



Predictors of functional outcome in individuals at high clinical risk for psychosis at six years follow-up



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ABSTRACT

Background: The long-term functional status of subjects at ultra high risk for psychosis (HR) is relatively under investigated. This study explores baseline predictors of long-term functional outcome in HR subjects who did not convert to psychosis during a 6 years follow-up period.

Methods: A total of 154 HR were followed up for an average of 6 years. The primary outcome variable was global assessment of functioning at the last follow-up visit as assessed with the Global Assessment of Functioning tool. A multinomial logistic regression was performed to identify potential predictors of functional outcome.

Results: Baseline and follow-up data on functioning was available for 92 HR. Twenty-four (43%) individuals who did not convert to psychosis reported poor functioning at follow-up. Baseline scores in the GAF ($\text{Exp}(b) = 0.857$; 95% CIs: 0.75/0.97), employment status ($\text{Exp}(b) = 0.029$; 95% CIs: 0.00/0.268), and CAARMS total scores ($\text{Exp}(b) = 1.976$; 95% CIs: 1.00/1.14) predicted functional outcome in HR subjects at 6 years.

Conclusions: Despite the preventive treatments received, many individuals who did not convert to full-blown psychosis in the longer term do not functionally remit. These individuals are lower functioning, unemployed and have higher symptom loading at the time of their presentation to the prodromal clinic. Our study suggests the need for innovative treatments targeting long term functional status beyond the prevention of psychosis onset in the HR population.

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1. Introduction

Schizophrenia and psychotic disorders continue to be debilitating and associated with lifelong impairment in social and role functioning (Clement et al., 2014). The duration of untreated psychosis has been proposed to strongly influence functional outcome (Perkins et al., 2005; Hegelstad et al., 2012). Operationalized criteria to detect the presence of a putative prodromal stage for psychosis have been largely tested and used worldwide (Fusar-Poli et al., 2013b). These criteria are known as Ultra High Risk

(UHR), Clinical High Risk (CHR), At Risk Mental States (ARMS) (hereafter referred as clinical high risk, HR) and allow the preventative identification of subjects with a 30% risk of developing psychosis over a two year period (Fusar-Poli et al., 2012), mostly schizophrenia spectrum psychoses (Fusar-Poli et al., 2013a). While much attention has traditionally been given to predict transition to psychosis, only few studies have investigated the functional status of HR subjects who do not convert at follow-up. Recently a meta-analysis of functioning in subjects at high risk for psychosis demonstrated that HR subjects had a very large impairment in functioning than HC, but only small to moderate better functioning than subjects with a frank diagnosis of psychosis (Fusar-Poli et al., 2015). Although available treatment may reduce the risk of psychosis onset (Stafford et al., 2013), their impact on long-term functional outcomes remains unclear, with previous evidence indicating that non-converting individuals may remain at a

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lower level of functioning than matched healthy comparisons (Addington et al., 2011). Moreover, where functional status of HR individuals at follow-up has been studied, most have focused on short-term periods (up to 24 months) (Jalbrzikowski et al., 2013; Niendam et al., 2007; Bearden et al., 2011; Eslami et al., 2011; Sabb et al., 2010; Salokangas et al., 2014; Schlosser et al., 2012). To our knowledge there is no consensus regarding the definition of long-term observation period in the HR subjects, in this manuscript we have adopted a definition of long term follow-up of more than five years. Following this definition, relatively few studies assessed long term functional outcome (Lin et al., 2011; Velthorst et al., 2013; Carrion et al., 2013; Ziermans et al., 2014). Previous studies have shown that functioning of at risk subjects is stable over time (Cornblatt et al., 2012) whereas others have found an improvement in non-converters particularly in the year following the identification (Addington et al., 2011). Moreover, functional outcomes appear to be independent from the psychosis status (Carrion et al., 2013). While a lot of effort has been made to identify predictors of conversion (Fusar-Poli et al., 2011, 2014c) so far not enough is known about the possible predictors of functional outcome. Evidence suggests that negative symptoms (Salokangas et al., 2014; Schlosser et al., 2012; Velthorst et al., 2013; Valmaggia et al., 2013; Demjaha et al., 2012), mood/anxiety symptoms (Salokangas et al., 2014; Velthorst et al., 2013) and motor disturbances (Carrion et al., 2013), as well as positive (Salokangas et al., 2014), and disorganized (Salokangas et al., 2014; Eslami et al., 2011; Carrion et al., 2013; Demjaha et al., 2012) symptoms at baseline predict the functional outcome at follow-up. The presence of formal thought content disorders (Bearden et al., 2011) and basic symptoms (Salokangas et al., 2014) showed also a predictive action. In addition individuals with low functioning at follow up had poor premorbid adjustment and working status (Salokangas et al., 2014), an impaired reciprocal social behaviour (Jalbrzikowski et al., 2013) at baseline and a prolonged duration of the untreated 'at risk' symptoms (Fusar-Poli et al., 2009). So far not enough is known about the functional outcome of HR subjects who do not convert to psychosis in a longer period of time, which is crucial to test the predictive validity of HR construct against other competing approaches.

