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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 with van Os and Reininghaus[1], although the prevalence of psychotic-like experiences in the population is still not clear, because it strongly depends on methodological issues, such as the definition of these experiences, the type of prevalence (e.g., annual or lifetime) reported, the representativeness of the study sample and the age group investigated, the method of assessment (usually self-rating questionnaires or standardized interviews administered by laypersons, which do not allow for checking alternative explanations for the psychotic experiences or for assessing the grade of certainty), and the consideration of influencing factors such as cannabis abuse[2,3].

The "continuity" of psychosis is not an exception in medicine. We know quite well that many people are sometimes depressed or anxious without ever developing a depressive or anxiety disorder, and that many people sometimes have a cough without developing a serious lung disease.

Regarding the continuity of psychosis, G. Huber[4] already in the 1980s described the "Vorpostensymptome" (“outpost symptoms”), basic and prodromal symptoms preceding the outbreak of frank psychosis, and we later replicated these findings in a large representative sample with Häfner and others[5].

Based on these findings and P. McGorry's initiative of assessing this insidious onset of psychosis prospectively, early detection of psychosis was established[6]. Thus, acknowledging the continuity of psychosis has opened the door for its early detection. Many centers in the world have in the meantime shown that transition to frank psychosis can be predicted with a relatively high accuracy by carefully assessing these early signs and symptoms in help-seeking individuals: about 37% of those fulfilling the risk criteria develop psychosis within three years, mainly schizophrenia spectrum disorders[6,7], although psychotic transition was most likely prevented in some patients by caring for them in the early intervention services.

The big question, however, always was: when do psychotic-like experiences really predict later transition to psychosis, when are they symptoms of another mental disorder, and when are they just harmless, transient phenomena?

Early detection research has established quite an elaborate set of criteria for this prediction and is continuously trying to refine them[6-8]: the individuals or one of their significant others need to be distressed and help-seeking; they have to belong to an age group at risk; they *concurrently* have to display psychotic-like experiences such as attenuated hallucinations, unusual thought content or suspiciousness *above a certain threshold of severity;* or they must have had full-blown psychotic symptoms for less than one week; or they have to show a genetic risk in combination with a recent marked social decline, or, in some studies, with newly developed unspecific prodromal signs[9]; and, most importantly, risk assessment is based on thorough examinations by specifically trained, specialized psychiatrists and psychologists. More and more, additional predictors are included, such as (subclinical) negative symptoms or neurocognitive decline.

Well aware of the fact that psychotic experiences can be "transdiagnostic" phenomena, patients in early detection services are usually diagnosed according to the diagnostic criteria they fulfil (mainly depressive or anxiety disorders) and, in addition to that, they are educated about their potential risk of going on to develop some sort of psychotic disorder. So, there is not a "mislabelling as ultra-high risk status", as stated by van Os and Reininghaus[1], but the transdiagnostic nature of psychotic-like experiences is taken into account, which is exactly what van Os and Reininghaus demand. Fortunately, about two thirds of these individuals do not develop frank psychosis and some of them completely recover. In these cases, early treatment may have been beneficial not only for their psychotic-like symptoms, but also for the other symptom dimensions.

Acknowledging continuity also offers a chance for destigmatization. Educating patients, their significant others and the general population about the continuity of mental health problems often brings great relief and opens the door for the "coming out" of those concerned and a better

understanding by those not (or not yet) concerned. At the same time, it is a step away from an old patriarchal psychiatry in which patients were not educated about their diagnoses and risks.

However, if we acknowledge that mental (not only psychotic) symptoms are often continuous – temporally as well as phenomenologically – and cross the borders of traditional categories, does that really mean that we need new diagnostic approaches?

Clearly defined, reliable diagnostic categories brought great progress into psychiatry – research and clinic – some decades ago. But are these categories really valid entities? We suppose we have to admit that they are not. What was a progress some decades ago is not satisfying anymore, because research in psychiatry has made significant progress in the meantime, enabling us to enter a process which other medical specialties such as internal medicine have entered much earlier. Our colleagues there are well beyond deriving diagnoses from the presenting symptoms only, such as different sorts of coughing, aspects of sputum etc., but have learned to also use the "biomarkers" of their patients by means of X-rays, bacteriological analyses etc. and thereby learned that one and the same symptom can have completely different aetiologies, which is the basis for their diagnoses (e.g., pneumonia, tuberculosis or lung cancer).

Psychiatry in the meantime also has developed this potential of identifying disorders based on aetiology or at least suspected pathogenetic mechanisms rather than only on presenting symptoms. The challenge is now to use emerging research findings for identifying new, valid, aetiologically defined disease entities. To this end, data from genetics, neuroimaging, neurocognition, neurophysiology, neuroendocrinology, immunology etc. should be used, but also data on psychosocial pathogenetic influences such as environmental stressors and triggers[8].

In order to derive such new, aetiologically valid entities, research has to be free from preconceived assumptions and specifications and should be purely data-driven in a first step. All the above-mentioned assessment modalities have to be integrated. Dimensional rather than categorical approaches should be used in a first step, in order to avoid loss of data. Furthermore, data have to be derived from large populations with mental problems and not from specific, pre-defined traditional and to some extent artificial categories of patients. Thinking in silos has rarely brought progress.

New statistical methods, e.g. latent variable mixture models[10] or unsupervised machine learning[11], could allow for such new transdiagnostic, assumption-free, multi-domain approaches, which are not just based on psychopathology but mainly on aetiopathogenetic factors – neurobiological as well as psychosocial ones.

Thus, expanding on van Os and Reininghaus' suggestions, we propose an even more radical paradigm shift in psychiatry. Hopefully, our discipline and our patients can, in the future, benefit from such new approaches in many ways: a) in the general population, a more dimensional concept of mental symptoms would foster destigmatization and early detection; b) in research, more valid, aetiologically defined disease entities could be identified; c) in the clinic, these new entities would hopefully allow for more causal therapies.

Anita Riecher-Rössler, Erich Studerus
Center for Gender Research and Early Detection, University of Basel Psychiatric Clinics, Basel, Switzerland

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