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FUNCTIONAL CHARACTERIZATION OF RAT PLASMA MEMBRANE MONOAMINE TRANSPORTER (PMAT) IN THE BLOOD-BRAIN AND BLOOD-CEREBROSPINAL FLUID BARRIERS

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ABSTRACT

This study investigated the expression and functional roles of rat plasma membrane monoamine transporter (rPMAT) in the blood-brain barrier (BBB) and blood-cerebrospinal fluid barrier (BCSFB) by using *in vitro* brain barrier model cells (TR-BBB13 and TR-CSFB3 cells) and multiple *in vivo* experimental techniques.[1)] Quantitative RT-PCR analysis showed relatively high expression of rPMAT mRNA in TR-BBB13 and TR-CSFB3 cells. 1-Methyl-4-phenylpyridinium (MPP^+) was transported into rPMAT-expressing cells in a sodium-independent manner. [^{3}H]MPP^+ was taken up concentration-dependently by TR-BBB13 and TR-CSFB3 cells with K_m values similar to that of rPMAT-expressing cells. [^{3}H]MPP^+ transports into these cells were markedly inhibited by serotonin, dopamine and cationic drugs. rPMAT siRNA significantly suppressed [^{3}H]MPP^+ uptake by TR-BBB13 cells. Intracerebrally injected [^{3}H]MPP^+ was eliminated from the brain parenchymal region, whereas brain [^{3}H]MPP^+ uptake did not increase with time during *in situ* brain perfusion, suggesting that the brain-to-blood transport across the BBB predominates over blood-to-brain transport. Brain microdialysis studies revealed that the elimination across the BBB was significantly decreased by co-perfusion of unlabelled MPP^+, serotonin or dopamine. [^{3}H]MPP^+ was also eliminated from the CSF. These findings suggest that PMAT in brain barriers functions as the brain-to-blood transporter to regulate brain concentrations of organic cations, including monoamines and cationic neurotoxins.