Psychiatry Research ■ (■■■■) ■■■–■■■

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Changes in verbal learning and memory in schizophrenia and non-psychotic controls in midlife: A nine-year follow-up in the Northern Finland Birth Cohort study 1966

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ARTICLE INFO

Article history:
Received 9 June 2014
Received in revised form
8 April 2015
Accepted 20 April 2015

Keywords:
Population-based birth cohort study
Schizophrenia
Cognition
California Verbal Learning Test
Follow-up

ABSTRACT

Findings on longitudinal change of cognitive performance in schizophrenia are extremely variable in the case of verbal learning and memory, and it is still unclear which dimensions of verbal learning and memory exhibit possible deterioration over the long-term. Our aim was to compare the change in verbal learning and memory in individuals with schizophrenia 10–20 years after the illness onset and healthy controls during a nine-year follow-up in a general population sample. Our sample included 41 schizophrenia spectrum subjects and 73 controls from the Northern Finland Birth Cohort study 1966. The California Verbal Learning Test (CVLT) was used to estimate the degree of change in verbal learning and memory during a nine-year follow-up from age 34-years to 43- years. Both cases and controls deteriorated. There was statistically significant decline in two out of 20 CVLT items among cases and in 13 out of 20 CVLT items among controls. With the exception of two variables, the decline in verbal learning and memory over nine years was not significantly larger in cases. We conclude that during midlife verbal learning and memory in schizophrenia mostly declines in a normative fashion with aging at the same rate as the general population.

1. Introduction

It is widely established that neurocognitive deficits are a core feature of schizophrenia, but controversy exists about whether and when further progression in neuropsychological impairment may occur (Ekerholm et al., 2012; Hedman et al., 2013). Individuals with schizophrenia show pronounced deficits in many areas of neurocognitive functioning including particularly memory functions (Ekerholm et al., 2012). When read a story or list of words they remember less than healthy controls (Saykin et al., 1991), and if the list or story is repeated, patients with schizophrenia learn much less than healthy controls. Even so, a sizeable proportion of individuals with schizophrenia have normal performance on any one test: for example, in one study, 44% of subjects with schizophrenia, schizoaffective disorder or delusional disorder had

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http://dx.doi.org/10.1016/j.psychres.2015.04.048
0165-1781/

normal learning ability as measured by the Rey Auditory Verbal Learning Test (RAVLT) (Karilampi et al., 2007).

In a meta-analysis of cross-sectional first-episode studies, cognitive impairments were reliably and broadly present by the first-episode or early phase schizophrenia, and were maximal in immediate verbal memory and processing speed, compared to other neuropsychological domains (Mesholam-Gately et al., 2009).

In a recent meta-analysis on change of global IQ, less prominent improvement in IQ in schizophrenia subjects compared to healthy controls was found (Hedman et al., 2013). Another meta-analysis showed large and generalized cognitive deficits in older individuals with schizophrenia, but these deficits did not decline over a 1–6 year period (Irani et al., 2010). A first-episode study followed up over 10–20 years presented that some domains of cognition might already have deteriorated by the first-episode, but do not progress over time; on the other hand other domains of cognitive functioning might be spared during the first-episode but deteriorate with time (Stirling et al., 2003). Taken together, these lines of evidence suggest that the neurocognitive impairments in general in schizophrenia do not deteriorate significantly during the midlife (Censits et al., 1997; Hoff et al., 2005). However, in the domain of the verbal learning and memory, there is some evidence of further deterioration over the long term, and there is a need for further studies on this topic (Bozikas and Andreou, 2011).

Findings on longitudinal change of cognitive performance are extremely variable in the case of verbal memory and learning. Some studies show less improvement with practice, or even deterioration in cases compared to controls on some measures of verbal memory (Hill et al., 2004; Hoff et al., 2005; Albus et al., 2006) while others report no difference (Censits et al., 1997; Heaton et al., 2001; Hoff et al., 2005; Albus et al., 2006; Leeson et al., 2009) or even greater improvement in cases compared to non-psychotic controls on at least some measures of verbal memory (Addington et al., 2005).

One reason for divergent findings may be differences in length of follow-ups. In short follow-ups (maximum two years) in first-episode samples both cases and controls improved in many cognitive domains, including verbal learning and memory (Addington et al., 2005; Mayoral et al., 2008). One possible explanation for this could be practice effect and improvement in symptoms. In contrast, in studies with follow-ups from two to 10 years, cases improved less compared to controls over time in memory functions (Hoff et al., 2005; Albus et al. 2006; Leeson et al., 2009; Ekerholm et al., 2012). In studies with longer follow-up (over 10 years) cases may perform more poorly or show deterioration compared to healthy controls in different measures of verbal learning and memory (Hoff et al., 1999; Hoff et al., 2005), but in some studies do not show evidence of cognitive decline in memory functioning over time (Caspi et al., 2003).

