Psychotic disorders are severe psychiatric conditions which are characterised by losses, namely the loss of touch with reality during which the patient may often experience auditory hallucinations, persecutory delusions, and which are often accompanied by a crippling loss of awareness about the need for treatment and ensuing social disability.\(^1\) The paradigmatic example of a psychotic disorder is schizophrenia which occurs in 1% of the population and the patient often suffers from a loss of ability to plan, work, and not infrequently, a loss of interpersonal relationships in the longer term.\(^2\) According to the World Health Organisation (WHO), schizophrenia lists amongst the top 10 leading causes of years lost to disability worldwide,\(^3\) and is one of the medical conditions with the highest disability weights.\(^4\) Due to the huge burden of illness for both patients and carers, there is a pressing need to better understand its underlying neurobiology so as to inform and hopefully reform treatment of these incapacitating conditions.

In the study of the pathophysiology of any complex neurobehavioural disorder including psychotic disorders, one seeks to look for unifying hypotheses which take into account 3 cardinal aspects, namely the context of continuing evidence, core neurobiology based on current investigations, as well as clinical relevance to the patient’s experience.\(^5\) In this regard, one such hypothesis posits that white matter brain changes underlie psychotic disorders and its clinical manifestations, and which can be studied with current neuroimaging modalities including structural magnetic resonance imaging (MRI) and diffusion tensor imaging.\(^6\) In terms of the continuity of evidence, there is mounting evidence to suggest that white matter anomalies underlie psychotic disorders and its clinical manifestations, and which can be studied with current neuroimaging modalities including structural magnetic resonance imaging (MRI) and diffusion tensor imaging.\(^8\) In terms of core neurobiology, there are several patterns that have been noted. In early onset schizophrenia, disruptions of white matter integrity were found in the cortical, subcortical brain regions and white matter associative and commissural tracts, suggesting that changes of cortical-subcortical white matter integrity were found at an early stage of the disorder.\(^13\) In more chronic schizophrenia, differences in the area and volume of the commissural white matter tract, corpus callosum, were greatest in patients whose condition was longstanding relative to patients with a first episode and controls.\(^14\) These findings emphasise the need to understand the wider brain network as well as progressive white matter changes over the illness course. Another area of interest regarding core neurobiology relates to sustained efforts to examine relationships between genetic biomarkers and intermediate phenotypes such as brain white matter changes. The proliferation of recent genome-wide association studies (GWAS) for the last few years encapsulates the vigour in trying to map out heritable biomarkers which may allow better detection of illness and delineation of disease mechanisms.\(^15\) Past GWAS have pointed to genetic signals related to neuronal communication, signaling, and neuroplasticity underlying schizophrenia.\(^16\) A recent landmark study involving 150,000 subjects, 300 collaborators and spanning 30 countries uncovered more than 80 novel genetic loci which have not been previously identified and which are related to body systems including the immune system and gut brain axis.\(^17\) This and other collaborative strategies in medicine would augur well for the future as resources are pooled together by different international groups to generate more generalisable findings in the united quest to advance our understanding of disease mechanisms which can later point...
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16. KW, Woon PS, Teo YY, Sim K. Genome wide association studies (GWAS) and copy number variation (CNV) studies of the major psychoses: what have we learnt? Neurosci Biobehav Rev 2012;36:556-71.


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