To examine the efflux transport of pentazocine (PTZ) from the brain across the blood-brain barrier (BBB), kinetic studies were performed by in vivo experiments using the Brain Uptake Index (BUI) method and the Brain Efflux Index (BEI) method. Rapid elimination of PTZ with the apparent elimination rate constant of $5.35 \times 10^{-2} \, \text{min}^{-1}$ (the BEI method) or $22 \times 10^{-2} \, \text{min}^{-1}$ (the BUI and washout study) suggests that PTZ is transported by a specific transport system(s) from the brain. The BBB efflux clearance of PTZ was $137 \, \mu\text{L/min/g brain}$, which was calculated from the apparent elimination rate constant ($5.35 \times 10^{-2} \, \text{min}^{-1}$) determined by the BEI method and the distribution volume in the brain ($2.56 \, \text{mL/g brain}$) determined by brain slice uptake study. Brain uptake of PTZ was increased by the coadministration of P-glycoprotein inhibitors such as cyclosporin A, quinidine, verapamil and vinblastine into the carotid artery. The PTZ efflux transport was significantly inhibited by microinjection into the Par2 region following the preadministration of injections containing quinidine or verapamil. In addition, the elimination of PTZ from the brain was significantly reduced by preadministration of organic cation compounds such as L-carnitine and tetraethylammonium (TEA), whereas organic anion compounds such as p-aminohippurate, probenecid and taurocholate did not affect the PTZ efflux transport. Therefore, in vivo studies suggest that PTZ is transported from the brain to the circulating blood via P-glycoprotein and L-carnitine/TEA–sensitive efflux transport system(s) across the BBB.