

Progressive Brain Changes in Schizophrenia

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For this theme issue, we have called upon experts in the field of study of brain changes in high-risk patients with prodromal symptoms or with a first episode of schizophrenia, whether it takes place in childhood, adolescence, or adulthood. The evidence—or lack thereof—that currently exists for progressive brain changes is discussed in this theme issue by some of the leading groups in the field.

The set of reviews starts with an elegant historical background on the cyclical issue of progressive brain changes in schizophrenia. The longitudinal magnetic resonance imaging studies from Edinburgh and Melbourne in prodromal subjects and subjects at increased genetic risk are then reviewed by their investigators. And finally, bringing us full circle, progressive changes after a first schizophrenia episode and in children and adolescents with early-onset psychosis are the last 2 reviews of this theme issue.

Overall, the different lines of evidence suggest that some structures appear abnormal before the first sign of any symptom and therefore during a first episode, while some of these same structures and others show a higher than expected volume loss over time and thus appear different at follow-up when compared with healthy controls. These progressive changes seem to be present during the initial years after the first episode and continue even in the more chronic phase of the illness.

The results of the different studies reviewed here could be explained by separate disease processes taking place at different times in the lives of patients with schizophrenia or a single ongoing process beginning during brain development and accelerating after maximum cranial volume is reached.^{1,2} Brain insults early in development, either in utero or ex utero, may affect maturational processes. In turn, early and late maturational processes, eg,

regressive or pruning processes, result in dynamic changes in the structure of the brain well into the second and third decade of life and even later.³ These normal processes of brain maturation, leading to decreased cortical volume, could be exaggerated in patients with schizophrenia and lead to greater than expected decreases in cortical volume and increases in sulcal cerebrospinal fluid, in the absence of neurodegeneration. Excessive brain volume loss occurring may also be a consequence rather than a cause of illness, with variables such as psychosis, stress, and drug treatment playing a role in brain volume loss.^{4–6} Therefore, if we attempt to integrate the findings from the studies reviewed in this issue, we would suggest that early and late neurodevelopmental abnormalities may be present in varying degrees in patients with schizophrenia. Some of these may be under genetic control, other may be the result of environmental effects. Finally, progressive changes need to be addressed, not only from the aspect of volumetric brain changes but also at the molecular, cellular, and neurochemical level, and the findings will need to be related to the influence of genetic and environmental factors.^{7–10}

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