subgroup.

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