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Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features

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Abstract

The identification of individuals at high risk of developing a psychotic disorder has long been a goal of clinicians because it is thought that early treatment of this group may prevent onset of the disorder. However, little is known of predictive factors of psychosis, even within a high-risk group. This study followed up 104 young people thought to be at 'ultra high risk' for schizophrenia and other psychotic disorders by virtue of having a family history of psychotic disorder combined with some functional decline or the presence of subthreshold or self-limiting psychotic symptoms. All subjects were therefore symptomatic, but not psychotic, at intake. Thirty-six subjects (34.6%) developed frank psychotic symptoms within 12 months.

Measures of symptom duration, functioning, disability and psychopathology were made at intake, 6 and 12 months. Poor functioning, long duration of symptoms, high levels of depression and reduced attention were all predictors of psychosis. A combination of family history of psychosis, a recent significant decrease in functioning and recent experience of subthreshold psychotic symptoms was also predictive of psychosis. Combining highly predictive variables yielded a method of psychosis prediction at 12 months with good positive predictive value (80.8%), negative predictive value (81.8%) and specificity (92.6%) and moderate sensitivity (60.0%).

Within our symptomatic high-risk group, therefore, it appears possible to identify those individuals who are at particularly high risk of developing a psychotic disorder such as schizophrenia. Given the very high PPV and low false positive rate with this two-step process, it may be justifiable to target these individuals for intensive monitoring of mental state and even low-dose neuroleptic medication or other biological and psychosocial treatments depending on clinical condition. This indicated prevention approach could be further developed and preventive strategies in the psychoses refined.

Keywords: Psychosis; Schizophrenia; Prevention; Prediction; High-risk; Prodrome

1. Introduction

Biological and subthreshold clinical features of physical and mental disorders are often thought to be precursors to the development of full-blown disorder (Helmchen and Linden, 2000; Magruder and Calderone, 2000). For example, individuals with

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'subclinical' or 'minor depression' are at risk of developing major depression (Pincus et al., 1999; Clarke et al., 2001). Indicated prevention refers to clinical intervention in individuals who display these putative markers in the hope that further progression of the illness process can be averted (Mrazek and Haggerty, 1994). We have previously described how individuals with subthreshold psychotic symptoms or other risk factors are at risk of developing a full-blown psychotic disorder (Yung et al., 2003) and have discussed the development and evaluation of possible preventive interventions aimed at this group of patients.

It is acknowledged that not all people with operationally defined subthreshold forms of psychosis will go on to develop a diagnosable psychotic disorder such as schizophrenia. Until individuals at risk of psychosis can be identified with nearly 100% certainty this will be the case with any predictive research. The challenge is to identify those individuals most likely to make this transition. These are the people in whom intervention at an early stage, in this case, before onset of frank psychosis, could be justified in order to prevent further deterioration and suffering.

Previous papers have described a method of identifying and recruiting individuals at high risk of developing a psychotic disorder to produce such an enriched sample (Yung et al., 1995, 1996, 1998a,b; Phillips et al., 1999; Yung and Jackson, 1999). We have deliberately avoided using the term 'prodromal' to refer to this group as that is a retrospective concept and therefore at odds with our prospective strategy of identification (Yung et al., 1996). That is, it is not clear at the time of their presentation whether psychosis will follow or not, a situation which is implied by the term 'prodromal'. Instead, we have used the term "at risk mental state" (ARMS) (McGorry and Singh, 1995) to refer to these individuals who appear to be at risk of psychosis but in whom psychosis is not inevitable.

In a previous study (Yung et al., 2003), the "natural history" of the ARMS criteria was examined. A transition rate of 41% was demonstrated. Some factors that predicted an increased likelihood of the development of psychosis over the course of a year within this high-risk group were found, including long duration of subthreshold ('prodromal') symptoms, poor functioning and high levels of depressive and attenuated psychotic symptoms. A limitation of that study was a small sample size ($n = 49$). The current paper continues that research by expanding the sample size to 104.

2. Method

2.1. Subjects

Subjects were recruited into this study from the Personal Assessment and Crisis Evaluation (PACE) Clinic, Melbourne, Australia (Yung et al., 1995, 1996). All referrals to the Clinic between March 1995 and January 1999 were screened for inclusion. Referral sources included general practitioners, psychiatric services, school and university counseling services, and other support agencies working with young people, such as drug and alcohol services. Subjects were included in the research program if they (a) were aged between 14 and 30 years, (b) met criteria for one or more of the groups outlined in Table 1, (c) had not experienced a previous psychotic episode, and (d) were living in the Melbourne metropolitan area. Exclusion criteria were: intellectual disability, lack of fluency in English, and presence of known organic brain disorder. The rationale for these intake criteria is described elsewhere (Yung et al., 1996, 1998a,b). Essentially there are three sets of separate intake criteria. "Group 1 Attenuated Psychotic Symptoms" defines a group of people who have symptoms that deviate from normal phenomena but which are not yet frankly psychotic. For example, overvalued ideas that people are laughing at or are hostile towards the subject, but the subject realizes that it is not really true. The duration of *attenuated psychotic symptoms* should be less than 5 years. This limit on the duration of the attenuated psychotic features was included as people who have very long durations of attenuated psychotic symptoms might best be conceptualized as having these as trait phenomena (schizotypal personality disorder) rather than as a more acute mental state change. However, subjects meeting this criterion might well have other symptoms, such as depressed mood or anxiety, lasting over 5 years. Thus the maximum duration of symptoms applies only to the actual psychotic-like phenomena.