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Stability of executive functions in first episode psychosis: One year follow up study

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ABSTRACT

Executive functioning is a multi-dimensional construct covering several sub-processes. The aim of this study was to determine whether executive functions, indexed by a broad range of executive measures remain stable in first episode psychosis (FEP) over time. Eighty-two patients and 107 age and gender matched healthy controls were assessed on five subdomains of executive functioning; working memory, fluency, flexibility, and inhibitory control at baseline and at 1 year follow-up. Results showed that patients performed significantly poorer than controls on all executive measures at both assessment points. In general executive functions remained stable from baseline to follow-up, although both groups improved on measures of inhibitory control and flexibility. In phonemic fluency, controls showed a slight improvement while patients showed a slight decline. Investigation of individual trajectories revealed some fluctuations in both groups over time, but mainly supports the group level findings. The implications of these results are discussed.

1. Introduction

Impairments in executive functioning are evident in the majority of schizophrenia spectrum patients, and are observed throughout all stages of the illness (Rund et al., 2007; Holmen et al., 2012b; Barder et al., 2013a, 2013b; Sanchez-Torres et al., 2013). Executive dysfunction is present already in the first year of the illness, even before the first contact with the public health care service (Hoff et al., 2005), and is a contributing factor to functional loss and disability. Executive functioning predicts degree of self-care, as well as social, interpersonal, community, and occupational functioning (Mcgurk and Mueser, 2003; Bowie and Harvey, 2006), and is associated with treatment success. Impairments in this domain are coupled with less engagement in therapy, poorer medication adherence, and longer hospital stays (McKee et al., 1997; Jackson et al., 2001; Robinson et al., 2002; Bowie and Harvey, 2006).

There is no established consensus of which tests are best suited to assess executive functions, nor is there any single test that assesses all components of executive function. Thus, some criticism has been directed towards an inconsistently defined executive domain (Bozikas and Andreou, 2011) and longitudinal studies have shown ambiguous findings (Liu et al., 2011). Executive functioning is a multi-dimensional construct covering several sub-processes including, working memory, fluency, flexibility, inhibitory control and problem-solving. In general, longitudinal studies of executive functioning have investigated a limited range of cognitive sub-processes, and yet refer to executive function as a whole (Frangou, 2010). This may lead to misinterpretations, since results may be more related to the sensitivity and psychometric properties of the specific test used rather than specificity to the executive process being measured. Several reviews of neurocognition in schizophrenia report a discrepancy in effect sizes across different executive measures (Szoke et al., 2008; Aas et al., 2014). This could be due to variability in the difficulty level of the specific tests or to the degree of dysfunction in the different sub-functions being measured in the patient group, underlining the importance of using a variety of tests.

There is still an ongoing debate as to whether schizophrenia is a neurodegenerative disorder with brain related changes after illness onset or a neurodevelopmental disorder with debut early in life (Rund, 2009). This is critical knowledge with implications for illness recovery and future functioning. Still, executive functions

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Table 1
Demographic and clinical characteristics for patients and controls. Means, standard deviations, and results from group comparisons are reported.

1a: Demographics	**Patients**	**Controls**	**Group comparison**	
Age (years)	26.7(7.6)	28.6(6.8)	−1.8	0.073
Education (years)	12.1(2.2)	14.1(2.1)	−6.6	< 0.001
Estimated IQ (WASI)	102.5(14.8) (n81)	114.8(16.0)	−5.4	< 0.001
IQ matched subsample (n62)	109.0(9.9)	110.7(9.5)	−1.0	0.318
Sex (m/f)	50/32	62/45	$x^2(1, N=189)=0.2$	0.674
1b: Clinical characteristics	**Baseline**	**Follow-up**		
Age at onset	23.5(7.4)			
DUP(median)	45(1–1040[a])			
Diagnoses				
Schizophrenia	35(43%)			
Schizophreniform	9(11%)			
Schizoaffective	4(5%)			
Other psychosis	25(30%)			
Major depressive disorder	9(11.0%)			
On anti-psychotic medication ≥ 1	64(78.1%)			
Months on antipsychotic medication	2.6(3.1)			
GAF function	45.3(13.9)	53.4(15.5)		
GAF symptom	41.9(12.2)	50.0(15.9)		
PANSS positive score	15.6(5.0)	13.2(5.0)		
PANSS negative score	15.2(6.4)	13.8(5.8)		

