No. 1926

The Role of Arcuate Nucleus Neurons in Salt-Induced Hypertension.

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Summary

The arcuate nucleus in hypothalamus plays a main role in regulating food intake and energy metabolism. In the arcuate nucleus, there are orexigenic Agouti-related peptide (AgRP) neurons and anorexigenic Proopiomelanocortin (POMC) neurons. Recently, dysfunction of both neurons has been clarified as one of the neuronal pathogenesis of obesity, impaired glucose tolerance, and dyslipidemia of metabolic syndrome. However, in hypertension associated with metabolic syndrome, the role of both neurons has not been established. We previously have shown that mice that have knocked out of an insulin signaling molecule PDK1 in AgRP neurons, exhibit hypertension via the hyper-activation of sympathetic nervous system after fed of high salt diet. It was suggested that AgRP neurons play a crucial role in blood pressure regulation during excessive salt intake.

We clarified whether AgRP neurons sense the extracellular Na^+ concentration and whether high salt diet feeding impairs this sensing function. The isolated neurons of the arcuate nucleus were prepared from male C57B6 mice, and intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) was measured by fluorescence imaging. When the extracellular Na+ concentration was increased from 134 to 144 mM, the increase in $[Ca^{2+}]_i$ was observed in about 10% of AgRP neurons. Expression of AgRP mRNA was significantly increased in arcuate of mice fed a high salt diet for 2 weeks. On the other hand, the expression of POMC was not altered. These results suggested that the increase of extracellular Na^+ concentration by excessive salt intake directly activated AgRP neurons.

In this study, we revealed that the AgRP neuron in arcuate nucleus, which is the primary sensing neurons of peripheral metabolic signal, is a new Na^+-sensing neuron. This suggests that dysfunction of a AgRP neurons may be involved in the pathologies of obesity, impaired glucose tolerance, dyslipidemia, and hypertension in metabolic syndrome.