Distress in relation to attenuated psychotic symptoms in the ultra-high-risk population is not associated with increased risk of psychotic disorder.

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Distress in relation to attenuated psychotic symptoms in the ultra high risk population

is not associated with increased risk of psychotic disorder

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Abstract

Background The 'ultra high risk' criteria identify a clinical population at substantially increased risk for progressing to schizophrenia and other psychotic disorders. While a number of clinical variables predictive of transition to psychotic disorder have been identified within this population, the predictive value of the level of distress associated with attenuated psychotic symptoms has not yet been examined. This was the aim of the present study.

Method The level of distress (0-100) associated with attenuated psychotic symptoms was recorded for 70 ultra high risk patients using the Comprehensive Assessment of At-Risk Mental State (CAARMS). Transition to psychosis was assessed over a 16-month follow-up period.

Results Of the 70 UHR patients, 15 transitioned to psychosis (21.4%). Of the 4 CAARMS subscales measuring attenuated positive symptoms, Perceptual Abnormalities was rated as the most distressing. There were no differences in CAARMS scales rated as the most distressing between those who transitioned to psychosis and those who did not. There was also no association between higher levels of distress associated with attenuated psychotic symptoms and transition to psychosis.

Discussion While the findings require replication, they indicate that the degree of distress associated with attenuated psychotic symptoms should not be used as a criterion for enriching UHR samples for risk of frank psychotic disorder.

Introduction

The detection of young people who are at heightened risk of developing psychotic disorders has significantly improved over the last two decades (1). This has been facilitated by the introduction of the "ultra high risk" (UHR; otherwise known as "clinical high risk" or "psychosis high risk") criteria. These criteria are based on a combination of state and trait risk factors, most prominently attenuated positive psychotic symptoms, in addition to help-seeking. A meta-analysis of rates of transition to psychotic disorder in the UHR population found a 22% transition rate after 1 year, increasing to 36% after 3 years (2). Our long term follow up study found a 34.9% transition rate over a 2.4-14.9 year follow up period (3). These rates are substantially higher than those seen in other clinical populations and in the general population.

A challenge has been to identify additional clinical and other predictors (such as neurocognitive, neurobiological, and genetic variables) within the UHR population that further enhance prediction of outcome. The clinical variables that have been identified as predicting transition to psychosis in UHR samples include: long duration of symptoms prior to treatment (3, 4), subthreshold positive symptoms (3-7), poor functioning (3-5, 7, 8), basic and negative symptoms (3, 5, 6, 9-11), depression (4, 11), schizotypal disorder (7), sleep disturbances (7), substance abuse (12), and genetic risk with functional decline (12).

However, an aspect of this clinical population that has not yet been addressed is the level of distress associated with attenuated psychotic symptoms, and whether increased distress in relation to these symptoms is associated with increased risk of transition. This issue is significant for several reasons. Firstly, most UHR patients (approximately 80%) enter clinics based on their attenuated psychotic symptoms, rather than one of the other risk groups

(BLIPS or trait vulnerability)(13). Therefore, improving our understanding of the significance of distress associated with these symptoms is important for our understanding of the UHR population generally. Secondly, if higher level of distress associated with attenuated psychotic symptoms corresponds to increased risk for transition to psychotic disorder then this may assist with "narrowing down" on UHR patients most likely to develop psychotic disorder. This is a salient issue given the decreasing transition rates in more recent UHR cohorts (2, 3, 14). Finally, the description of "Attenuated Psychosis Syndrome" in DSM-5, modelled on the UHR criteria, assumes a clinically significant level of distress associated with the attenuated psychotic symptoms (*"Symptom(s) is sufficiently distressing and disabling to the individual to warrant clinical attention"*). However, this has not been established in UHR cohorts, who are often in fact referred to clinical services for other, non-psychotic complaints (15).

In this study, we aimed to examine whether the level of distress associated with attenuated psychotic symptoms predicts transition to psychotic disorder in the UHR population.

