Involvement of glycine binding site of NMDA receptor in the prefrontal cortex of SHRSP/Ezo as an AD/HD animal model

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Background: Attention deficit/ hyperactivity disorder (AD/HD) is a mild developmental disorder. We previously reported that stroke-prone spontaneously hypertensive rat/Ezo (SHRSP/Ezo) had high validity as an AD/HD animal model, because of its behavioral phenotype. It was reported that AD/HD had the front-cortical dysfunction, hypofrontality. Based on these reports, we hypothesized that SHRSP/Ezo as AD/HD animal model has some fronto-cortical incompetence. Thus, we evaluated the excitatory synaptic function in the PFC of SHRSP/Ezo using electrophysiological and pharmacological methods.

Methods: At 6 weeks old, SHRSP/Ezo and its genetic control, WKY/Ezo were anesthetized and immediately decapitated. Using acute coronal brain slice, we recorded excitatory postsynaptic potential (EPSP) in layer V pyramidal neurons in the PFC by whole-cell patch clamp recording method to assess synaptic plasticity in the form of long-term potentiation (LTP). We also performed N-methyl-D-aspartic acid (NMDA) receptor binding assay in the PFC and hippocampus with radio-labeled NMDA receptor antagonist [³H]MK-801 using homogenized membrane tissue.

Results: Theta burst stimulation induced long-lasting EPSP enhancement, LTP, in the PFC of WKY/Ezo, whereas failed to induce LTP, in that of SHRSP/Ezo. The K_d value of [³H]MK-801 binding for NMDA receptors in the PFC of SHRSP/Ezo was higher than in the WKY/Ezo. Neither the B_{max} nor K_d of [³H]MK-801 binding in the SHRSP/Ezo hippocampus were significantly different to WKY/Ezo. When we added 100 μ M glycine into the incubate solution to assess the function of glycine binding site of NMDA receptor in each rat, there was no significant difference of K_d value in the PFC of SHRSP/Ezo.

Conclusion: These results suggest that the AD/HD animal model SHRSP/Ezo has NMDA receptor dysfunction in the PFC, but not the hippocampus. Moreover, some ligands for glycine binding site in NMDA receptor can be a possibility of new drug for AD/HD treatment.