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Review

What drives poor functioning in the at-risk mental state? A systematic review

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ABSTRACT

Background: Transition to psychotic disorder has been the traditional outcome of interest for research in the at-risk mental state (ARMS). However, there is growing recognition that individuals with ARMS may function poorly regardless of whether they develop psychosis. We aimed to review the literature to determine whether there are specific factors associated with, or predictive of, functional impairment in the ARMS population.
Method: An electronic database search of MEDLINE, PsycINFO and Embase from inception until May 2014 was conducted using keyword search terms synonymous with the at-risk mental state and functioning. Eligible studies were original peer-reviewed English language research articles with populations that met validated at-risk diagnostic criteria and examined the cross-sectional or longitudinal association between any variable and a measure of functioning.
Results: Seventy-two eligible studies were identified. Negative symptoms and neurocognitive impairment were associated with poor functioning in cross-sectional studies. Negative and disorganised symptoms, neurocognitive deficits and poor functioning at baseline were predictive of poor functional outcome in longitudinal studies. Positive symptoms were unrelated to functioning in both cross-sectional and longitudinal studies. Functional disability was persistent and resistant to current treatments.
Conclusions: Negative and disorganised symptoms and cognitive deficits pre-date frank psychotic symptoms and are risk factors for poor functioning. This is consistent with a subgroup of ARMS individuals potentially having neurodevelopmental schizophrenia. Treatments aimed at improving functioning must be considered a priority on par with preventing transition to psychosis in the development of future interventions in the ARMS group.

1. Introduction

Criteria have been developed to identify individuals vulnerable to developing a psychotic disorder (Yung et al., 1996, 1998; Miller et al., 2002). These have been referred to as the prodromal, ultra-high risk (UHR), clinical high-risk (CHR) and at-risk mental state (ARMS) criteria (Fusar-Poli et al., 2013). In brief, the standard at-risk criteria are the presence of subthreshold psychotic symptoms and/or full threshold psychotic symptoms that resolved spontaneously and/or a trait risk factor for psychotic disorder (such as positive family history) combined with significant deterioration in mental state. The UHR criteria have been widely used and are associated with a high risk of developing psychotic disorder. A recent meta-analysis found that rates of onset of psychosis are 22% in 1 year, 29% in 2 years and 36% after 3 years (Fusar-Poli et al., 2012).

In addition to the development of psychosis (Yung et al., 2003; Mason et al., 2004; Thompson et al., 2011; Cornblatt et al., 2012), there has recently been a growing interest in poor functioning as an outcome of interest in itself (Yung et al., 2010; Barbato et al., 2013; Fulford et al., 2013; Kim et al., 2013; Lin et al., 2013) and in identifying factors predictive of long-term functional disability (Fusar-Poli et al., 2009; Lin et al., 2011; Carrión et al., 2013; Meyer et al., in press). For a large proportion of ARMS patients functioning remains impaired, regardless of transition to full-threshold psychosis or symptomatic remission (Addington et al., 2011a; Schlosser et al., 2012; Carrión et al., 2013; de Wit et al., 2014). It is important to establish whether particular aspects of illness consistently underlie functional disability in order to improve our understanding of this patient group. Therefore, the aim of this review was to systematically appraise the literature to identify variables associated with, or predictive of, functional impairment in the ARMS population.

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2. Method

This review was conducted in line with the PRISMA guidelines for reporting systematic reviews (Moher et al., 2009).

2.1. Eligibility criteria

Eligible studies were original research articles published in peer-reviewed journals, with populations that met the diagnostic criteria for being 'at-risk', 'ultra-high risk' or at 'clinical-high risk' (or similarly defined) of psychosis based on a clinically validated instrument. Studies were included that examined the cross-sectional relationship between any variable and a measure of functioning, or reported the longitudinal relationship between baseline variables and subsequent functional outcome. For the purposes of this review, functioning was defined as measures relating to the frequency of, quality of, or satisfaction with social, academic or occupational activity. Intervention studies that examined functioning pre- and post-intervention were eligible.

Studies that included only subjects at genetic risk who had not met the formal diagnostic criteria for being at ultra-high risk (or similarly defined) of psychosis, case studies and non-English language articles were excluded.

2.2. Search strategy

On the 1st of May 2014 an electronic database search of Ovid MEDLINE, PsycINFO and Embase using the following keywords was conducted: "at risk mental state" or "ultra high risk", "UHR", "clinical high risk", "CHR", "prodrom*" and "psychos*" or "psychot*", "schizo*" and "social function*" or "role function*", "global function*", "psychosocial function*", "functional outcome", "academic function*", "community function*", "occupational function*", "school function*", "work function*". Reference lists of retrieved articles were also reviewed by hand for additional relevant publications not identified in the initial electronic search.

