

Certainly, the evidence based on family studies suggests that subclinical psychotic experiences are influenced by genetic risk factors. In theory this may offer a unique prospect to develop a screening test based on genetic composition. Indeed, similarly to the asserted nature of the extended psychosis phenotype, the genetic risk for psychosis is distributed on a continuum at the highest end of which are affected individuals followed by their healthy relatives¹¹. Although these results support the premise of being able to detect those at risk based on their genetic make-up, recent attempts of linking genetic risk score for schizophrenia to an intermediate phenotype in non-clinical populations have so far been contradictory¹².

The importance of the transdiagnostic and extended psychosis phenotype in relation to diagnosis, aetiology, prevalence and outlining the future direction for research is indeed noteworthy. However, without a clearly established and scientifically validated threshold defining pathology, as well as markers indicative of susceptibility to the illness, the borderline between normality and psychopathology will remain contested.

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The authors are supported by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London.

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DOI:10.1002/wps.20327

Psychotic experiences and their significance

The term “psychotic experiences” generally refers to subthreshold forms of hallucinations and delusions. However, this term is used inconsistently, sometimes referring to psychotic symptoms (i.e., full threshold positive phenomena), at other times including both sub- and full threshold positive symptoms. van Os and Reininghaus¹ use the term “subclinical psychotic experiences” to discuss their views on psychotic experiences along the extended psychosis phenotype. Here we present a clinical perspective from the ultra high risk (UHR) paradigm, that aims to identify people at high risk of psychotic disorder by the presence of psychotic experiences and associated help-seeking and functional impairment.

van Os and Reininghaus assert that “most individuals with psychotic experiences have a current diagnosis, primarily one of mood or anxiety disorder”¹. We do not believe this is true. For example, Varghese et al² found that major depressive disorder was absent in the majority of individuals with psychotic experiences, including those scoring in the highest quartile for these experiences. Similarly, anxiety was absent in most people with psychotic experiences, even for those in the highest quartile. Morgan et al³ showed that 46% of their community sample with psychotic experiences had no common men-

tal disorder, and a large German general population study found that only 43% of individuals with psychotic experiences at baseline had at least three symptoms of depression 3.5 years later (note that at least three depressive symptoms is not necessarily diagnostic).

In fact, many of the studies cited by van Os and Reininghaus as evidence for their assertion are examining a different research question, that is, the prevalence of psychotic experiences in people with mood and anxiety disorders. Indeed, individuals with common mental disorder *are* more likely to have psychotic experiences than their counterparts with no psychiatric disorder⁴, and such experiences in mood and anxiety disorders predict more severe illness course⁴.

While psychotic experiences may not always be associated with mental disorder in the general population, some people with psychotic experiences are at increased risk of psychotic disorder, including schizophrenia. This has been shown in both general population studies⁵ and the UHR group⁶. A meta-analysis of UHR research found that risk for psychotic disorder was 22% within one year of identification, rising to 36% after three years⁶. Therefore, while van Os and Reininghaus argue that individ-

uals in the community with psychotic experiences are more likely to develop a mood or anxiety disorder than a psychotic disorder, these phenomena actually predict psychotic disorders far more strongly⁵. This is because mood and anxiety disorders are much more common than psychotic disorders and frequently occur in the absence of psychotic experiences⁴. Consistent with this, as van Os and Reininghaus note, evidence from a Danish birth cohort study showed that psychotic experiences at age 11-12 years were strongly associated with a family history of psychotic disorder, but not of common mental disorder. Thus, just as the UHR state is relatively specific to psychotic disorders (compared to non-psychotic disorders)⁷, this is also the case with psychotic experiences in the general population.

So, how are we to understand these psychotic experiences? It is important to recognize that not all positive psychotic symptoms are the same. Previous research has identified four factor (persecution, bizarre experiences, hallucinations, and paranormal beliefs/magical thinking)⁸ and five factor (hallucinations, delusions, paranoia, grandiosity, paranormal beliefs)⁹ models of psychotic experiences. Persecution, bizarre experiences and

hallucinations are more likely to be associated with distress and disability than paranormal beliefs/magical thinking⁸. Further, the type of experience may play a role in determining if an individual develops psychotic disorder or more common mental disorder. The finding that most individuals with psychotic experiences have no mental disorder may be because they have the more benign paranormal beliefs/magical thinking. This remains to be investigated.

