

Effects of natriuretic polypeptides and sodium-related peptides on the hypothalamic neurosecretory neurons: molecular and physiological aspects

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Summary

The hypothalamus and neuroendocrine system is known to have an important role in the integrative regulation of sodium balance in a body. We have examined the effects of natriuretic polypeptides and sodium-related peptides on the hypothalamic neurosecretory neurons, using morphological, electrophysiological and molecular techniques. In the present study we examined the effects of adrenomedullin (AM) that is a new potent hypotensive and natriuretic peptide on membrane potential, excitatory postsynaptic currents (EPSCs), intracellular Ca^{2+} concentrations and the expression of the *c-fos* gene in the rat hypothalamic neurosecretory neurons. The outward currents were observed in the adult rat supraoptic (SON) neurons of the slice preparation, using perforated patch-clamp technique. On the other hand, the recorded EPSCs were not affected by the administration of AM in the perfused solution. Ca^{2+} imaging method using fura-2 revealed that AM caused a marked increase of intracellular Ca^{2+} concentrations in the neuron isolated from the immature rat SON. The effects of central administration of AM on the expression of the *c-fos* gene in the hypothalamus were also examined by *in situ* hybridization histochemistry. Intracerebroventricular (icv) administration of AM caused a remarkable increase in the expression of the *c-fos* gene in the SON and paraventricular nucleus (PVN) in a dose and time dependent manner. The induction of the *c-fos* gene reached the peak at 30 min after central administration of AM. The effects of AM on the induction of the *c-fos* gene was blocked by pretreatment with AM receptor antagonist (AM22-52). These results suggest that AM may have an important role to modulate the neuronal activity of neurosecretory neurons in the hypothalamus and be involved in the central regulation of sodium balance in a body.