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Cognitive reserve as a predictor of two year neuropsychological performance in early onset first-episode schizophrenia

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ABSTRACT

Introduction: The concept of cognitive reserve (CR) has been defined as individual differences in the efficient utilization of brain networks which allow some people to cope better than others with brain pathology. CR has been developed mainly in the field of aging and dementia after it was observed that there appears to be no direct relationship between the degree of brain pathology and the severity of clinical manifestations of this damage. The present study applies the concept of CR to a sample of children and adolescents with a first episode of schizophrenia, aiming to assess the possible influence of CR on neuropsychological performance after two year follow-up, controlling for the influence of clinical psychopathology.
Methods: 35 patients meeting DSM-IV criteria for schizophrenia or schizoaffective disorder (SSD) and 98 healthy controls (HC) matched for age and gender were included. CR was assessed at baseline, taking into account premorbid IQ, educational–occupational level and leisure activities. Clinical and neuropsychological assessments were completed by all patients at two year follow-up.
Results: The CR proxy was able to predict working memory and attention at two year follow-up. Verbal memory and cognitive flexibility were not predicted by any of the variables included in the regression model. The SSD group obtained lower scores than HC on CR. CR measures correctly classified 79.8% of the sample as being SSD or HC.
Conclusions: Lower scores on CR were observed in SSD than in HC and the CR measure correctly classified a high percentage of the sample into the two groups. CR may predict SSD performance on working memory and attention tasks.

1. Introduction

The concept of cognitive reserve (CR) has developed in the field of aging and dementia after it was observed that people with the same amount of brain damage could show different clinical expressions depending on their compensatory capacity. CR has been defined as "individual differences in how people process tasks which allow some to cope better than others with brain pathology" (Stern, 2009). This concept is focused on the ability to optimize performance based on more efficient brain network utilization, and may vary depending on environment and lifetime exposure to certain environmental factors.

Although it has been used primarily in the fields of dementia and brain injury, this concept could potentially be applicable to a whole range of neurological and psychiatric conditions. For example, CR could play an important role in the expression of symptoms and functional outcome of schizophrenia patients (Barnett et al., 2006). Studies have shown that patients with schizophrenia with better performance on cognitive tests have better social and functional outcomes (Green et al., 2000; Munro et al., 2002). Holthausen et al. (2002) studied a

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sample of 118 first episode of psychosis patients and classified them according to the presence or absence of cognitive deficits. Results showed that patients with normal cognitive functioning had higher scores on IQ measures and higher educational levels than patients with cognitive difficulties. The authors suggested that the observed differences may have been due to the higher compensation capacity or higher CR of the group with normal cognitive functioning.

An important caveat when investigating CR is the absence of any single measure of this concept. Variables such as occupational and educational attainment, leisure activity and IQ have been used as CR proxies (Stern, 2009). Staff et al. (2004) tested three possible CR proxies (head size, education and occupational attainment) and observed that while education and occupational attainment contributed to CR, intracranial volume did not. There is no consensus as to which CR measures (premorbid IQ, education, occupation or leisure activities) could be the most representative. In the present study, CR was measured with the main CR proxies used in previous literature (i.e. Scarmeas and Stern, 2003; Stern et al., 2005), premorbid IQ, which is thought to partially reflect an 'innate reserve capacity', and educational–occupational attainment and leisure activity, which more directly reflect lifetime exposure to particular environmental factors that help develop mental capacities.

Studies in child and adolescent samples with a first episode of schizophrenia have observed a broad range of neuropsychological difficulties in cognitive domains such as attention, working memory, executive function, verbal learning and memory (Kenny et al., 1997; Fagerlund et al., 2006; Mayoral et al., 2008; Zabala et al., 2010). Most of these deficits have been associated in young adults with premorbid functioning and educational and occupational levels (Silverstein et al., 2002; Norman et al., 2005; Rund et al., 2007), which are considered part of CR. However, studies in young patients have also observed that clinical manifestations such as negative symptoms play an important role in neuropsychological performance (Bilder et al., 2000; Fitzgerald et al., 2004). Taking this previous research into account, the aim of the present study was, first, to employ the concept of CR with a sample of children and adolescents with a first episode of schizophrenia in order to compare them to control subjects. The second aim was to assess the influence of CR on neuropsychological performance after a two year follow-up of schizophrenia patients while controlling for the influence of clinical psychopathology.

