

Study shows genetic link for schizophrenia

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Gene mutations governing a key brain enzyme make people susceptible to schizophrenia and may be targeted in future treatments for the psychiatric illness, according to MIT and Japanese researchers.

The work, by scientists from MIT's Picower Institute for Learning and Memory and Japan's RIKEN Brain Science Institute, will be reported in the early online edition of the *Proceedings of the National Academy of Sciences* on Feb. 20.

According to the National Institute for Mental Health, an estimated 51 million people worldwide suffer from schizophrenia. Although 80 percent of schizophrenia cases appear to be inherited, the specific genetic components underlying individuals' susceptibility and pathology are largely unknown.

By studying genetically engineered mice and the genetic makeup of schizophrenic individuals, the MIT and Japanese scientists pinpointed the PPP3CC gene and other genes in the early growth response (EGR) gene family (specifically, EGR3) as likely suspects for causing the disease.

These genes are critical in the signaling pathway for the brain enzyme calcineurin. Calcineurin is prevalent in the central nervous system, where it plays a role in many neuronal functions whose disturbances would play into the disorganized thinking, attention deficits, memory and language problems that characterize schizophrenia.

The researchers confirmed that the PPP3CC gene is involved in diagnosed schizophrenia in Caucasian, African-American and Japanese individuals. EGR3 involvement was confirmed through a separate test.

“These data suggest that the brain signals governed by calcineurin stand at a convergent point of the molecular disease pathology of schizophrenia, and the involvement of the EGR genes reinforces this,” said co-author Takeo Yoshikawa of the RIKEN Brain Science Institute. This knowledge could lead to new schizophrenia therapeutics targeting the calcineurin system, he said.

“This study provides genetic and biological evidence that PPP3CC and EGR3, both constituents of the calcineurin signaling pathway, may independently elicit increased risk for schizophrenia,” said co-author Susumu Tonegawa, Picower Professor of Biology and Neuroscience at MIT. “These findings raised a novel and potentially important role for EGR genes in schizophrenia pathogenesis.”

Source: Massachusetts Institute of Technology

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