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Comorbid diagnoses for youth at clinical high risk of psychosis

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ABSTRACT

Several studies have demonstrated that youth at clinical high risk (CHR) of developing psychosis have a high prevalence of comorbid psychiatric disorders. Less is known about the impact of comorbid diagnoses on later conversion to psychosis and the change over time. The aim of this study was to determine the frequency and distribution of psychiatric diagnoses at baseline and over time in the North American Prodrome Longitudinal Study (NAPLS 2) and the role of comorbid diagnoses in conversion to psychosis. The NAPLS 2 sample consisted of 744 CHR youth and 276 healthy controls. Only 21% of the CHR group did not have a comorbid diagnosis with many have 2–3 DSM-IV comorbid diagnoses. The most common diagnoses were anxiety and depressive disorders, which did improve over time. The only diagnosis at baseline that differentiated the converters from the non-converters was cannabis misuse. Comorbidity, except for cannabis use, was essentially independent of clinical outcome. It is possible that those with comorbid diagnoses are preferentially the help-seeking individuals that present for help in our clinics and research projects and that those who are at risk but do not have a comorbid diagnosis may not be seeking help in the prodromal phase.

1. Introduction

Studies of young people at high risk of developing psychosis are prominent in the psychosis literature. These young people are at clinical high risk (CHR) of psychosis since the criteria are based on clinical symptoms that include the presence of sub-threshold psychotic symptoms, brief intermittent psychotic symptoms, or the pairing of genetic risk with a decline in functioning (McGlashan et al., 2010; Yung and McGorry, 1996). Interestingly, studies of those at CHR consistently report that these individuals have a high prevalence of comorbid psychiatric diagnoses and, in particular, mood disorders (Fusar-Poli et al., 2013). In the first North American Prodrome Longitudinal Study (NAPLS), the prevalence of any DSM-IV diagnosis of anxiety or depression or both in 377 help-seeking CHR participants was 69% (Woods et al., 2009). In 2012, the European Prediction of Psychosis Study (EPOS) (Salokangas et al., 2012), which included 245 individuals at CHR, reported that 71% of participants were given at least one life-time diagnosis and 62% were assessed as having one or more current diagnoses. Rates of a current depression or anxiety disorder were reported in 34% and 39% respectively of the sample. A more recent study, which included 509 individuals at CHR reported the presence of comorbid Axis I diagnoses in 73% of the sample. More specifically 40% had a depressive disorder, either on its own (26%) or with an anxiety disorder (14%), and 8% had only an anxiety disorder (Fusar-Poli et al., 2014). Additionally, of 226 individuals at CHR who were followed-up between 2 and 14 years following first presentation, 90% of them had a non-psychotic

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disorder at baseline, which persisted at follow-up for 52% of the sample (Lin et al., 2014). A meta-analysis of 11 studies from 2014 that included 1684 CHR individuals calculated the prevalence of depression and anxiety disorders as 41% and 15% respectively (Fusar-Poli et al., 2014).

Comorbid diagnoses are of concern in that they have been reported to increase the subjective burden of attenuated psychotic symptoms in those at CHR, and to predict poorer long-term outcomes (Wigman et al., 2012). Notably, the distress of depression and anxiety can overshadow that caused by attenuated psychotic symptoms to such an extent that depression and anxiety are most often the primary complaint when CHR individuals are first seeking help (Falkenberg et al., 2015). Furthermore, their role in later conversion to psychosis has not been conclusively explored. In NAPLS-1, except for substance use, comorbid diagnoses were not associated with conversion to psychosis (Woods et al., 2009). In the EPOS study, current bipolar, somatoform and depressive disorders were shown to predict conversion to psychosis, while anxiety disorders predicted non-conversion to a psychotic disorder (Salokangas et al., 2012). In a meta-analysis, during an average follow-up of 3.7 years, no association was found between additional diagnoses at baseline and conversion to a psychotic disorder in 509 CHR individuals (Fusar-Poli et al., 2014). More recently, emergence of non-psychotic disorders, namely mood and anxiety disorders, was reportedly independent of the psychosis risk status whereby individuals at CHR had the same level of risk as their help-seeking counterparts who did not meet criteria for CHR syndrome or psychosis (Fusar-Poli et al., in press; Webb et al., 2015).

In NAPLS 2, we have previously published on anxiety disorders and substance use. In the first paper, it was reported that 51% of CHR study participants presented with an anxiety disorder but there was no association between baseline anxiety disorder and later conversion to psychosis (McAusland et al., 2015). In the second paper, those at CHR had an increased level of severity of cannabis use with respect to their healthy peers, but did not use cannabis more frequently and no association was reported between cannabis use and later conversion to psychosis (Buchy et al., 2015). However, this paper only focused on ratings of severity and frequency of substance use and not DSM-IV diagnoses.