Method

Setting

Orygen Youth Health clinical program (OYH-CP) is a public mental health service for young people aged between 15-24 years in the catchment area of western and northwest Melbourne, Australia. The clinical service has four components: EPPIC (Early Psychosis Prevention and Intervention Centre, a first episode psychosis service), PACE (Personal Assessment and Crisis Evaluation, a UHR clinic), Youth Mood Clinic (a mood disorder clinic), and HYPE (Helping Young People Early, a clinic for borderline personality pathology). Referrals to

OYH-CP are received from a range of sources including school counselors, GPs, other healthcare providers, family, friends, and young people themselves. Individuals referred to OYH-CP are assessed at a central triage point, which directs patients to the appropriate clinic. Individuals referred to PACE from triage then undergo an entry assessment, at which stage the Comprehensive Assessment of At Risk Mental States (CAARMS) is administered to assess UHR status. The CAARMS is administered by trained clinicians – either psychiatrists, psychologists or other allied health staff.

Participants

The recruitment period was 20/5/2006-21/6/2009. Over this period, the PACE clinic received 340 referrals, of which 311 were accepted into the clinic. Of this cohort, CAARMS and distress data were available on 70 cases. Inclusion criteria were: being aged between 15 and 24 years, living in the OYH catchment area, and meeting UHR criteria(4). Exclusion criteria were: previous diagnosis of a psychotic disorder, known organic cause of symptoms, or if relevant data were not available.

Assessments

The CAARMS consists of four attenuated positive psychotic symptoms sub-scales: Unusual Thought Content (UTC), Non-Bizarre Ideas (NBI), Perceptual Abnormalities (PA), and Disorganised Speech (DS). Each of these are rated on a 0-6 scale for intensity and frequency. In addition to this rating, participants were also rated on how distressed they were by these attenuated psychotic symptoms. This was established in the course of the CAARMS semi-structured interview. Distress was measured using a Likert scale from 0 (not at all distressed) to 100 (extremely distressed). If the participant rated on multiple attenuated psychotic symptoms the highest distress rating was used in data analysis. Baseline functioning was

assessed using the Global Assessment of Functioning (GAF). Participants were treated at the

PACE clinic for approximately one year. They were regularly monitored by their treating

psychiatrist and case manager for onset of psychotic disorder. This is defined as per previous

research as clear full-threshold positive psychotic symptoms for longer than one week.

Data Analysis

Statistical analyses were conducted using the statistical package IBM SPSS for Windows,

version 22.0. An alpha level of <0.05 was set. Cox regression was used to assess the

association between distress rating (0-100) and time to transition. The cox regression

adjusted for GAF score as poor functioning as previously been found to predict transition to

psychosis.

Results

Baseline characteristics

Sample characteristics are presented in Table 1. There were no differences in gender or age

between the cohort and PACE patients who did not have the required data available (n=241).

Insert Table 1 about here

Transition to psychosis

Transition to psychosis data were available for the full cohort. Fourteen participants

transitioned to psychosis within 12 months, and an additional individual transitioned within

16 months, yielding an overall transition rate of 21.4%.

Distress in relation to transition

Cox regression, adjusting for GAF score, indicated that level of distress in relation to attenuated psychotic symptoms did not predict transition to psychosis (beta=-.002, SE=.013, p=.904).

Distress in relation to type of attenuated psychotic symptom

An exploratory analysis was conducted to assess if higher distress ratings associated with type of attenuated psychotic symptom (UTC, NBI, PA, DS) was associated with transition to psychosis. PA were rated as the most distressing (n=32, 46%) and more frequent PA showed a weak but significant correlation with higher distress (r=.26, p=0.03). NBI were the second most distressing (n=21, 30%), followed by UTC (n=14, 20%), and DS (n=3, 4%). A cox regression adjusting for GAF score indicated that higher distress associated with type of attenuated psychotic symptoms, using UTC as the reference, did not predict transition (p=.853).

