MedicalXpress

Neuroscientists identify synaptic defect in brain area involved in Fragile X syndrome

June 7 2010

Researchers at India's National Centre for Biological Sciences (NCBS) and New York University's Center for Neural Science have identified novel synaptic defects in an area of the brain that is involved in the debilitating emotional symptoms of Fragile X Syndrome (FXS). FXS is the leading known genetic cause of autism and mental retardation.

The study, which appears in the journal the Proceedings of the National Academy of Sciences, is also of potential therapeutic significance—it showed that a brief pharmacological treatment is capable of correcting some of these synaptic deficits in mice genetically engineered to model FXS.

Individuals with FXS, which is caused by a mutation in a gene on the X chromosome, suffer from a range of problems, such as learning disabilities, attention deficit and hyperactivity, seizures, and emotional problems related to anxiety and mood instability. To investigate the cellular and molecular basis for the emotional problems associated with FXS, neuroscientists from NCBS and NYU studied how neurons and synapses in the amygdala—a small, almond-shaped part of the brain known to mediate emotion's influence on memory—are affected in FXS model mice.

Using electrophysiological recordings from neurons in the amygdala, Sumantra Chattarji, a professor at NCBS, and Aparna Suvrathan, an NCBS graduate student, determined that there were defects on both sides of synapses in the amygdala—that is, its neurons were not properly

communicating with each other. NYU Professor Eric Klann and Charles Hoeffer, a former postdoctoral fellow in the Center for Neural Science and now at NYU School of Medicine, identified the molecular correlates of these defects, giving the researchers a firm understanding of where the breakdown occurs. Together, these deficits impair the ability of neurons in the amygdala to communicate and encode information.

Their next step was to consider how to normalize communication between neurons. To do so, they focused on group I metabotropic glutmate receptors (mGluRs), which have been shown to be involved in synaptic dysfunction in other brain areas in FXS. mGluRs are receptors for glutamate, the major neurotransmitter in the brain. Specifically, the researchers found that some of the synaptic deficits could be reversed when the amygdala neurons in adult FXS model mice were treated with a drug that blocks these receptors. By blocking the functionality of these receptors, normal communication between neurons could occur.

The findings hold promise for addressing FXS.

FXS is a developmental disorder that arises early in childhood, so the results suggest that synaptic defects can be corrected pharmacologically even after the disease has had time to alter the brains of the FXS mice. The findings follow recent reports that pharmaceutical companies have conducted clinical trials in FXS individuals using compounds that block mGluRs.

Provided by New York University