

Why the concept of schizophrenia is still alive and kicking

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In their paper ‘The slow death of the concept of schizophrenia’ Guloksuz and Van Os have elegantly written about the (ir)relevance of the schizophrenia diagnosis. They make the point that this diagnosis not only carries the negative connotation of poor outcome and (hence) stigma; they also argue that schizophrenia is non-specific, showing overlap with (amongst others) bipolar disorder. How much more useful and more humane would it be, in their eyes, to focus on the more prevalent phenotype: psychosis.

There is much value, both clinically and scientifically in their proposition to study psychosis in the population, and the various component parts of this phenotype, such as hallucinations and delusions. Similarly, their statement rings true that the (ultra) high risk concept of schizophrenia, focusing on psychosis as it does, has been proven inadequate in predicting transition to schizophrenia – especially because of this limited focus and even more narrow outcome (Cannon *et al.* 2016). Indeed, in adolescence the route to psychiatric illness is broad and rather ill-defined (Mesman *et al.* 2013) providing an interesting field of research into the pathways to psychiatric illness, a field that has indeed been hampered by the aforementioned constricted definition of high-risk.

However, their main thesis that the diagnosis of schizophrenia is neither valid nor useful is not as well supported by the data as they would like to suggest. First, bipolar disorder and schizophrenia show many more differences than the response to lithium (which they cannot and do not dispute; that lithium reduces the affective symptoms of schizophrenia is of course not the same as being effective as a monotherapy for schizophrenia, which it is not). High IQ is a risk factor for bipolar illness; in schizophrenia the risk is increased by low IQ (Maccabe *et al.* 2010;

Vreeker *et al.* 2016). Intracranial volume is reduced in schizophrenia (Haijma *et al.* 2013), in bipolar illness it is increased (Hulshoff Pol *et al.* 2012), suggesting differences in brain development between both disorders. And finally, the often-quoted genetic overlap between both disorders is smaller than the difference in genetic risk profiles, both for common and rare variants (Neale & Sklar, 2015). In short, schizophrenia does not differentiate from bipolar disorder, clinically as well as biologically.

However, the Achilles heel in their argument is the basis on which it is founded: that schizophrenia should be understood as a form, severe or not, of psychosis. Indeed, they argue that Kraepelin’s dichotomy is a false one, since psychosis is part of both schizophrenia and bipolar illness; that both disorders are cyclical and that schizophrenia can have a good outcome. All are true and uncontested. However, as they could have read, Kraepelin did *not* define schizophrenia on the basis of psychosis. He delineated the illness on the basis of the cognitive decline *preceding* the onset of psychosis – by many years. Indeed, in his original description of the illness, his account of the cognitive (and social) decline literally precedes the discussion of psychotic symptoms by many pages, indicating the relative priority – both in chronology and in relevance – he attributed to cognition rather than psychosis. Indeed, whether based on population-wide samples (Kendler *et al.* 2016), birth cohorts (Meier *et al.* 2014) or longitudinal high-risk studies (Seidman *et al.* 2016), all studies show that it is the cognitive decline *preceding* psychosis, much more than psychotic symptoms *per se*, that predict the onset of schizophrenia. That is why, on the basis of these and other data, we have argued that schizophrenia should be conceptualized as a cognitive, rather than a psychotic disorder (Kahn & Keefe, 2013).

In summary, Goloksuz and van Os come up short in their argument that the concept of schizophrenia is slowly dying. Yes, when viewed through the narrow prism of psychosis, schizophrenia is not unique and

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not a useful concept. Indeed, if psychosis it is we want to study, we should follow the lead Guloksuz and van Os provide in their paper: study the phenotype in the population in all their aspects of severity. However, if the goal is understanding, the illness that starts with cognitive and social decline – with psychosis a late (albeit prominent) symptom – we cannot do without the concept first delineated by Kraepelin. In fact, elucidating the causes and consequences of cognitive decline in psychiatric illness may not only be necessary to understand schizophrenia; it will help to differentiate this syndrome from the others it is confused with (Keefe & Kahn, 2017). A need amply demonstrated by the paper of Guloksuz and van Os. The questions they raise are relevant, their proposed solutions are not.

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