Discussion

To the best of our knowledge, this is the first study to address the level of distress in relation to attenuated psychotic symptoms and risk for transition to psychosis in a UHR sample. There was no association between level of distress in relation to attenuated psychotic symptoms and transition to psychosis. Perceptual abnormalities were the most distressing, with more frequent perceptual abnormalities correlating with higher distress, and disorganised speech the least distressing attenuated psychotic symptom. There was no relationship between higher levels of distress in relation to particular types of attenuated psychotic symptoms and transition to psychosis.

These results provide preliminary evidence that distress in relation to attenuated psychotic symptoms is not a good indicator of risk for subsequent psychotic disorder in UHR patients. This suggests that help-seeking UHR young people who are not significantly distressed by their attenuated psychotic symptoms are just as likely to develop first episode psychosis as those who are significantly distressed by these symptoms, and therefore should receive clinical care and be recruited to UHR research studies.

Although this issue has not previously been examined in UHR cohorts, the results are somewhat at odds with data from a large Dutch general population study (16). In the NEMISIS study 8% of the cohort who had an incident psychotic experience had a subclinical outcome two years later, and 8% had a psychotic clinical outcome two years later. Emotional appraisal and degree of intrusiveness of the psychotic experience, which may index level of distress, were strong modifiers of the clinical outcome, but not the subclinical outcome. The current data are also not consistent with cognitive models of psychosis that posit that interpreting anomalous perceptual or cognitive experiences in an anxiety or distress-provoking manner may exacerbate psychotic symptoms (17, 18).

Recent evidence indicates that only 52% of UHR patients find their attenuated psychotic symptoms distressing, with social and functioning difficulties and depressive symptoms being the most prominent sources of distress in this population (19). Thus the distress and help-seeking in this population is attributable to a wide range of reasons, rather than being solely attributable to attenuated psychotic symptoms. This suggests that the requirement in the DSM-V Attenuated Psychosis Syndrome that the attenuated psychotic symptoms are "sufficiently distressing and disabling to warrant clinical attention" would identify a

significantly different group than that which is currently recruited in UHR studies. The

finding that a higher level of distress associated with attenuated psychotic symptoms is not

associated with a higher risk for psychosis also suggests that this criterion for Attenuated

Psychosis Syndrome would *not* identify a group at enriched risk for psychotic disorder.

The current study suffers from a number of limitations. The sample with available data was a

subset of the overall sample of UHR patients seen over the recruitment period. While the

demographic data indicate that this sub-set was representative of the age and gender of the

overall pool of patients, it is possible that the larger pool of patients may have differed on

other variables not captured, possibly resulting in a selection bias. Second, the type of

treatment that the UHR patients received was not taken into account in analysis. The

particular type of treatment, for example cognitive-behaviour therapy directed towards

reducing distress associated with attenuated psychotic symptoms, may have moderated the

risk for transition to psychotic disorder. Finally, distress was measured as a single

"snapshot" at entry to the clinic. This measurement may have been influenced by factors

such as self-stigma, shame associated with symptoms, patients' coping style, sufficient

rapport and engagement not yet established with the clinical team, and so on. Future work

may wish to adopt a more thorough approach to measuring distress associated with

symptoms.

Conclusion

These findings indicate that perceptual abnormalities are the attenuated positive psychotic

symptoms most distressing to UHR patients at entry. Higher levels of distress associated

with symptoms is not associated with transition to psychotic disorder over the subsequent 1.5

years. While the findings require replication, they indicate that the degree of distress

associated with attenuated psychotic symptoms should not be used as a criterion for enriching

UHR samples for risk of frank psychotic disorder.

References

1.   Fusar-Poli P, Borgwardt S, Bechdolf A, Addington J, Riecher-Rossler A, Schultze-Lutter F, et al. The psychosis high-risk state: a comprehensive state-of-the-art review. JAMA Psychiatry. 2013;70(1):107-20.

2.   Fusar-Poli P, Bonoldi I, Yung AR, Borgwardt S, Kempton MJ, Valmaggia L, et al. Predicting Psychosis: Meta-analysis of Transition Outcomes in Individuals at High Clinical Risk. Archives of general psychiatry. 2012;69(3):220-9.

