

Immaturity of the brain may cause schizophrenia

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The underdevelopment of a specific region in the brain may lead to schizophrenia in individuals. According to research published today in BioMed Central's open access journal *Molecular Brain*, dentate gyrus, which is located in the hippocampus in the brain and thought to be responsible for working memory and mood regulation, remained immature in an animal model of schizophrenia.

Professor Tsuyoshi Miyakawa of Fujita Health University, National Institute for Physiological Sciences (NIPS), and Kyoto University led a research team in Japan, with support from the CREST program of Japan Science and Technology Agency (JST). First, the team investigated behaviors by conducting a systematic and well-defined behavioral test battery with alpha-CaMKII mutant mice, an animal model of schizophrenia..

These mice showed abnormal behaviors similar to those of schizophrenic patients. Next, the team found the dentate gyrus neurons in hippocampus of the brain of these mice were not matured morphologically and physiologically. By a gene expression analysis, changes of gene expression related to the maturation of dentate gyrus neurons were also found in the brains of schizophrenic patients. Taken together, the immaturity of the dentate gyrus may be an underlying cause for schizophrenia.

Among their findings, mice heterozygous for a null mutation of the alpha-isoform of calcium/calmodulin-dependent protein kinase II show profoundly dysregulated behaviors, including a severe working memory deficit and an exaggerated infradian rhythm (cycle of increases and decreases in locomotor activity in their home cage; 2-3 weeks/cycle), which are comparable to the symptoms observed in patients with schizophrenia, bipolar disorder and other psychiatric disorders.

Despite extensive research, the brain mechanisms of schizophrenia remain largely unknown. According to Professor Miyakawa, one reason for this is that clinical diagnosis in the area of psychiatry is based solely on subjective observations and not on biologically or objectively solid criteria, "As a result of this limitation, most of the psychiatric disorders currently diagnosed as a single disorder are likely to comprise several biologically distinct heterogeneous populations. Therefore, the identification and investigation of more reliable biomarkers that characterize a single subpopulation of a specific psychiatric disorder are essential for increasing the understanding of the pathogenesis/pathophysiology of such disorders." The authors note that "'Immature dentate gyrus' could provide a basis for such biomarkers that may help produce new diagnosis and treatment for shizophrenia patients".

Source: National Institute for Physiological Sciences

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