PANSS: Positive and Negative Syndrome Scale.
GAF: Global Assessment of Functioning Scale.
[a] Range.

are reported as relatively stable from treatment start in patients with first episode psychosis (FEP). Longitudinal studies without a control sample generally report minor improvements over the first years, but an overall stability over longer periods (Rund et al., 2007; Cohen et al., 2012; Barder et al., 2013a, 2013b). The same stability is observed when patient samples are compared to healthy control subjects (Hoff et al., 2005; Bozikas and Andreou, 2011; Sanchez-Torres et al., 2013). In studies in which improvements are observed in patients (Addington et al., 2005; Hoff et al., 2005; Mayoral et al., 2008; Rodriguez-Sanchez et al., 2008; Szoke et al., 2008), the same pattern is most often also seen in the control subjects, indicating that changes may be due to practice effects or the natural development and maturation within the samples (Goldberg et al., 2007).

To ensure that possible findings are not the result of practice effects of repeated measurements, it is thus important to have an age and gender matched control group. This can also help to determine whether stability among patients actually reflects lack of development. Although practice effects which are often reported in patient studies might mask such a lack of development, relatively few studies include a control group (Szoke et al., 2008). An additional step in detecting actual changes in longitudinal studies is to calculate reliable change indices (RCI). This could provide information as to whether changes seen on the group level exist on the individual level, and whether these changes are reliable and unlikely to be caused by measurement error or practice effects (Heaton et al., 2001; Iverson, 2001; Parsons et al., 2009; Duff, 2012). Thus, the aim of this study was to determine whether executive functions remain stable over one year in first episode patients compared to a healthy age and gender matched control group, using a broad range of executive tests covering the executive subdomains of working memory, fluency, flexibility, and inhibitory control. Our main objective was to investigate performance in these functions over time and to define the magnitude of reliable changes on the individual level.

2. Methods

2.1. Participants

This study included 82 patients with first episode psychosis (FEP), defined as less than one year since starting their first adequate treatment for a DSM-IV diagnosis of schizophrenia (42.7%), schizophreniform disorder (11.0%), schizoaffective disorder (4.9%), major depression with mood incongruent psychotic symptoms (11.0%), and other psychosis (30.5%), as well as 107 healthy control participants from the ongoing Thematic Organized Psychosis (TOP) research in Oslo, Norway. All participants were recruited between 2005 and 2012. The average test-interval time between baseline and 12 months follow-up was 406.3 days (SD 66.5).

Diagnostic assessment was based on the "Structured Clinical Interview for DSM-IV, axis 1 (SCID-1; (First et al., 1995)) and symptom assessment on the Positive and Negative Syndrome Scale (PANSS; (Kay et al., 1987)). Psychosocial functioning was assessed with the Global Assessment of Functioning Scale split version (GAF-S; (Pedersen et al., 2007)). Age at first psychotic episode was calculated based on age at first psychotic symptoms (23.5 years, SD 7.4), DUP was measured as the time from onset of psychotic symptoms (the first week with PANSS score of 4 or above on the last one (item) of the Positive Scale items 1, 3, 5, 6 or general item 9) until start of first adequate treatment. The DUP median was 45 weeks (SD 198.4, range 1-1040). Medication use is reported in current usage of one or more antipsychotic drugs, in addition number of months the participants had been on their main antipsychotic medication.

The healthy control group was randomly selected from the same catchment area as the patient group using statistical records. Exclusion criteria for both groups were traumatic brain injury, neurological disorders and other medical condition interfering with brain functioning, or signs of mental retardation (IQ < 70). Also to ensure valid test performance all participants had a score ≥ 15, on the CVLT forced recognition task (CVLT-II (Delis et al., 2004). The healthy controls were screened before participating,