3.   Nelson B, Yuen HP, Wood SJ, Lin A, Spiliotacopoulos D, Bruxner A, et al. Long-term Follow-up of a Group at Ultra High Risk ("Prodromal") for Psychosis: The PACE 400 Study. JAMA Psychiatry. 2013:1-10.

4.   Yung AR, Phillips LJ, Yuen HP, Francey SM, McFarlane CA, Hallgren M, et al. Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group. Schizophrenia Research. 2003;60(1):21-32.

5.   Mason O, Startup M, Halpin S, Schall U, Conrad A, Carr V. Risk factors for transition to first episode psychosis among individuals with 'at-risk mental states'. Schizophr Res. 2004;71(2-3):227-37.

6.   Haroun N, Dunn L, Haroun A, Cadenhead K. Risk and protection in prodromal schizophrenia: ethical implications for clinical practice and future research. Schizophr Bull. 2006;32:166-78.

7.   Ruhrmann S, Schultze-Lutter F, Salokangas RK, Heinimaa M, Linszen D, Dingemans P, et al. Prediction of psychosis in adolescents and young adults at high risk: results from the prospective European prediction of psychosis study. Archives of general psychiatry. 2010;67(3):241-51.

8.   Yung AR, Stanford C, Cosgrave E, Killackey E, Phillips L, Nelson B, et al. Testing the Ultra High Risk (Prodromal) criteria for the prediction of psychosis in a clinical sample of young people. Schizophrenia Research. 2006;84:57-66.

9.   Simon AE, Dvorsky DN, Boesch J, Roth B, Isler E, Schueler P, et al. Defining subjects at risk for psychosis: a comparison of two approaches. Schizophr Res. 2006;81:83-90.

10.   Yung AR, Yuen HP, McGorry PD, Phillips LJ, Kelly D, Dell'Olio M, et al. Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. Australian & New Zealand Journal of Psychiatry. 2005;39(11-12):964-71.

11.   Johnstone EC, Ebmeier KP, Miller P, Owens DG, Lawrie SM. Predicting schizophrenia: Findings from the Edinburgh High-Risk Study. British Journal of Psychiatry. 2005;186(1):18-25.

12.   Cannon TD, Cadenhead K, Cornblatt B, Woods SW, Addington J, Walker E, et al. Prediction of psychosis in youth at high clinical risk: a multisite longitudinal study in North America. Arch Gen Psychiatry. 2008;65(1):28-37.

13.   Nelson B, Yuen K, Yung AR. Ultra high risk (UHR) for psychosis criteria: are there different levels of risk for transition to psychosis? Schizophrenia research. 2011;125(1):62-8.

14.   Yung AR, Yuen HP, Berger G, Francey S, Hung TC, Nelson B, et al. Declining transition rate in ultra high risk (prodromal) services: dilution or reduction of risk? Schizophr Bull. 2007;33(3):673-81.

15.   Nelson B. Attenuated Psychosis Syndrome: Don't jump the gun. Psychopathology. 2014;In press.

16.   Hanssen M, Bak M, Bijl R, Vollebergh W, van Os J. The incidence and outcome of subclinical psychotic experiences in the general population. British Journal of Clinical Psychology. 2005;44(2):181-91.

17.   Morrison AP. The interpretation of intrusions in psychosis: An integrative cognitive approach to hallucinations and delusions. Behavioural and Cognitive Psychotherapy. 2001;29:257- 76.

18.   Morrison AP, Wells A. Relationships between worry, psychotic experiences and emotional distress in patients with schizophrenia spectrum diagnoses and comparisons with anxious and non-patient groups. Behav Res Ther. 2007;45(7):1593-600.

19.   Rapado-Castro M, McGorry PD, Yung AR, Calvo A, Nelson B. Sources of clinical distress in young people at ultra high risk of psychosis. Under review. 2014.