Abstract of Presentation

Presentation Title

The metabolic control of vesicular neurotransmitter transporters

Name (Underline the family name)

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Abstract

Fasting has been used to control eplilepsy since biblical times, but the mechanism of coupling between metabolic state and excitatory neurotransmission remains unknown. Previous work has been shown that vesicular glutamate transporters (VGLUTs) required for exocytotic release of glutamate undergo an unusual form of regulation by Cl^-. Using functional reconstitution of the purified VGLUTs into proteoliposomes, we demonstrated that Cl^- acts as an allosteric activator, and the ketone bodies that increase with fasting and intake of the ketogenic diets inhibit glutamate release by competing with Cl^- at the site of allosteric regulation. Consistent with these observations, acetoacetate reduced quantal size at hippocampal synapses and suppresses glutamate release and seizures evoked with 4-aminopyridine. These results indicate an unsuspected but strong link between metabolic state and excitatory neurotransmission through anion-dependent regulation of VGLUTs. Vesicular nucleotide transporter (VNUT) that generate the signal output through vesicular storage of ATP also possesses Cl^- binding site similar to that of VGLUT, and thus purinergic neurotransmission can be metabolically controlled. In the former part of my talk, I will update our studies on the Cl^- and ketone bodies-mediated regulation of vesicular neurotransmitters. In the latter part of my talk, I will update our JST-MOIST study to establish a platform to study the structure and function of neurotransmitter transporters involved in human neurotransmission using the breakthrough technology on the expression and preparation of membrane proteins developed by Israel group.