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Premorbid IQ subgroups in first episode non affective psychosis patients: Long-term sex differences in function and neurocognition

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ABSTRACT

Background: Low IQ has been associated with schizophrenia, even to the point of being posited as a possible causal factor for psychosis. However, individuals with normal and high IQ also develop psychotic illnesses. The aim of this study was to characterize premorbid IQ subgroups at first episode of psychosis (FEP).
Methods: The study sample comes from a large epidemiological, 3-year longitudinal, intervention program on psychosis containing individuals living in a catchment area in Spain. Estimated premorbid IQ (epIQ) scores were used to build low (<90), normal (90–110) and high (>110) epIQ subgroups in samples of FEP patients (N = 292) and healthy controls (N = 199). The epIQ subgroups were compared in sociodemographic, neuropsychological, clinical and premorbid characteristics. Long-term functional and cognitive outcome, with a focus on sex differences, were also explored.
Results: Low-epIQ was more frequently found in FEP patients (28.8%) than in healthy controls (14.6%). Low-epIQ patients were more likely to have worse premorbid adjustment, belong to low socioeconomic status families, have less years of education, and to be single, unemployed, and younger. They presented more severe impairments in processing speed, executive and global cognitive function. Female patients with low-epIQ showed better baseline function and more stable outcome than males.
Conclusions: Our results indicate that low premorbid IQ is a morbid manifestation, easily detected in a subgroup of FEP patients that predicts poorer outcome particularly in males. This perspective provides important information for the tailoring of subgroup-specific early intervention programs for psychosis.

1. Introduction

The study of intelligence in schizophrenia has a long history. A meta-analysis of the research on this topic, carried out by Aylward and colleagues (1984) in the early 1980s, found that the risk of developing both early and adult-onset schizophrenia was associated with intellectual deficits across the lifespan, and that several indices of prognosis were related to IQ. The hypothesis was echoed by Andreasen and Olsen (1982), who suggested that patients suffering from structural central nervous system impairment and concomitant cognitive deficits would be identifiable long before the first onset of psychotic symptoms, in terms of premorbid adjustment and premorbid IQ. More recent meta-analyses have confirmed the association between low premorbid IQ and increased risk for schizophrenia. Years before illness onset, individuals with schizophrenia, as a group, demonstrate mean IQ scores approximately one-half of a standard deviation below that of healthy comparison subjects (Woodberry et al., 2008). The largest meta-analysis to date, which included 4396 cases and over 745,000 controls from 12 independent longitudinal studies, confirmed that a lower premorbid IQ increased the risk of schizophrenia as a consistent dose-response effect of 3.7% for every point decrease in IQ (Khandaker et al., 2011). However, the nature of the association between IQ and schizophrenia is not known and cannot be ascertained from these studies.

Researchers in the cognitive epidemiology field argue that intelligence measured at an early age is an important predictor of later health and mortality differences (Wraw et al., 2015). Meier and colleagues (2014) conducted a premorbid to post-onset study that found that individuals with schizophrenia exhibit declines in IQ within a range of

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mental functions (particularly in processing speed), and that the deficits increased gradually from the age range of 7–13 to age 38. Other prospective studies confirmed that individuals who developed schizophrenia in later life are significantly impaired on non-verbal and verbal intelligence tests from the age of 8 (Jones et al., 1994). These results clearly indicate the presence of detectable cognitive abnormalities in childhood, which pre-date the development of the illness. Furthermore, recent meta-analyses showed the mean weighted baseline IQ was 97.20 for schizophrenia patients and 109.26 for controls, showing patients less prominent improvement in IQ over time (Hedman et al., 2013). Contrary to these findings, Ayesa-Arriola and colleagues (2013) reported the presence of a subgroup of patients (around 40%) who did not present cognitive impairment during the first episode of psychosis (FEP). From the perspective of a theory of schizophrenia that postulates cognitive dysfunction as a feature of the diagnostic entity, the existence of a subset of cases with above normal cognitive performance should be regarded as an anomaly. MacCabe et al. (2012) proposed that schizophrenia patients who have markedly superior premorbid intellectual level may constitute a discrete subgroup of schizophrenia who have suffered less neurodevelopmental damage. Germaine to this proposal, Cernis and colleagues (2015) found a high-IQ subgroup of patients markedly associated with fewer negative symptoms. These analyses of subgroup characteristics remind us of the fact that individuals with schizophrenia are heterogeneous in nature and that a research approach that considers subsample definitions might explain some of the heterogeneity.

