SODIUM AND HYDROGEN IONS AS MODULATORS OF SYNAPTOSOMAL MEMBRANE TRANSPORT ACTIVITY

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The transfer of choline through the membrane of the neuron is a specific, high affinity, sodium-dependent process, a rate-limiting and regulatory step in acetylcholine synthesis. In synaptosomes it was observed that high-affinity but Na^+-independent choline uptake proceeds concurrently to Na^+-dependent transport. The aim of this study was to reveal some regulatory mechanisms of high-affinity choline transport through the synaptic striatal membrane in Na^+-containing and Na^+-free media. We studied choline transport kinetics in synaptosomes as well as conformational transitions in isolated membranes (changes of the microviscosity and polarity of both the bulk and annular lipids) in the presence of hemicholinium-3 (HC-3), a known inhibitor of choline transport. It was shown that HC-3 inhibited Na^+-dependent and Na^+-independent transport in different ways. This fact seems to provide evidence for the relative independence of these two processes. The effects of HC-3 depend on the presence or absence of sodium ions in the medium. In the presence of 0.1, 1 and 5 μM HC-3, the microviscosity of the bulk lipids is significantly lower in the Na^+-containing medium than in the Na^+-free medium. At HC-3 concentrations of 0.1 μM, the microviscosity of the annular lipids is significantly lower in the Na^+-containing medium than in the control.

In the pH range from 6.0 to 7.0, an inversion of the Na^+-dependent and Na^+-independent processes may occur during nerve conductance. In this pH range, the alterations in the choline transport system did not correspond to the total structural changes in the synaptosomal membrane, as monitored via intristic tryptophan fluorescence. There is a structural transition of the synaptosomal membrane at pH above 7.7 in the Na^+-containing medium, as revealed by an increase in tryptophan fluorescence intensity and a short-wave shift in its maximum position. This transition was not found for the Na^+-free medium. The pH-evoked choline transport changes may be due to specific alterations in the choline transport-related proteins.

Our data suggest sodium and hydrogen ions play an important role as regulators of synaptosomal membrane structure and functional properties.