2.3. Study selection and data extraction

Two reviewers (J.C. and J.F.) independently screened articles for eligibility. Any disagreements were resolved through discussion. For all eligible studies, a standardised tool was developed to record: (1) study characteristics (study design, year of publication, country where the work was performed); (2) sample demographics (sample size, gender composition, mean age); (3) the at-risk screening instrument used to assess eligibility; (4) functioning data (measure(s) used, mean sample scores); (5) variables examined for their association with functioning; and (6) summary of study findings. For intervention studies, we also recorded: (7) intervention and comparator arms; and (8) treatment duration.

3. Results

The study selection and exclusion process are summarised in Fig. 1. Our initial database search retrieved 384 unique citations after the removal of duplicates. Of these, 271 were excluded at the title–abstract stage and a further 55 following full-paper screening. Full text articles were excluded due to the use of ineligible populations (n = 9), studies not examining the relationship between functioning and any other variable (n = 44) or not being original research studies (n = 2). Fourteen additional papers were identified from reviewing reference lists of articles. Seventy-two papers met the full inclusion criteria, and fell broadly into the categories of observational (Table 1) and intervention studies (Table 2). These were conducted in North America (n = 35), Europe (n = 20), Australia (n = 10) and South Korea (n = 7). There were 12 different measures of functioning used by studies within this review, which are briefly summarised in Supplementary Table 1. These included 'global' measures such as the Global Assessment of Functioning (GAF; Hall, 1995) and Social and Occupational Functioning Assessment Scale (SOFAS; Goldman et al., 1992), which provide a single score indicative of overall impairment. Functioning was also examined using separate measures of social and role (occupational/educational) functioning, such as the Global Functioning: Social (GFS; Auther et al., 2006) and Role (GFR; Niendam et al., 2006a) scales.

3.1. ARMS subgroup

One study found that patients meeting the genetic risk and deterioration subgroup criteria had significantly better global functioning than those presenting with attenuated psychotic symptoms in the year prior to entering the study. However, due to rapid deterioration, functioning in these groups did not differ at study inception (Miller et al., 2003). This is consistent with research reporting no significant differences in global functioning between ARMS diagnostic sub-groups (Lemos-Giráldez et al., 2009).

3.2. Symptoms

Positive psychotic symptoms are sub-threshold and often transient in ARMS patients. These were associated neither with functioning in cross-sectional studies, nor with long-term functional outcome (Niendam et al., 2006b; Shim et al., 2008a; Carrión et al., 2011; Corcoran et al., 2011; Eslami et al., 2011; Lin et al., 2011; Barbato et al., 2013; Carrión et al., 2013; Kim et al., 2013; Walder et al., 2013; Meyer et al., in press).

Cross-sectional evidence indicated that negative symptoms (Niendam et al., 2006b; Cornblatt et al., 2007; Svirskis et al., 2007; Willhite et al., 2008; Velthorst et al., 2010; Raballo et al., 2011; Valmaggia et al., 2013; Walder et al., 2013; Meyer et al., in press) and disorganised and general symptoms (Cornblatt et al., 2007; Comparelli et al., 2010; Velthorst et al., 2010; Corcoran et al., 2011; Fulford et al., 2013; Kim et al., 2013; Walder et al., 2013; Meyer et al., in press) were consistently associated with a broad range of global, social and role functioning measures. When each of these symptom clusters was entered into regression analyses, only negative symptoms remained significantly associated with poor functioning (Corcoran et al., 2011; Fulford et al., 2013; Kim et al., 2013; Meyer et al., in press). However, longitudinal evidence indicated that both negative (Lin et al., 2011; Schlosser et al., 2012; Meyer et al., in press) and disorganised symptoms at baseline (Bearden et al., 2011; Eslami et al., 2011; Carrión et al., 2013; Ziermans et al., 2014) were also amongst the strongest independent predictors of long-term functional outcome.

A key methodological limitation of this area is that negative symptom items in the Structured Interview for Prodromal Syndromes (SIPS; Miller et al., 2002) overlap with measures of functioning. This is one of the main instruments used to characterise ARMS patients, particularly in North American studies. Meyer et al. (in press) reported that removal of two SIPS negative items from the functional assessment resulted in a substantial drop in the magnitude of association between negative symptoms and social and role functioning both at baseline and at follow-up (Meyer et al., in press). This also greatly increased the strength of association between neurocognition and disorganised symptoms and functioning in the cross-sectional and longitudinal analyses. Future studies should take this potential confounding of items into account when performing analyses.

3.3. Duration of symptoms

Global functioning did not significantly differ between patients with long (>1 year) and short (<1 year) durations of untreated attenuated psychotic symptoms (Chung et al., 2010). However, a longer duration of prodromal symptoms was associated with increased impairment on the 'Interpersonal behaviour' and 'Prosocial activities' subscales of the Social Functioning Scale (Shim et al., 2008a). A longer duration of