

Chronic psychosis and its prevention

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Opinion

Nothing is more challenging in psychiatry than the management of chronic psychosis. Indeed, this issue may shape the future of psychiatry in the long run. Today there is excessive pessimism in the field about our ability to influence the outcome of chronic schizophrenia. In my opinion we need a long term vision with emphasis on prevention, early detection and a good dose of optimism. Winston Churchill once said: “for my self I am an optimist – it does not seem to be much use in being anything else.”

Why chronic psychosis?

Being free of hallucinations, delusions or anxiety are important to our patients, but things that they care about the most, such as going to school, work or raising children are out of the reach for the majority in spite of the best treatments.

Here is a short history of chronic psychosis: at the turn of the last century there were large public institutions for tuberculosis, leprosy and chronic psychiatric illnesses, especially schizophrenia. After enough progress was made in infectious diseases, institutions for TB and leprosy became obsolete. When chlorpromazine was discovered in 1954 there was hope that deinstitutionalization would occur in psychiatry as well. This belief led to the Community Mental Health Act (passed by the U.S. Congress in 1963). However, as of today public institutions treating chronic psychoses remain standing. To put it simply, treatment of these conditions has not made enough progress as to warrant the abolition of hospitals for their long term treatment.

Being mindful of our limitations

At this point you may not agree with me, after all antipsychotics are very efficacious, aren't they? Indeed, they are, but only for positive symptoms and acute psychosis. If you filter out the noise and the spin of the industry, this is what remains standing: neither first nor second generation antipsychotic medications do much for returning our patients to leading productive and healthy lives.¹ In other words we are unable to influence the chronicity or disability caused by schizophrenia and other chronic psychoses and we should acknowledge our limitations.

In order to take a long view at psychiatry, let's pause for the moment in the shade of an old olive tree on the road from Athens to Megara in Ancient Greece. It also happens that Socrates sits there resting from the scorching sun of Attica. Being mindful of our limitations, explains Socrates, is part of the Socratic method of thinking. This approach has a long pedigree, dating all the way back to 327 B.C. and the publication of the world's first work on introspection: Plato's Apology.

As you may recall, Socrates was on trial – and ultimately sentenced to death – for corrupting the youth of Athens. He had done no such thing, of course. What he had done was educate and inspire students, teaching them to challenge arguments from authority and question what they knew to be true. In the process, he frustrated and embarrassed many powerful people with his persistent line of questioning, known today as the Socratic method.

Why was he such a gadfly? According to the Apology, the oracle at Delphi had pronounced Socrates the wisest man in Athens. Yet no one was more astonished – or more disbelieving – than Socrates himself. So he immediately set out to disprove the oracle by finding a wiser man. He started by examining a politician with a reputation for great wisdom (and the ego to go with it). Not only was the politician unable to justify his beliefs, he resented Socrates' challenge to his authority. “So I left him,” Socrates laments, “saying to myself, as I went away: Well, although I do not suppose that either of us knows anything really beautiful and good, I am better off than he is, for he knows nothing, and thinks that he knows; I neither know nor think that I know. In this latter particular, then, I seem to have slightly the advantage of him. Then I went to another who had still higher pretensions to wisdom, and my conclusion was exactly the same. Whereupon I made another enemy of him, and of many others besides him”. In the end, Socrates discovered he was indeed the wisest man in Athens. Not because of how much he knew, but because he understood how much he didn't know.

Socrates makes an important point. He tells us to acknowledge our limitations, to face up to our own ignorance. How much we need Socrates in psychiatry today. The tectonic plates under our discipline are shifting and we are called to adapt our thinking and practices. Armed with the Socratic method let us bid farewell to Socrates and take a long view at psychiatry vis-à-vis the treatment of chronic psychoses. Two pillars appear immediately in our sight: prevention and rehabilitation both anchored in neuroscience.

Prevention – the first pillar of the future treatments

Throughout the past two centuries we have been treating psychosis after we diagnose it, meaning after the fact. You would not start treating schizophrenia in the absence of delusions, hallucinations or negative symptoms, right? Even our diagnostic criteria insist on “continuous signs of the disturbance persisting for at least six months”. However a look at preventative interventions demonstrates that in medicine more progress was made by preventative as opposed to curative interventions. Hand washing saved more lives than antibiotics. More than 60% reduction in mortality due to coronary artery disease

(1.1million deaths each year) was achieved by controlling the blood pressure, diet and cholesterol.