Several authors have previously used an IQ subgrouping approach as a strategy to explore variability related to intellectual levels of competence. In Kremen et al. (2001), schizophrenia patients (N = 36) and matched control subjects (N = 36) were subgrouped into low (81–94) and average IQ (95–119), showing that even those with normal IQ had neurocognitve deficits. Badcock et al. (2005) identified subgroups of schizophrenia patients with preserved (N = 45), deteriorated (N = 47) and compromised (N = 17) intellect, controlling for estimated premorbid IQ and current IQ differences. In the same vein, Ammari and colleagues (2014) assessed schizophrenia and schizoaffective disorder patients (N = 101) and control participants (N = 80), showing that patients with deteriorated and compromised patterns were equivalent to controls, while preserved patients presented cognitive impairments relative to controls. Vaskinn et al. (2015) showed evidence of deficits in a superior intelligence subgroup of schizophrenia patients (N = 20) by comparing the neuropsychological profile with IQ-matched healthy controls (N = 50). However, longitudinal studies with FEP patients subgrouped by premorbid IQ are less frequent and certainly needed. Leeson et al. (2011) conducted a 3-year follow-up study of 129 FEP individuals (25% showed stable low IQ, 31% stable IQ in the average/high range, and 44% intellectual deterioration). The low IQ group demonstrated no change in IQ, whereas both the deteriorated and the preserved IQ groups improved.

Subgrouping by sex is another research strategy approach we have previously used (Ayesa-Arriola et al., 2014). Flaum et al. (1994) found IQ and sex-related differences in brain structure/function in schizophrenic patients versus normal control subjects, showing female patients a pattern of correlations similar to that of normal control subjects while no such relationship was apparent among the male patients. Most studies have shown better premorbid functioning, and social adjustment for women compared with men (Thara and Kamath, 2015). Thus, sex differences in the course of schizophrenia seem to be determined by a complex pattern of interactions between biological and behavioural differences, the consequence of age at illness onset and course (Mendrek and Mancini-Marie, 2016). To the best of our knowledge, no previous studies have addressed sex differences in outcome related to premorbid IQ.

The aim of the present study was to characterize subgroups of low, normal and high premorbid IQ in a large and homogeneous sample of first episode non-affective psychosis patients. We hypothesized that the FEP patients with low premorbid IQ would be characterized as a distinct subgroup of schizophrenia with poorer cognitive and functional outcome, and that this outcome would be more salient for males.

2. Methods

2.1. Participants

The study sample comes from a large epidemiological, 3-year longitudinal intervention program on first-episode psychosis (PAFIP) at the University Hospital Marques de Valdecilla (Santander, Spain). Ethical approval was obtained from the local Ethics Committee. A more detailed description of PAFIP has been previously given (Crespo-Facorro et al., 2006; Pelayo-Teran et al., 2008).

The patient group consisted of 397 medication-naive subjects (age: 15–60, M: 29.84) included in the first-episode psychosis program of Cantabria, Spain, (PAFIP) recruited between February 2001 and February 2011. Written informed consent was obtained from all participants after a complete description of the study. The patients met the following criteria: 1) 15–60 years of age; 2) lived within the catchment area; 3) were experiencing a first episode of psychosis; 4) had no prior treatment with antipsychotic medication or, if previously treated, a total life-time of antipsychotic treatment of <6 weeks; and 5) met the DSM-IV criteria for brief psychotic disorder, schizophreniform disorder, schizophrenia or not otherwise specified (NOS) psychosis. The diagnoses were confirmed through the use of the Structured Clinical Interview for DSM-IV (SCID–I) (First et al., 1996), conducted by an experienced psychiatrist within six months from the baseline visit.

A group of 221 healthy volunteers (age: 15–51 years, M: 29.58) were recruited from the community through advertisements. They had no current or past history of psychiatric, neurological or general medical illnesses, including substance abuse and significant loss of consciousness. The abbreviated version of the Comprehensive Assessment of Symptoms and History (CASH) (Andreasen et al., 1992) was completed by a trained interviewer.

2.2. Definition of premorbid IQ subgroup

Vocabulary, as a measure of crystallized intelligence, has been extensively used to generate an estimate of the intelligence quotient (IQ) (Ringe et al., 2002). The WAIS-III Vocabulary subtest (Wechsler, 1997) was used to estimate premorbid IQ in the first episode psychosis (FEP) patients and as a measure of estimated IQ in the healthy controls (HCs) (Lezak, 1995). The choice of WAIS-III Vocabulary as a proxy measure for premorbid intelligence was based on it being a measure of crystallized intelligence associated with an individual's knowledge base, which includes linguistic information such as the phonology and semantics of the intended speaker's native language. As stated by de Oliveira and colleagues (2014), ideal premorbid IQ measures should be little impacted by a neurocognitive disease. These authors confirm the stability of Vocabulary during the progression of dementia. Estimated premorbid IQ scores (epIQ) were calculated using centiles correspondence for standard scores. Following Wechsler's (Wechsler, 1997) classification based on the deviation from the median level of performance within the group, both FEP patients and HCs were stratified into three epIQ subgroups: low (epIQ < 90), normal (epIQ = 90–110), and high (epIQ > 110).

2.3. Premorbid and sociodemographic information

Premorbid and sociodemographic information was recorded from interviews with patients, their relatives and from medical records at admission. Sex, age, age of psychosis onset (defined as the age when the emergence of the first continuous [present most of the time] psychotic symptom occurred), and duration of untreated psychosis (DUP, defined as the time from the first continuous [present most of the time]

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