

Challenges in the early detection and intervention of the psychosis-risk syndrome

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Summary: The concept of a clinical high-risk state for psychosis has been used to describe individuals who have prodromal symptoms of psychosis and, thus, are at high-risk of developing psychosis. This high-risk concept promotes a more detailed developmental understanding of the evolution of psychosis and provides a theoretical basis for providing necessary mental health services to people at clinically high-risk of developing psychosis. Early detection and intervention can potentially change the course of psychotic conditions and, thus, prevent or minimize the associated disability. This is a relatively new area of interest, so more studies are needed to fully understand this high-risk condition.

Keywords: clinical high-risk state for psychosis; psychosis risk syndrome; attenuated psychosis syndrome; schizophrenia

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The concept of a clinical high-risk state for psychosis (HR) has recently gained popularity in clinical psychiatry as a means of describing individuals with prodromal psychotic symptoms who are at the cusp of developing a full-blown psychosis. Several labels have been used for this condition, including 'psychosis risk syndrome' (PRS), 'prodromal psychosis', or 'very high-risk state'. Due to controversies around this concept, DSM-5 does not list HR as a diagnosis, but it does include 'attenuated psychosis syndrome' (APS) in the appendix as a condition worthy of further study. We believe use of the APS category can help in the early detection and intervention of psychotic disorders.

1. Epidemiology and clinical features

Clinical studies support the existence of a high-risk state for psychosis, which is associated with impaired functioning and an increased risk of suicide. Previous reports indicate that the majority of patients with psychotic disorders experience a prodromal period of gradually declining functioning prior to the onset of full-blown psychosis that, on average, lasts for five

years.^[1] The reported incidence of the HR state in the general population is 2%, and it is much higher among individuals 11 to 13 years of age.^[2] Individuals with this HR condition typically experience progressively more severe negative symptoms, impairments in social and work functioning, interpersonal difficulties, and mild cognitive impairments that results in a declining quality of life.^[3] MRI studies of these individuals find decreased brain volumes in the hippocampus and anterior cingulate.^[4] And a study by Hutton and colleagues^[5] reported that 47% of help-seeking patients with the HR condition had attempted suicide at least once before seeking treatment.^[5] The early detection and management of this HR condition provides an important opportunity to prevent or delay the evolution of the condition into a fully-blown psychosis.

2. Conversion from high-risk state to psychosis

The reported conversion rate from HR to psychosis has varied widely. A previous meta-analysis with a pooled sample size of 2500 individuals estimated conversion

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rates of 18% during the first 6 months, 22% in 1 year, 29% in two years, 32% in 3 years, and 36% for follow-up periods greater than 3 years.^[6] We believe these results under-estimate the true conversion rates of the HR condition. Our reasons are as follows:

- (a) The existing tools used to identify the HR state over emphasize the importance of positive symptoms and underestimate the importance of negative symptoms. Gradual decline in social and role functioning and mild cognitive impairment are key features of prodromal psychosis,^[7] but these symptoms are more difficult to reliably identify than the positive symptoms of psychosis (i.e., hallucinations, delusions and bizarre thoughts or behaviors) so they are either absent or given less importance in the available screening scales for the HR state. As a consequence, screening tools for the HR condition may miss many persons with prodromal psychosis who have prominent negative symptoms but lack positive symptoms. If these negative symptoms are more important predictors of conversion to full-blown psychosis than positive symptoms, this weakness in available screening tools would result in relatively low rates of conversion.
- (b) Interventions provided to individuals experiencing the HR state could decrease their conversion rate and, thus, lead to an under-estimate of the true conversion rate. Most studies that assess the conversion rate of the HR state are conducted in help-seeking individuals, so many of them receive psychological or medical treatment during the follow-up period that could reduce the rate of conversion to full-blown psychosis.^[8]
- (c) The follow-up periods of previous studies are not long enough. Although some studies have found that individuals in an unconverted HR state have better clinical outcomes and social functioning than those who convert to a full-blown psychosis, whether these differences are permanent or temporary is unknown without long-term follow-up data.^[9] A 15-year follow-up study found that conversion to psychosis can happen as long as 10 years after the onset of the HR condition. Other long-term studies with an average of 9 years of follow-up reported conversion rates between 65 and 79%.^[4]

3. The possibility of early detection and intervention

The conversion of the HR state to psychosis is not unpredictable. Conversion-related clinical predictors include genetic risks combined with decreased social functioning, prominent eccentric thought content, a

high level of suspicion or paranoia, and a history of substance abuse.^[10] Combining multiple predictive factors can greatly improve the accuracy of the prediction. These predictive factors include family history of psychosis, cognitive decline, clinical symptoms combined with abnormal EGG or brain imaging, and certain personality traits.^[4] A multi-center study in the United States of 291 teenagers with prodromal symptoms followed for 2.5 years reported that their risk of developing schizophrenia was 405-fold greater than that of healthy controls; the concurrent presence of three risk factors for conversion (including genetic factors, strange thoughts/paranoia, social dysfunction, etc.) accurately identified 74 to 81% of the individuals who converted to schizophrenia within the 2.5-year follow-up period. The joint use of other predictors such as neuropsychological tests and certain biomarkers (e.g., functional or structural brain imaging, reaction time, linguistic memory, etc.) can also increase the accuracy of predicting the conversion of the HR state to a full-blown psychosis.^[11]

Early intervention for HR individuals is both feasible and effective. The latest meta-analysis of randomized controlled trials reported that the pooled risk ratio of developing full-blown psychosis over a one-year period in the intervention group compared to that in the control group was 0.34; six individuals experiencing the HR state need to be treated for one year to prevent one case of full-blown psychosis (i.e., number needed to treat [NNT]=6).^[4] The effect of early intervention for APS is analogous to the early intervention for coronary heart disease to prevent sudden cardiac arrest; such interventions can potentially significantly decrease the number of individuals who progress from the HR state to first-episode psychosis.^[11]

Despite these potential benefits of identifying and treating individuals in the HR state, many questions remain. The relationship between psychopathology, social dysfunction, cognitive decline, and structural change in the brain during the evolution of psychosis remains a mystery. Unraveling this mystery may take decades. At this early stage in our understanding we believe efforts should focus on (a) improving the reliability of the HR diagnosis by identifying the clinical characteristics and biomarkers that predict conversion from the HR state to psychosis; and on (b) identifying medication and non-medication interventions that can effectively prevent progression from the HR state to psychosis.

Conflict of interest

The authors declare no conflict of interest.

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精神病风险综合征——早期诊断与干预的挑战

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概述: 精神病临床高风险状态的概念已用于描述具有精神病前驱症状而处于高发病风险的个体。这一高风险概念促使人们更深入理解精神病的发展转归, 并在为精神病临床高风险人群提供必要的精神卫生服务方面提供了理论依据。早期诊断和干预可能会改变精神病性状态的病程, 从而防止相应功能损害的发生, 或将功能损害减少到最小程度。这是相对较新的研究领

域, 需要更多的研究才能充分理解这种高风险状态。

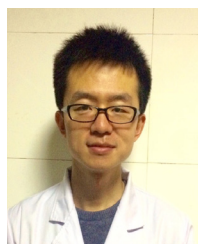
关键词: 精神病临床高风险状态, 精神病风险综合征, 轻微精神病综合征, 精神分裂症

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