Adenoviral MeCP2 Gene Therapy Partially Improves Neurological Symptoms of Rett Syndrome in Mice

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Rett syndrome (RTT) is a neurological disorder mainly caused by mutations in methyl-CpG-binding protein 2 (MeCP2). Obviously, gene therapy, i.e., gene transfer of intact MeCP2 gene, is a potential candidate for curative therapy for MeCP2, however, its possibility or potential has not yet been studied for Rett syndrome. Alteration of dopaminergic function was suggested in Rett syndrome, and local delivery of therapeutic gene into the nigrostriatal system experimentally revealed promising therapeutic effects in certain neurological disorders such as Parkinson's diseases. As a first study, we explored the therapeutic potential of adenoviral gene therapy that targets the nigrostriatal system and their neighboring neurons for Rett syndrome using MeCP2-null mice. Behavioral studies (open field test) showed that Ad.MeCP2 injection into MeCP2-/y (hemi) male mice on day 39 transiently but significantly inhibited progressive loss of motor skill in comparison with control Ad.LacZ. Beneficial effects on body weight gain and survival extension were small. On the other hand, adenoviral gene therapy for MeCP2-/+ (hetero) female mice, which were suffering from RTT-like symptoms, resulted in more prominent therapeutic effects than those in MeCP2-/y male; reduced motor skills and self-injury behavior were drastically improved during much longer periods. The present results for the first time showed therapeutic potentials of gene therapy for RTT patients, with important implications on the necessity of further development of gene therapy strategy.

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- Asian & Oceanian Child Neurology Association
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Symposium title

Neurochemistry of Autism

Infantile autism (IA) is considered and categorized one of the pervasive developmental disorders (PDD). The behavioral, emotional, and cognitive symptomns of autism indicate that central nervous system dysfunction may be involved. Recent advance of neurochemical and neurotransmitter studies including monoamines (dopamine, norepinephrine, and serotonin), biopterine, neuropeptides, amino acids/organic acids, mineral, secretin and others compounds have been reported.
Brains of some patients with IA are enlarged both by weight and volume. Volumetric magnetic resonance imaging studies (MRI), CT, positron emission tomography (PET), and SPECT neuroimaging sutdies also enabled us to reveal the pathophysiology of IA. The most frequently reported findings in the autistic brain have been assymmetry of right and left hemisphere size, unusually small, closely packed neurons and increased cell packing density in portion of limbic system, , cingurate gyrus, amygdala, and temporal lobe, and cerebellum and brainstem. neuropathological studies showed that age-related abnormalities have been observed in the deep cerebellar nuclei and inferior olivery nucleus of the brainstem. In this symposium, I would like to review the neurochemical and neurotransmitter studies of IA. I laso reviewed the neuropathological, neuroimaging studies and discuss the possible involvement of theses neurocircuits and clinical symptoms.