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Research paper

Persistence or recurrence of non-psychotic comorbid mental disorders associated with 6-year poor functional outcomes in patients at ultra high risk for psychosis

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ABSTRACT

Background: Patients at ultra-high risk for psychosis (UHR) are a highly heterogeneous group in terms of clinical and functional outcomes. Several non-psychotic mental disorders co-occur together with the UHR state. Little is known about the impact of non-psychotic comorbid mental disorders on clinical and functional outcomes of UHR patients.

Methods: The sample included 154 UHR help-seeking patients (identified with the CAARMS, comprehensive assessment of the at-risk mental state), evaluated at baseline on the Ham-D, Ham-A (Hamilton depression/anxiety rating scale), and PANSS (positive and negative syndrome scale). 74 patients completed the 6-year follow-up assessment (mean = 6.19, SD = 1.87). Comorbid disorders at follow-up were assessed with the SCID I and II. Global functioning was rated on the global assessment of functioning (GAF) scale.

Results: In the present sample, 6-year risk of psychosis transition was 28.4%. Among non-transitioned UHR patients, 28.3% reported attenuated psychotic symptoms (APS) and 45.3% remained functionally impaired at follow-up (GAF < 60). 56.8% patients were affected by at least one comorbid disorder at follow-up. Among UHR patients who presented with some comorbid disorder at baseline, 61.5% had persistent or recurrent course. Incident comorbid disorders emerged in 45.4% of baseline UHR patients. The persistence or recurrence of non-psychotic comorbid mental disorders was associated with poorer global functional outcomes at follow-up.

Limitations: A substantial proportion of the initial sample was not available for follow-up interviews and some groups in the analyses had small sample size. Predictors of longitudinal outcomes were not explored.

Conclusions: Among UHR patients, persistence or recurrence of non-psychotic comorbid mental disorders, mostly affective disorders, is associated with 6-year poor functional outcomes.

1. Introduction

Preventative strategies in psychosis have received growing attention since the introduction of psychometric criteria for identifying patients at ultra-high risk for psychosis (UHR) (McGlashan et al., 2010; Yung et al., 2005). Current psychometric instruments allow the preventative identification of subjects with an enhanced 36% risk of developing psychosis after 3 years (Fusar-Poli et al., 2012a), a risk which peaks within the first two years since initial assessment (Kempton et al., 2015). However, since most of those initially deemed at risk will not actually transition to full-blown psychosis, and given that the transition risk appears to be declining over the recent years (Fusar-Poli et al., 2015d), it is

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crucial to address the clinical and functional outcomes of UHR patients beyond transition to psychosis.

The UHR state tends to co-occur with other non-psychotic mental disorders (Fusar-Poli et al., 2013a; Salokangas et al., 2012; Svirskis et al., 2005). Our previous multicentre study found that at presentation about 73% of UHR patients had at least one comorbid Axis I diagnosis in addition to the UHR, with the most common one being of depressive and/or anxiety disorders (Fusar-Poli et al., 2014a). These comorbid disorders were impacting the baseline functional level of UHR patients, with an accumulating effect of concurrent anxiety and depressive disorders (Fusar-Poli et al., 2014a). These results suggest that UHR patients suffer from mental difficulties which are distressing and disabling *per se*, regardless of the development of a psychotic disorder. Indeed, the presence of psychopathological symptoms other than attenuated psychotic symptoms (APS) is the most common subjective complaint triggering help-seeking behaviours in this population (Addington et al., 2002; Falkenberg et al., 2015; Stowkowy et al., 2013).

Despite the above findings exploring the impact of non-psychotic comorbid mental disorders on baseline UHR presentation, less is known about their impact on the long-term outcomes. Only a few papers have addressed the impact of comorbid disorders on longitudinal outcomes at 12mo (Lim et al., 2015; Niendam et al., 2009; Ryan et al., 2015; Van Dael et al., 2011), 24mo (Thompson et al., 2012; Van Dael et al., 2011), 44mo (Fusar-Poli et al., 2014a), and 84mo (de Wit et al., 2014; Fontenelle et al., 2011, 2012; Lin et al., 2015). These studies confirmed high percentages of co-occurrence of the UHR state with non-psychotic comorbid mental disorders at baseline, with meta-analytical prevalences of 40.7% (95% CI 32.5–49.4%) for depressive disorders and 15.3% (95% CI 8.9–25%) for anxiety disorders (Fusar-Poli et al., 2014a). Other non-psychotic mental disorders consistently observed in UHR samples were obsessive-compulsive disorders, pervasive developmental disorders, substance use disorders, and borderline personality disorders, with baseline prevalence of up to 14% (Niendam et al., 2009), 38.6% (de Wit et al., 2014), 8% (Fusar-Poli et al., 2014a), and 25% (Ryan et al., 2015), respectively. High comorbidity rates were also found over follow-up assessments. For example, Lin, et al. found that 68.1% of their initial UHR patients presented at least one non-psychotic comorbid mental disorder over 7-year follow-up, the more frequent being mood disorders (48.7%), anxiety disorders (34.5%), and substance use disorders (29.2%) (Lin et al., 2015). In their UHR sample, non-psychotic comorbid mental disorders tended to persist or recur (51.6% persistent/recurring course vs 26.0% remittent course). Incident non-psychotic comorbid mental disorders developed in 37.5% UHR patients, leaving only 7.3% of the baseline UHR patients with no experience of any comorbid disorders (Lin et al., 2015) over follow-up time. Overall, these studies showed that baseline non-psychotic comorbid mental disorders were not predicting subsequent transition to psychosis (Fontenelle et al., 2011; Fusar-Poli et al., 2014a; Lim et al., 2015; Niendam et al., 2009; Ryan et al., 2015; Thompson et al., 2012), whereas their presence during follow-up was associated with lower GAF scores at one-year follow-up (Lim et al., 2015).

