

Role of astrocytic histamine *N*-methyltransferase in brain functions

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Histamine *N*-methyltransferase (HNMT), which inactivates histamine to 1-methylhistamine, plays an important role in the regulation of histamine concentration and brain functions. Although previous studies indicated the possible involvement of neurons and astrocytes in brain histamine inactivation, the contribution of each cell type to the histamine inactivation was not fully elucidated. In the present study, we phenotyped astrocytes-specific *Hnmt* knockout mice (cKO) to reveal the importance of astrocytic histamine inactivation for brain functions. First, we generated cKO mice by crossing *Hnmt flox* mice and Gfap-Cre mice which expressed Cre recombinase specifically in astrocytes. Increase in brain histamine concentration of cKO mice was modest compared to that of conventional *Hnmt* knockout mice, indicating the limited contribution of astrocytes to histamine metabolism. Behavioral test battery showed the lower locomotor activity of cKO mice in novel environment and home cages, although anxiety-like behaviors and depression-like behavior were not changed by *Hnmt* deletion in astrocytes. These results demonstrated that astrocytic *Hnmt* maintained normal locomotor activity despite of its minor role in histamine clearance.