Article: 0572
Topic: EPW01 - e-Poster Walk Session 01: Child and Adolescent Psychiatry, Mental Retardation part 1

Autism Spectrum Disorders: Focus On Neuronal Synapses (literature Review)

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Introduction: Advancements in human genetics are revealing a large number of genetic variants involved in Autism spectrum disorder (ASD). This genetic variability affects mostly proteins involved in synaptic function.

Methods: The Medline database was searched using the following keywords: ‘synapses’; ‘autism’. Animal as well as human models of ASD were included.

Results: Nowadays, ASD are considered genetically influenced neurodevelopmental disorders, with abundant evidence pointing to dysfunction at the level of the synapse in the early stages of cerebral development. Potential mechanisms underlying ASD are neuroanatomical abnormalities, extracellular factors, excitatory and inhibitory imbalance and synaptic signaling.

I. **Neuroanatomical abnormalities**

Mutations of *Tsc1 (tuberous sclerosis 1)* and *nlgn3 (neuroligin3)* lead to alterations of synapses in the cerebellum and could explain signs of autism in mice.

II. **Extracellular factors**

Growth factors and neurotrophic factors are associated with ASD such as: HGF, BDNF and WNT2.

III. **Excitatory and inhibitory imbalance**

Defects in synaptic proteins would lead to defective transmissions at excitatory and inhibitory synapses, a key mechanism implicated in ASD. Synaptic molecules involved: neuroligin, neurexin, shank, but also Glutamatergic system, GABAergic system and Serotonergic system.

IV. **Synaptic signaling**

NF1 (Neurofibromin 1), *TSC1/TSC2* (tuberous sclerosis complex 1 and 2), and *PTEN* (phosphatase end tensin homolog) are tumor suppressors genes associated with ASD.

Conclusion: An alternative but not mutually exclusive hypothesis is that environmental factors interact with genetic susceptibilities to influence ASD risk, clinical phenotype and/or treatment outcome.

https://doi.org/10.1016/S0924-9338(15)31912-X Published online by Cambridge University Press