We hypothesized that the schizophrenia spectrum disorder group (SSD) would show lower CR measures than healthy controls (HC). Moreover, we expected that neuropsychological variables after two years could be predicted by baseline CR measures.

2. Methods

This research was part of the Child and Adolescent First-episode Psychosis study (CAFEPS), a multi-center, longitudinal study aimed at evaluating different clinical, neuropsychological and biological factors, as well as treatment and prognostic factors in these patients; the corresponding methodology has been described previously in detail (Castro-Fornieles et al., 2007). The CAFEPS study included 110 patients aged between 9 and 17 years diagnosed with a first episode of psychosis, and 98 matched healthy controls. Patients were recruited from child and adolescent psychiatry units at six university hospitals and assessed by mental health professionals with experience diagnosing and evaluating subjects with semi-structured interviews and clinical scales. Inclusion criteria for patients were: a) an onset of positive psychosis symptoms less than 6 months prior to baseline assessment and b) age between 7 and 17 years. Exclusion criteria included: a) presence of another concomitant Axis I disorder at the time of assessment that could account for the psychotic symptoms, including substance-induced psychotic disorder, post-traumatic stress disorder, or acute stress disorder; b) IQ below 70 with impaired functioning; c) pervasive developmental disorder d) neurological disorders, including history of head trauma with loss of consciousness; and e) pregnancy. Occasional and regular substance use was not an exclusion criterion if positive symptoms persisted for more than two weeks after a negative urine toxicology test and a substance-induced psychotic disorder was not diagnosed. Socioeconomic status of the whole sample was estimated with the Hollingshead Redlich Scale (Hollingshead and Redlich, 1958).

The healthy control group was matched by age and gender to patients. Sample recruitment and description of both patients and healthy controls have been detailed previously (Castro-Fornieles et al., 2007).

The study was approved by the Ethical Review Board of each hospital. All patients and controls and their parents or legal guardians provided written informed consent.

2.1. Subjects

Patients were given clinical and CR assessments at baseline and neuropsychological assessments at two year follow-up. To homogenize the sample and guarantee the stability of the diagnosis, only subjects diagnosed with schizophrenia or schizoaffective disorder (SSD) at the two-year follow-up were included in the study. This group comprised only 35 patients from the total CAFEPS sample. A healthy control group (HC) of 98 subjects matched for age and gender was also recruited.

2.2. Clinical assessment

Clinical assessment at baseline consisted of:

- Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version (K-SADS-PL) (Kaufman et al., 1997) using the Spanish validated adaptation; This is a semi-structured interview, which was administered by psychiatrists trained in the use of the instrument and in the assessment of children and adolescents. Parents and children from both the patients group and control group were interviewed separately.
- Positive and Negative Syndrome Scale (PANSS): This is a 30 item rating scale which aims to assess the symptom severity of patients with psychosis. It is subdivided into three subscales-positive, negative and general psychopathology- and a total score (Kay et al., 1987; Peralta and Cuesta, 1994). Each subscale is evaluated from 1 to 7 according to the severity of the symptoms.

2.3. Assessment of cognitive reserve

Our determination of the main proxies of CR was based on recent literature in the field, with special consideration given to the areas most commonly included in cognitive reserve questionnaires (Bartres-Faz et al., 2009; Sole-Padulles et al., 2009; Bosch et al., 2010). As a result, the CR measure was composed of an estimation of premorbid IQ and a measure of education–occupation levels and lifetime leisure-social activities.

- Premorbid IQ was assessed between 4 and 8 weeks after admission when patients had reached clinical stability. Premorbid IQ was estimated using the Vocabulary subtest of the Wechsler Adult Intelligence Scale—III Revised (WAIS III) (Wechsler, 2001) or the Wechsler Intelligence Scale for Children—Revised (WISC-R) (Wechsler, 1974), depending on the subject's age. Direct scores of the subscale were translated to standard scores, which have a mean of 10 and a standard deviation of 3.
- Education–occupation (EO). Education–occupation was assessed taking into account the number of years of obligatory education that subjects had completed, school performance before the beginning of the disorder, parents' educational level and questions about the children's development in terms of language, reading, writing and motor functions. EO could have values between 0 (low level of CR) and 33 (high CR).