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論文要約

学位論文題目

（和文）グルタミン酸作動性と GABA 作動性パルバルブミン陽性ニューロンの
外側手綱核における局在とトポグラフィックな編成

（英文） **Topographic Organization of Glutamatergic and GABAergic Parvalbumin-Positive Neurons in the Lateral Habenula**

氏名　NGUYEN THI VAN TRANG

〔目的〕

Parvalbumin (PV) neurons are well known to be involved in neuronal plasticity as GABAergic fast spiking neurons; on the other hand, they were also reported glutamatergic. The PV neurons are also a key for understanding the lateral habenula (LHb) plasticity; fewer PV neurons are shown in adult mice with anxiety and depression-like behaviors caused by early-life stress. To date, it has been unknown in the LHb what proportion of the neurotransmission machinery of the PV neurons is constituted. To clarify the characteristics of the PV neurons in the LHb, I investigated the PV neurons with expression of GABAergic, glutamatergic, serotonergic, cholinergic, and dopaminergic neurotransmitter markers.

〔方法並びに成績〕

Expression of cell type markers was examined by combining mRNA in situ hybridization chain reaction (HCR) and immunohistochemistry (IHC) on C57BL/6J mice. I elucidated the percentages of the glutamatergic markers (*vglut1*, *vglut2*, *vglut3*) and GABAergic markers (*gad1*, *gad2*, *vgat*, *gat*) positive PV neurons. In the LHb, the large percentage of the PV neurons were glutamatergic; 76.08 ± 1.20% was *vglut2* positive. In contrast, the percentage of GABAergic neurons was small: *gad1* (1.42 ± 0.33%), *gad2* (2.93 ± 0.57%), *vgat* (1.14 ± 0.22%), and *gat* (4.52 ± 1.27%). Moreover, there existed the *vglut2* and *gad2* double positive PV neurons (2.51 ± 0.48%) in the LHb. Therefore, the PV neurons in the LHb consisted of following subsets: glutamatergic, GABAergic, and both glutamatergic and GABAergic double positive. These proportions were different from other regions: the cingulate cortex, hippocampus, and basolateral amygdala. In addition, I did not detect the other neurotransmission markers in the LHb PV neurons.

The LHb were topographically different with the subsets of the PV neurons. The medial and lateral LHb were different in the expression of *vgat*; the percentages of the *vgat* positive PV neurons were significantly higher in the lateral LHb than in the medial LHb. On the other hand, the *vglut2* positive PV neurons are evenly distributed in the medial and lateral LHb. The anterior and posterior LHb were topographically different in the glutamatergic and GABAergic expressions. The percentage of the *vglut2* positive PV neurons was significantly higher in the posterior LHb, and the percentages of the GABAergic PV neurons (*gad1*, *gad2*, *vgat*, and *gat*) were significantly higher in the anterior LHb.

〔総括〕

I demonstrated that the PV neurons in the LHb are heterogenous although they are mainly glutamatergic. The proportions of the PV neuron subsets differ between the LHb and other brain regions. The GABAergic PV neurons were distributed mainly in the medial LHb, and the GABAergic and glutamatergic PV neurons were mainly distributed in the anterior and posterior LHb, respectively. The subsets of the PV neurons were topographically organized mediolaterally and anteroposteriorly inside the LHb, indicating their different function.