Development of Psychosis: Gray Matter Loss and the Inflamed Brain

Findings from a new study in Biological Psychiatry

Philadelphia, PA, January 13, 2015 – The thickness of cortical brain tissue progressively reduces as individuals develop psychosis, according to researchers of a large, multi-site study of young adults at clinical high risk.

Onset of psychosis typically occurs during the transition from adolescence to early adulthood, a period of time when the brain is also maturing. Brain tissue is commonly divided by its appearance on magnetic resonance imaging (MRI) into gray matter, the component of cortical tissue containing nerve cell bodies, and white matter, the component of cortical tissue containing the axons or projections from these nerve cell bodies.

Prior neuroimaging research has established that individuals who convert to psychosis have more rapid and more pronounced gray matter loss, compared to non-converters and healthy individuals. However, since the long-term effects of antipsychotic medications on cortical gray matter are not well understood and nearly all patients are treated with these medications, it has been difficult to distinguish the effects of antipsychotic drug treatment from the progression of schizophrenia.

Dr. Tyrone Cannon, Professor of Psychology and Psychiatry at Yale University, and his collaborators in the North American Prodrome Longitudinal Study Consortium have now provided important new insights into cortical changes associated with the development of psychosis. Their work is published in the current issue of Biological Psychiatry.

They conducted a longitudinal MRI study across 8 U.S. sites. They recruited 274 individuals at clinical high risk for psychosis and 135 healthy controls. Each participant received an initial (baseline) scan and a second scan either one year later or at the time of conversion to psychosis.

Thirty-five individuals ultimately converted to psychosis and they showed a steeper rate of thinning in prefrontal cortex compared with those who did not convert and the healthy control group. Importantly, this tissue loss was not explained by exposure to antipsychotic drugs.

“Because this differential rate of tissue loss was observed among subjects who had never been exposed to psychiatric drugs, we can conclude that the brain changes are part of the natural course of the disorder rather than being a consequence of treatment,” explained Cannon.

Interestingly, the tissue loss observed in the converters was correlated with levels of proinflammatory cytokines in plasma, suggesting the presence of systemic neuroinflammation.

“The findings are also important in showing that markers of proinflammatory cytokines at the baseline assessment predicted the rate of gray matter loss among the individuals who converted to psychosis, suggesting that activation of microglia was involved in the tissue loss,” he added. “This could mean that psychosis is associated with an abnormal acceleration in the processes underlying normal synaptic pruning during late adolescence/early adulthood, or that some kind of immune-related process is involved in psychosis onset, or both.”

“Inflammation is increasingly recognized as a contributing factor to the emergence of progression of disease in every organ in the body,” said Dr. John Krystal, Editor of Biological Psychiatry. “This report suggests that neuroinflammation may be a process that in some cases ‘tips people over’ from the at-risk state into psychosis.”

The authors recommend that future work be conducted to evaluate whether inflammation precedes and perhaps even predicts such gray matter loss, or whether it is a consequence of such loss.

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Notes for editors
Full text of the article is available to credentialed journalists upon request; contact Rhiannon Bugno at +1 214 648 0880 or Biol.Psych@utsouthwestern.edu. Journalists wishing to interview the authors may contact Dr. Tyrone Cannon at +1 203 436 1545 or tyrone.cannon@yale.edu.

The authors’ affiliations, and disclosures of financial and conflicts of interests are available in the article.

John H. Krystal, M.D., is Chairman of the Department of Psychiatry at the Yale University School of Medicine, Chief of Psychiatry at Yale-New Haven Hospital, and a research psychiatrist at the VA Connecticut Healthcare System. His disclosures of financial and conflicts of interests are available here.

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Media contact
Rhiannon Bugno, Editorial Office
+214 648 0880