Understanding the longitudinal changes in cognitive performance is important for the etiological investigation of schizophrenia and for treatment purposes, but the number of studies in this area is small. Generally, long-term follow-up of general population-based samples with inclusion of controls and individuals with schizophrenia, especially in a later phase of the illness, are still scarce. Furthermore, it is still relatively rare to have similar cognitive measures in both cases and controls at two-time points. In this same Northern Finland Birth Cohort study 1966 (NFBC 1966) sample Kobayashi et al. (2014) found that between the ages of 34 and 43 the schizophrenia group exhibit progressive cognitive decline in executive function, but there were no differences between cases and controls in rate of change of visual object learning or change in one indicator of verbal learning. Kobayashi et al. (2014) studied only one of the several items from the California Verbal Learning Test (CVLT). Verbal learning and memory in schizophrenia has received considerable attention by cognitive neuropsychology and severe verbal learning impairment has been established. However, it is still unclear in which dimensions of verbal learning and memory deterioration over the long follow-up occurs.

The aim of our study was to compare the change in several dimensions of verbal learning and memory in individuals with schizophrenia in midlife 10–20 years after the illness onset and healthy controls during a 9-year follow-up in the general population-based NFBC 1966. We had the opportunity to study the changes in verbal learning and memory in schizophrenia and non-psychotic controls in midlife from age 34 to age 43 in large, unselected, epidemiologically sound sample. To our knowledge, there are no previous studies on this topic with this length of follow-up in this age group. Our research hypothesis was that subjects with schizophrenia would experience less improvement, or more deterioration, in measures of verbal learning and memory when compared to healthy controls.

2. Methods

2.1. Participants

The NFBC 1966 is an unselected general population birth cohort ascertained during mid-pregnancy. The NFBC 1966 consist of 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 these, 83 individuals did not consent to the use of their data and have been excluded. The Faculty of Medicine Ethics Committee of the University of Oulu keeps the study design of the NFBC 1966.

A psychiatric field study including diagnostic interviews and the CVLT was conducted in 1999–2001 (baseline, around age 34 years), with follow-up in 2008–2010 (around age 43 years). Participants were given a complete description of the study and had an opportunity to refuse to participate at baseline and follow-up. All participants provided written informed consent.

2.2. Case identification

The nationwide Finnish Hospital Discharge Register (FHDR) covers all mental and general hospitals, as well as beds in local health centers and private hospitals nationwide. All cohort members over 16 years appearing on the 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). Altogether 160 individuals with known psychotic episodes until the year 1999 were detected. The detection of cases and validation of diagnoses are described in Moilanen et al. (2003). Fourteen psychosis cases (8.8%) had died by the year 2001 (Alaräisänen et al., 2006).

At baseline, during 1999–2001 around age 34-years all 146 living cases (62 females, 42%) and 187 controls (71 females, 38%) were invited to participate in the field study. Altogether 92 (63%) cases (73 (79%) with schizophrenia spectrum disorders) and 104 (56%) controls participated. Controls were randomly selected from the NFBC 1966 members who were living in Oulu area, and who did not have any history of psychotic disorder (Haapea et al., 2007).

The Structured Clinical Interview for DSM-III-R, (SCID I; Spitzer et al., 1989) was used for diagnostic assessment, together with all available anamnestic information including individual hospital notes. SCID I was performed for both cases and controls at both baseline and follow-up assessments. At baseline, after diagnostic interviews a total of 61 cases with a lifetime diagnosis of schizophrenia and 12 cases with other schizophrenia spectrum disorder were detected. Hereafter in this paper we use term “schizophrenia” meaning schizophrenia and other schizophrenia spectrum disorders (in our study including schizophreniform disorder, schizoaffective disorder and delusional disorder). Mean duration of illness was 10 years (S.D. 4.3) at baseline. The field study in 1999–2001 is presented in detail in Haapea et al. (2007).

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. Of the individuals with schizophrenia 44 (60%) and 76 (73%) of the control subjects participated in the follow-up. The mean duration of illness until the follow-up study was 20.0 years (S.D. 4.1). The SCID I interview (First et al., 2002) was performed in the follow-up as well. The original diagnosis was upheld at follow up for all participants with schizophrenia on the basis of the SCID I interview and case note review.

Please cite this article as: Rannikko, I., et al., Changes in verbal learning and memory in schizophrenia and non-psychotic controls in midlife: A nine-year follow-up in the.... Psychiatry Research (2015), http://dx.doi.org/10.1016/j.psychres.2015.04.048