EDITORIAL

Psychotic Experiences in the General Population
Symptom Specificity and the Role of Distress and Dysfunction

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It has been more than 125 years since Eleanor Mildred Sidgwick first reported an unusually high rate of hallucinations in a general census of the population of Cambridgeshire, England.[1] Yet despite the endorsement of prominent psychologists of the day, such as William James, MD—and likely in part because of Mrs Sidgwick's affiliation with the Society for Psychical Research—this observation played little discernable role in the development of the emerging, predominantly categorically defined nosology of psychosis. Nonetheless, the lifetime incidence of psychotic experiences among individuals in the general population has been repeatedly estimated to be greater than 5% across large international samples.[2] Many affected individuals do not seek psychiatric help and yet report experiences remarkably similar to those seen in classically defined psychosis, with some notable and informative exceptions.[3]

Related article

Although the existence of psychotic experiences in nonpsychiatric samples is now widely acknowledged, the extent and nature of their association with those of individuals with a diagnosable psychotic illness remains a topic of active debate: should we interpret individuals with psychotic experiences, such as voice hearing, in the general population as being on the tail of a gaussian distribution of nonpathological experiences, or might they represent higher-functioning individuals within the psychosis spectrum? Are psychotic experiences a nonspecific marker of general psychiatric distress, as a fever is a nonspecific marker of illness in somatic disease, or does the expression of psychotic experiences depend on multiple interacting predispositions that define both symptom development and ability to function?

In this issue of *JAMA Psychiatry*, Legge et al[4] take a substantial step toward identifying genetic contributions toward risk for psychotic experiences in a general population sample from the UK Biobank and subsequently associate them with genetic risk factors for psychiatric illness. While they[4] highlight the genetic commonalities underlying psychotic experiences and disorders traditionally thought to be on the psychosis spectrum, such as schizophrenia and bipolar disorder, they also found commonalities with attention-deficit/hyperactivity disorder, major depressive disorder, and autistic spectrum disorder. Fittingly, the authors[4] found that the presence of distress associated with psychotic experiences strengthened genetic associations not only with schizophrenia but with each of these psychiatric illnesses. This finding speaks to the possibility that some of the genetic contributions identified by the authors may not be associated with the psychotic experiences themselves but rather with susceptibility to distress or dysfunction caused by these and other psychiatric symptoms.

Penetrance of the genes in question likely depends at least in part on environmental influences, some of which have been studied extensively. Recently, some have proposed risk stratification by *exposome*,[5] a composite score of relevant exposures that may increase risk for psychosis and is analogous to the polygenic risk score used by Legge et al.[4] The inclusion of both genetic and environmental risk factors may aid in risk stratification for those deemed at clinical high risk for psychosis. However, the low discriminant capacity of both exposome and polygenic risk scores would likely limit their utility for this purpose; the addition of stress-based measures did not contribute significant independent associations in a recently published risk calculator.[6] Nonetheless, the persistence of attenuated psychotic symptoms in some individuals who are at clinical high risk for psychosis but do not convert has been well described.[7] Although these individuals remain at elevated risk of conversion,[8] understanding the factors that allow them to maintaining functioning while continuing to experience symptoms will be important for future attempts at risk stratification.

The combination of environmental and genetic composite scores may lead to improved insight into individualized pathways toward psychotic experiences, highlighting genetic vulnerabilities to specific stressors likely to lead to phenotypic expression. Ultimately, this will require a more sophisticated mapping between phenomenology and biology than currently exists. To enable this, genetic approaches should be combined with deep phenotyping and behavioral analysis within a theoretical framework capable of linking all relevant explanatory levels, from symptom expression to neurophysiology. One such framework is predictive processing theory, which is linked closely with the free energy principle and the Bayesian brain hypothesis[9] and attempts to explain perceptual and cognitive phenomena as manifestations of a drive to maintain as accurate an internal model of one's surroundings as possible by minimizing prediction errors. This relatively simple scheme makes specific—and, importantly, falsifiable—assessments of the mathematical signatures of neurotypical processes and the ways they might break down to produce specific psychiatric symptoms.

With colleagues, I recently undertook a series of experiments[10] meant to elucidate the computational processes underlying hallucinations. Using behavior from a novel task meant to safely produce hallucinations of faint tones

embedded in white noise, contingent on the presence of a concurrently presented visual stimulus, we fit parameters of a predictive processing theory–based generative model of perception. In this model, perception is seen as a process of unconscious inference in which both incoming sensory evidence and prior experiences of the world are combined according to their respective precisions. Thus, within this model, hallucinations (ie, perceptions in the absence of incoming sensory evidence) may be seen as the result of overly precise prior experiences or weighing one's expectations about the world too heavily during perception. Consistent with this hypothesis, the study found that individuals with daily auditory hallucinations were especially susceptible to conditioned auditory hallucinations and that this susceptibility was the result of a tendency of these individuals to overly weigh their prior experiences during perception.

Importantly for the current discussion, these findings[10] applied not only to people who heard voices and had a schizophrenic spectrum illness but also to people who heard voices daily without a diagnosable psychotic illness. These individuals, who self-identified as mediums, exhibited low levels of distress associated with their voice hearing and interpreted their voices spiritually—hearkening back to Mrs Sidgwick's first descriptions of people who heard voices but did receive clinical care. Despite the fact that the study model was meant to identify differences in a specific parameter associated with the relative precision of prior experiences, which was thought to underlie hallucinations, higher-level model parameters encoding beliefs about volatility in the stimulus associations were lower (and thus less accurate) in clinical vs nonclinical groups. Model parameter trajectories were then used to link specific, clinically relevant computational functions to activity in brain regions involved in hallucinatory perception. This example demonstrates the power of generative modeling to link levels of description. However, it should be noted that its power lies in the ability to focus transdiagnostically on a specific symptom that can be proposed to arise because of specific information-processing deficits. Progress in understanding psychotic experiences in the general population, then, may depend on researchers' ability to focus on each of these symptoms in turn, using sufficiently complex hierarchical models to understand the associations between development of these symptoms and the distress and dysfunction that sometimes arise from them.

Distress and dysfunction continue to be convenient, ethical, and ecologically valid markers of a need for intervention. These constructs may themselves be proxies for other phenomena, such as control over symptoms,[11] or computational concepts, such as impaired volatility encoding and belief updating.[10] Regardless, they likely represent a potentially separate target for intervention that may be independent of individual symptom expression. Paradoxically, however, alleviation of distress or dysfunction in some cases may depend on addressing specific symptom experiences. The field's task going forward will be to target both distress and the pathophysiology of distinct experiences; the goal must be to alleviate suffering in patients, but the key to doing so may often depend on understanding the development and persistence of distinct, distressing symptoms.

ARTICLE INFORMATION

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