The goal of the present study was to add evidence to the above by 1) establishing the proportion of non-converting HR individuals with a good functional outcome within the time frame of the study; and 2) identifying baseline predictors of functional outcome in these non-converting HR subjects.

2. Methods

2.1. Setting and procedure

Outreach And Support In South London (OASIS) is a service for young people aged 14–35 at high risk for psychosis whose methods have been fully described elsewhere (Fusar-Poli et al., 2013c). In brief, the OASIS is specifically designed to cater for patients served by the South London and the Maudsley (SLaM) National Health Service (NHS) Foundation Trust. This area has one of the highest rates of psychosis in the world (Kirkbride et al., 2006). HR clients are seen by the team over a period of two years, during which a range of interventions including cognitive behavioural therapy, advice on medication and practical support around housing, benefits, social inclusion and general care coordination are offered (Fusar-Poli et al., 2013c). For the present study patients were followed up for a period ranging from 3 to 11 years (average 6.6 years) and repeated measures were collected at baseline and at follow-up.

2.2. Ethical approval

The study was carried out in accordance with the latest version of the Declaration of Helsinki, and was reviewed and approved by the SLaM ethical committee.

Each participant gave written informed consent after receiving a complete description of the study.

2.3. Participants

The sample included 154 referrals to the OASIS clinic in the period 2001–2010 meeting HR criteria according to the Comprehensive Assessments of the At Risk Mental State (CAARMS) (Yung et al., 2005) interview and who had at least one follow-up assessment. An individual meets HR criteria if he displays one or more of the following: (i) 'attenuated' positive symptoms (APS); (ii) frank psychotic symptoms that last less than one week and resolve without treatment (BLIP); (iii) a recent decline in function coupled with either schizotypal personality disorder or a first-degree relative with psychosis (GRDS). OASIS exclusion criteria are: a history of frank psychotic episodes, previous exposure to antipsychotic agents, deficits in general intelligence (IQ < 70), neurological disorders and an absence of help-seeking behaviour.

2.4. Measures

Socio-demographic and psychosocial variables were recorded during the clinical assessment at baseline using an unstandardized questionnaire modelled on the Census 2001 collection form.

The Comprehensive Assessment of the At Risk Mental State (CAARMS) (Yung et al., 2005) is a semi-structured interview designed to assess putative prodromal psychotic symptoms in help-seeking individuals. The CAARMS has good to excellent reliability (Yung et al., 2005).

The SCID-I (First et al., 2012) and SCID-II (First et al., 1997) are used both to assess any comorbid diagnoses. Quantitative measures of psychopathology are further obtained using the Hamilton Depression (Hamilton, 1960) and Anxiety scale (Hamilton, 1959).

For a global rating of psychological, social and occupational functioning, the Global Assessment of Functioning Scale (GAF; APA, 1994) (Hall, 1995), recently dropped from the DSM-5 (APA, 2013), was used.

The primary outcome variable of interest was functional outcome at follow-up. Hence the sample was subdivided in three groups: those who converted to psychosis (HR-C), those who did not convert and had a good functional outcome (HR-GF) and those who did not convert and had a poor functional outcome (HR-PF). All three groups were retained in the study to compare subjects with a good functional outcome with both those who develop psychosis and those who, even if not psychotic, continue to have moderate to severe impairment after a long period of time. Transition to psychosis was defined according to the CAARMS criteria (Fusar-Poli and Van Os, 2013) as at least one fully positive psychotic symptom several times a week for more than 1 week. Good Functional Outcome (HR-GF) was defined as current GAF score of 61 and higher during the follow-up assessment (Schennach-Wolff et al., 2009; Harrison et al., 2001; Bachmann et al., 2008). This cut-off was chosen because the 60–70 range corresponds to the presence of "some difficulty in social or occupational functioning but [the subject] generally functions pretty well, has some meaningful interpersonal relationships" (Hall, 1995). Poor Functional Outcome (HR-PF) was defined as current GAF score of 60 or lower, indicating "moderate to severe impairment" (Hall, 1995).

2.4.1. Candidate baseline predictors

Based on the existing evidence mentioned in the introduction, candidate baseline predictors of functional outcome were positive,

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