Medical Science / Neuroscience
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Molecular Basis of Human Mind and Mental Disorders

Speaker:

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Novel molecular targets for stress in the hippocampus

Prolonged exposure to stress can have important consequences for the brain, conferring susceptibility to psychiatric disorders such as human depression. The hippocampus is a brain region important for memory and learning which possesses a remarkable degree of plasticity and is particularly sensitive to stress. Our work focused first on the discovery of novel molecular targets for the stress/antidepressant response in the hippocampus. Through the construction and analysis of cDNA subtractive hybridization libraries, we identified a number of genes regulated by chronic psychosocial stress in the hippocampus of tree shrews (*Tupaia belangeri*). These gene regulations could also be detected in the hippocampus of chronically stressed mice and, in both models, the stress effect was counteracted by antidepressant treatment. Among the genes identified, we selected the neuronal glycoprotein M6a, a highly expressed protein in the CNS which biological function remained unknown. M6a expression levels were decreased in hippocampus of animals exposed to chronic stress and we decided to study the cellular phenotypes caused by M6a overexpression and knock down. We found that M6a plays an important role in neurite outgrowth and filopodium/spine formation, and it might also be involved in synapse formation. These results suggested that this protein could be, at least in part, responsible for the plastic alterations found in the hippocampus of stress/antidepressant treated animals. Thus, we could identify a key molecule that links our previous findings on gene regulation in stressed animals with the morphological alterations and the processes of neuronal remodeling occurring in the hippocampus during chronic stress/depression.