Treating psychosis after the fact may be too little and too late. For example, in neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease and Huntington's disease changes in the brain precede changes in behavior sometimes by more than a decade. In Parkinson's disease symptoms only emerge after 80% of dopamine cells have been lost.²

Birth cohort studies demonstrate that individuals who develop schizophrenia later on differ from the general population on a range of developmental indices some of which occur as early as the first year of life, so why wait?³

But how can we proceed to treat psychosis prior to its onset? As a psychiatrist my knee-jerk reaction is to think: "shall I start prescribing medications before someone shows signs or symptoms of psychosis?" Again, too much simplification leads to an unsophisticated view of life. Who mentioned medications?

Diagnosis of schizophrenia in its prodromal phase is done by psychological testing such as Structured Interview of Prodromal Symptoms (SIPS), Neurocognitive Test Batteries for at Risk Mental States (ARMS) or Cognitive Perceptive Basic Symptoms (COPER). These tests were found to have a positive predictive power for conversion to psychosis of 75%.²

What about prodromal treatment? Here too the approach is psychological. Cognitive rehabilitation (or remediation) is believed to be a key component of early intervention programs in the prodromal phase of the disease.⁴

Maintenance treatment of chronic psychosis: the second pillar of future treatments

Throughout our training we were thought that maintenance antipsychotics treatment should never be stopped, after all you would not discontinue insulin in a diabetic type one patient, would you? All of us can recall schizophrenic patients from our practices who went off their medications and suffered disastrous consequences. But maintenance treatment of chronic psychosis may be changing.

Results from recent outcome studies suggest that antipsychotic maintenance may have limited efficacy for the outcomes that matter to our patients: full return to well-being and a productive place in society.^{5,6} In Europe only 20% of people diagnosed with schizophrenia are able to hold a job for more than one year. Moreover a recent study seems to suggest that at least a subgroup of patients with schizophrenia had superior recovery rates when maintenance medications were discontinued.⁷

A study published last year demonstrates via neuroimaging that both schizophrenia and some antipsychotics may cause brain gray matter loss^{8,9}. Thus it appears that despite successful treatment of delusions and hallucinations some schizophrenias (because there are many) progress unabated towards disability and cognitive deficit.

This is where cognitive rehabilitation fits in. Most psychiatrists today may not be familiar with cognitive rehabilitation even though it is rapidly emerging in being as important, if not more important, than psychopharmacological interventions¹⁰.

As an optimist, I see opportunity rather than gloom. Provided a right vision of the future in terms of prevention, and rehabilitation, psychiatry is poised for major advances. These advances are

driven by the advent of highly sophisticated neuroimaging and neurophysiological methods and tools for studying brain functions and how changes in brain function relate to neuropsychiatric illness. For example, mapping the white matter tracts of the brain has revealed impairments in salience network in both chronic schizophrenia and frontotemporal dementia^{11,12}

In medicine many acute conditions resolve after being treated and never become chronic. Others become chronic in spite of early and adequate interventions. For example, most acute infections remain localized, and never turn into sepsis, but sepsis occurs when early inflammation fails to shut down.¹³

Aging favors inflammation as older patients are more prone to developing sepsis than their younger counterparts. For the same reason, these individuals also develop delirium after urinary tract or other minor infections. This suggests that in regards to inflammation the brain is not a privileged organ, but there are constant two way communication between the CNS and the periphery. Indeed, peripheral inflammation can spread to the brain and vice versa. For example, cerebral ischemia is known to trigger peripheral inflammation. In Alzheimer's disease the peripheral lymphocytes respond poorly to mitogenic stimulation. The same phenomenon was found in chronic schizophrenia.¹⁴⁻¹⁶ This may open a diagnostic window for early detection and prevention of these conditions (first pillar of interventions).

On the other hand, patients with symptoms of chronic psychosis may benefit from cognitive neuroscience and rehabilitation. Tertiary prevention can be applied to chronic psychiatric conditions as they aim to reduce the burden of established disorder by optimizing treatment and rehabilitation.¹⁷

Conclusion

Throughout the history of medicine, prevention has saved more lives than did curative interventions. Treatment of hypertension and adequate diet has prevented more strokes and heart attacks than medications administered after the fact. AIDS and many cancers are currently considered chronic diseases, partially because of prevention. Today we are learning how to identify psychosis early by sensitive testing. For example, the Copenhagen Perinatal Cohort documented that individuals who later in life develop schizophrenia can be identified as early as the first year of life.¹⁸ With the same token, we are learning to identify antenatal risk factors such as viral infections affecting offspring gene expression and epigenetic control of gene expression via microRNAs (miRs).¹⁹⁻²⁰ In the future it may be possible not only to diagnose psychosis early by to silence pro-inflammatory genes, preventing manifestation of psychosis.

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Conflicts of interest

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