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Iron is a crucial element for our fundamental metabolic processes. Transferrin (Tf), an iron-binding protein, facilitates iron uptake in brain endothelial cells (ECs) and subsequent transport across the blood-brain barrier (BBB). Apo-Tf first binds with ferric iron to form holo-Tf, which is then internalized through receptor-mediated endocytosis. The iron-containing vesicles are sorted within the early endosomes, where some of them are recycled in cerebral capillaries and the rest are directed to the basolateral membrane for exocytosis to brain parenchyma. In this study, we have developed a detailed pathway based mathematical model of these processes. The developed model includes both Tf-bound and non Tf-bound iron transcytosis from cerebral capillaries to brain parenchyma. Our simulation results indicate that the developed model can successfully reconstruct in vitro experimental results of bovine brain ECs. Moreover, we studied the effects of cerebral iron and transferrin concentration as well as receptor density on the cell surface to predict iron accumulation inside the cell and exocytosis from the EC. We found that the transcytosis of iron through EC is mainly regulated by extracellular Tf-bound iron and expression of Tf-receptors on the luminal surface of ECs. (Received February 28, 2017)