From Electrophysiology to Chromatin: A Bottom-Up Approach to Angelman Syndrome

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Abstract:
Angelman syndrome is one of the most studied human diseases related to a gene that is expressed on the maternal chromosome only in at least some brain cells. It is caused by inactivation of the UBE3A gene in the brain due to various abnormalities of the 15q11-q13 chromosome inherited from the mother. It is characterized by severe developmental delay, seizures, virtual absence of speech, motor impairment, and a particular behavioral phenotype. Studies of cortical, electromyographic and cerebellar electrophysiology in patients with Angelman syndrome and a mouse model revealed unique rhythmic neurophysiological activities in the cerebral cortex, cerebellar cortex, and muscles. The oscillatory patterns may be linked to molecular pathophysiology of the syndrome involving dysregulation of synaptic neurotransmission through UBE3A-related modulation of functional GABAA receptor complexes.

Key Words: genomic imprinting • DNA methylation • Angelman