There are other factors which are likely to be significant predictors of whether an individual develops a clinical disorder or not, and whether that disorder is schizophrenia, another psychotic disorder or common mental disorder. These include the intensity, persistence and frequency of symptoms, related distress, attributional style, the presence of negative symptoms and cognitive dysfunction, history of childhood maltreatment, demographic features (such as social deprivation), and genetic risk. These factors are likely to influence each other.

Consistent with this, van Os and Reininghaus postulate that some psychotic experiences are associated with and are risk factors for psychotic disorder (the “specific extended psychosis phenotype”), while some are non-specific and are risks for both psychotic and non-psychotic disorders (the “transdiagnostic psychosis phenotype”). This is similar to a model we have previously described⁸, where we posited three groups. We proposed that: a) some psychotic experiences may indicate underlying vulnerability to schizophrenia (psychosis-specific); b) some may be “incidental” to common mental disorders such as anxiety and depression (similar to the “transdiagnostic phenotype”); and c) some may not be associated with any clinical disorder and may never come to clinical attention. This third group accounts for the finding that many indi-

viduals with psychotic experiences have no clinical disorder.

It is important to also account for the dynamic nature of symptoms. Individuals with psychotic experiences and common mental disorder may still be at risk of psychotic disorder. Mood and anxiety symptoms are common in the prodrome of schizophrenia, and individuals who meet the UHR criteria often have concurrent mood and/or anxiety disorder⁷. In the UHR population, mood and/or anxiety disorders may persist over time, often in the presence of continued psychotic experiences, without the individual ever developing frank psychotic disorder. This suggests that the psychotic experiences are part of these “neurotic” illnesses (the “transdiagnostic” or “incidental symptoms” group). For those with both psychotic experiences and mood/anxiety disorders, it is not possible to determine the direction of causality.

People with psychotic experiences that co-occur with mood and anxiety symptoms may seek help, and van Os and Reininghaus claim that these people will be “mislabelled as UHR”. We do not agree with this. These individuals will meet UHR criteria and *are* at high risk of full-blown psychotic disorder. They are also at risk of persistent or recurrent mood and anxiety disorder, of impaired psychosocial functioning and of persistent psychotic experiences. It is also true that they may not be at risk of any disorder, and symptoms and functioning might resolve over time⁷. We acknowledge that the UHR group is heterogeneous. The clinical approach to treating this group is to manage current symptoms and reduce distress. Cognitive behavioural therapy is useful both to manage mood and anxiety symptoms and assist people to better deal with psychotic experiences. It can therefore be seen as a “transdiagnostic” treatment, where therapy focuses on the issues that the clients themselves identify as being important targets.

Understanding more about the UHR group and what predicts different trajec-

ties is an ongoing challenge for research in this area. Negative symptoms and cognitive dysfunction appear to predict poor long-term functioning in the UHR group¹⁰. Similarly, in the general population, negative symptoms and worse cognition are associated with poor functioning in those with psychotic experiences¹¹. Ultimately, we need to be able to distinguish these and other risks in both the general population and those in the UHR group, regardless of whether the outcome is a psychotic or non-psychotic disorder.

General population and UHR sampling approaches can complement each other in examining psychotic experiences, their aetiopathology, associations with possible mediating factors (such as negative symptoms, cognition, childhood maltreatment and substance use), and their clinical significance. van Os and Reininghaus’ paper stimulates thought in this area, and robust, ongoing debate and discussion are to be welcomed.

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DOI:10.1002/wps.20328

High time for a paradigm shift in psychiatry

There is no doubt that several people, especially during their childhood and

adolescence, have some sort of psychotic-like experiences, and that only a minority

of them go on to develop a serious psychiatric disease. We completely agree on this