However, it is not known how non-psychotic comorbid mental disorders might impact outcomes other than psychosis onset. For example, recent studies have shown that a substantial proportion of the UHR patients - up to 50% - continue suffering from APS over the follow-up period (Lee et al., 2014; Lemos-Giraldez et al., 2009; Velthorst et al., 2011), but the impact of affective anxiety or depressive disorders on APS persistence is underinvestigated. Because of the persistence of conjoint APS and non-psychotic comorbid mental disorders, functional level in UHR may be impaired (Addington et al., 2011). Indeed, there is recent meta-analytical evidence indicating that the UHR, as a whole group, is characterized by baseline functional impairments and quality of life deficits that are comparable to other mental disorders (Fusar-Poli et al., 2015c).

The current study followed the methodological approach described in previous analyses (Lin et al., 2015) to investigate the long-term impact of non-psychotic comorbid mental disorders on several clinical outcomes in UHR patients. Our primary aim was to describe the broader spectrum of long term clinical outcomes of UHR patients. This included transition to psychosis, persistence of APS, prevalence and type of non-psychotic comorbid disorders, persistence of functional impairment as well as complete clinical remission. Our secondary aim was then to address the longitudinal course of non-psychotic comorbid disorders and their association with clinical and functional outcomes in UHR patients.

2. Methods

2.1. Setting and study participants

OASIS is a specialist clinic for patients at UHR for psychosis. Currently it covers a wide urban area of about 1.18 million citizens in South London in three different boroughs (Lewisham, Lambeth, Southwark) (Fusar-Poli et al., 2013b). It is known that South London has very high psychosis rates (Kirkbride et al., 2006).

The service is aimed at 14–35 help seeking UHR patients meeting the comprehensive assessment of the at-risk mental state (CAARMS) criteria (Yung et al., 2006) for: (1) Genetic risk and deterioration syndrome (GRD, schizotypal personality disorder or history of psychosis in a first degree relative); (2) APS (symptoms which do not reach threshold levels for psychosis due to subthreshold intensity or frequency); (3) brief limited intermittent psychotic symptoms (BLIPS, recent history of frank psychotic symptoms that resolved spontaneously within one week). In addition participants have to experience a decline in functioning sustained for at least one month in the past year or a low level of functioning sustained over the past year (Yung et al., 2006). All the subjects assessed at the OASIS clinic (Fusar-Poli et al., 2013b) in the period 2001–2012 and deemed to endorse a UHR state were considered eligible for this study.

All patients signed an informed consent to use data about clinical measures and treatment.

2.2. Baseline assessment

UHR patients were identified according to the CAARMS criteria (Yung et al., 2005). The CAARMS composite score was computed by weighting intensity (I) of symptoms by their frequency (F) within the three domains of positive symptoms measured by the CAARMS: disorders of thought content (DTC), perceptual abnormalities (PA) and disorganized speech (DS), according to the formula (I-DTC*F-DTC)+(I-PA*F-PA)+(I-DS*F-DS) (Morrison et al., 2012). Higher scores indicated more severe APS.

Comorbid lifetime and current non-psychotic mental disorders were established using the CAARMS and the Hamilton depression and anxiety scales (Ham-D, Ham-A) (Hamilton, 1959, 1960). In this study, comorbidity was defined as fulfilling the criteria for both UHR and at least one non-psychotic mental disorder.

Psychopathology was also investigated quantitatively at baseline with Ham-D, Ham-A (Hamilton, 1959, 1960) and positive and negative syndrome scale (PANSS) (Kay et al., 1987).

Global functioning in the past week was rated on the global assessment of functioning (GAF) scale (Hall, 1995). We used the GAF scale, which encompasses both psychopathology and social and role functioning, because the majority of our sample was recruited before the introduction of the social and occupational