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Transport of choline and its relationship to transport of cationic drugs in immortalized rat brain capillary endothelial cell line

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Choline serves critical roles in the CNS both as a precursor of neurotransmitter and as an essential component of membrane phospholipids. The long-term maintenance of brain choline concentration is dependent on choline transport across the blood-brain barrier (BBB). And, we examined to elucidate the characteristics of transport of choline across the BBB using conditionally immortalized rat brain capillary endothelial cell line (TR-BBB) in vitro. The [^{3}H]choline in TR-BBB was increased by time dependently, but independent on Na^+, and the transport process is saturable with Michaelis-Menten constrant, K_m of about 26 μM. The uptake of [^{3}H]choline is susceptible for inhibition by various organic cationic compounds including hemicholinium-3, tetraethylammonium chloride (TEA) and ℓ-carnitine. Also, we investigated the relationship of transport of choline and cationic drugs. The uptake of [^{3}H]choline is inhibited by antioxidant, α-phenyl-n-tert-butyl nitrone (PBN) with IC_{50} of 1.2 mM. and by Alzheimer's disease therapeutics, such as acetyl ℓ-carnitine, tacrine and donepezil. Also, choline uptake presented competitive inhibition with PBN, donepezil and acetyl ℓ-carnitine in Lineweaver-Burk plot. In conclusion, TR-BBB cells express a saturable transport system for uptake of choline, and several cationic drugs may be transported into the brain by BBB choline transporter.