S17-5 Identification of a vesicular aspartate transporter

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The aspartate, natural ligand of the NMDA receptors, is enriched in synaptic vesicles of hippocampal neurons and synaptic-like microvesicles (SLMVs) of pinealocytes, and exocytosed. Although evidence increasingly supports the occurrence of aspartergic neurotransmission, this process is still debated because the mechanism(s) for the vesicular storage of aspartate is unknown. Among the many anion transporters, sialin (SLC17A5), a lysosomal H^+/sialic acid transporter, is one of the appropriate candidates of vesicular aspartate transporter, because sialin is highly expressed in non-lysosomal compartments of cells found in various regions of the central nervous system, and the amino acid sequence is similar to the vesicular glutamate transporter (VGLUT). Upon reconstitution into liposomes, sialin transports aspartate in $\Delta\tilde{\psi}$dependent fashion. Immunohistochemistry indicated that sialin is present in synaptic vesicles of hippocampal neurons and SLMVs of pinealocytes. In addition, suppression of sialin expression by RNA interference decreased exocytosis of aspartate in pinealocytes. These results indicate that sialin acts as a vesicular aspartate transporter. Because sialin also transports glutamate, we named it vesicular excitatory amino acid transporter (VEAT). We discuss the physiological significance of sialin/VEAT on Salla disease.