Here, we focus on the prevalence of Axis I DSM-IV diagnoses in the NAPLS-2 cohort. We have throughout this paper referred to the clinical diagnoses that meet DSM-IV criteria as "comorbid diagnoses". We appreciate that since the CHR criteria is not an established DSM-V disorder that the use of the term "comorbid" could be misleading. However, it is widely used in the high-risk literature meaning, as we do here, that the individual meets criteria for one or more DSM-IV disorders in addition to meeting the criteria for CHR. The aims of the current study are to determine, first, the frequency and distribution of psychiatric diagnoses at baseline in those at CHR as compared to their healthy peers; secondly, whether there are differences in the baseline prevalence of psychiatric diagnoses between those who developed psychosis and those who did not; and finally, changes in diagnoses over time will be examined.

2. Methods

2.1. Participants

Participants were recruited as part of the multi-site NIMH funded NAPLS-2 study. CHR participants were help-seeking and were referred from health care providers, educators or social service agencies, or were self-referred in response to community educational efforts. Each site advertised for healthy controls. The NAPLS 2 sample consisted of 764 CHR individuals (436 males, 328 females) and 279 healthy controls (HC) (141 males, 138 females) recruited across the eight NAPLS 2 sites. Study participants were evaluated using the Structured Interview for Psychosis-risk Syndromes (SIPS) (McGlashan et al., 2010) to determine if they met the Criteria of Psychosis-risk Syndromes (COPS) i.e. one or more of the following high risk syndromes: attenuated psychotic symptoms syndrome; brief intermittent psychotic symptoms syndrome; and genetic risk and deterioration syndrome. Seven hundred and forty-three of the CHR participants met Criteria of Psychosis-risk Syndromes (COPS). A further 21 CHR participants were considered high risk due to the presence of schizotypal features and age <18 years. Of the total NAPLS 2 sample, 744 CHR and 276 HCs had complete baseline data for the SCID and thus will be the sample described in this paper. Participants had to be between 12 and 35 years of age. Participants were excluded if they met criteria for any current or past Axis I psychotic disorder, or had an IQ below 70, or past or current history of a clinically significant central nervous system disorder. HCs were excluded if they had a first-degree relative with a current or past psychotic disorder. We have previously reported a more detailed description of recruitment procedures, ascertainment, and inclusion and exclusion criteria (Addington et al., 2015).

2.2. Measures

The Structured Interview for Psychosis-risk Syndromes (SIPS) (McGlashan et al., 2010) was used to determine whether an individual met COPS criteria. The Scale of Psychosis-risk Symptoms (SOPS) consisting of 19 items in 4 symptom domains (i.e. positive, negative, general, and disorganized symptoms) was used to rate the severity of attenuated psychotic symptoms.

The Structured Clinical Interview for DSM-IV (SCID) (First et al., 1995) was used to determine the presence of current and past psychiatric diagnoses, including conversion to a psychotic disorder.

Conversion to psychosis was determined by meeting the Presence of Psychotic Symptoms (POPS) (McGlashan et al., 2010) criteria. POPS requires that at least one of the five SOPS positive symptoms reached a psychotic level of intensity (rated 6) for a frequency of ≥1 h per day for 4 days per week, or that symptoms seriously impacted functioning (e.g. disorganizing or dangerous to self or others).

Clinical outcome at each follow-up assessment was determined in the following way: (i) remission (remission from all CHR syndromes, which means scores of 2 or less on all five positive symptoms on the SOPS scale, or for those who have only GRD, "in remission" will require GAF to have returned to 90% of previous best GAF); (ii) symptomatic (not currently meeting criteria for a prodromal risk syndrome but having ratings of 3–5 on any one of the five positive symptoms on the SOPS, or with the no change in the GAF); (iii) prodromal progression (currently meeting criteria for one of the at risk syndromes; APSS, GRD, BIPS) and (iv) psychotic (currently meeting criteria for a psychotic disorder or evidencing scores of 6 on one or more positive symptoms of the SOPS) (Woods et al., 2014).

2.3. Procedures

Both CHR individuals and HCs were recruited for the study, which was approved by the Institutional Review Boards of all eight NAPLS-2 sites. Written informed consent, including parental consent, was obtained from all adult participants and parents/guardians of minors.

After the initial screening assessment that included administering the SCID and the SIPS, vignettes were developed for each CHR participant to obtain a consensus diagnosis. The attenuated psychotic symptoms rated on the SOPS are described at length and include both recent and longstanding symptoms. The vignettes are written so that raters from all eight sites can review the information under each symptom category and provide a reliable rating. Once approved at the site level, the vignette is presented on a conference call for a consensus decision on the symptom ratings as well as the diagnosis. The NAPLS-2 consensus call, chaired by JA, was held once a week and attended by the clinical raters from each of the eight sites. Submitted vignettes are individually reviewed and a consensus must be reached on each symptom rating, diagnosis and ultimate admission into the study. Clinical raters were experienced research clinicians. Gold standard post-training

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