Reduction of LAT1 mRNA expression at the blood-brain barrier in the mouse model of Parkinson’s Disease.
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Parkinson’s Disease (PD) is a neurodegenerative disorder associated with a loss of dopamine neurons in the substantia nigra (SN), which results in depletion of dopamine in the striatum (ST), and severe motor symptoms. Elucidating the changes in blood-brain barrier (BBB) transport in PD is important for understanding the pathophysiological roles of the BBB and altering drug permeability to treat the disease. The purpose of this study was to examine the changes in transporter gene expression at the BBB in the mouse model of PD. In this PD model, male C57BL/6 mice received 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and the expression of mRNA was measured by real time RT-PCR. At 7 days after MPTP treatment, a motor deficit and a loss of dopamine neurons were observed by behavioral testing, real-time RT-PCR and immunostaining. These results suggest that the conditions suffered by the MPTP-treated mice are similar to those in PD patients. In MPTP-treated mice, the mRNA expression of LAT1 throughout the brain capillaries isolated by the glass bead column method was significantly reduced by 63 % compared with the controls. Moreover, the mRNA expression of LAT1 throughout the whole brain was also reduced by 35%. These results suggest that LAT1 expression is reduced in PD patients. In contrast, the mRNA expression of GLUT1, SERT and TAUT was not affected in the MPTP-treated mouse. LAT1 mediates the transport of large neutral amino acids and L-dopa across the BBB. Therefore, this study suggests that the reduced LAT1 expression at the BBB in PD patients may affect the amino acid supply from the circulating blood and distribution of L-dopa into the brain.