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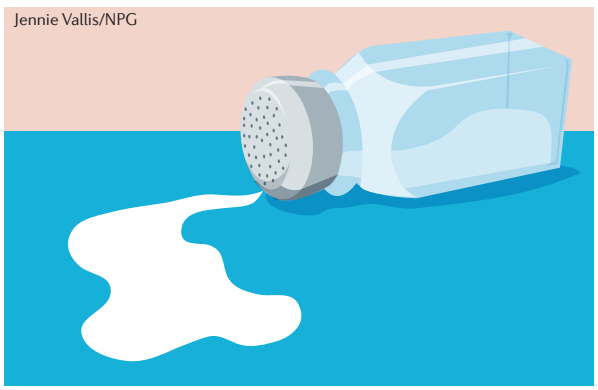
AUTONOMIC NERVOUS SYSTEM

Go easy on the salt!

> high dietary salt induces hypertension by disrupting baroreceptor feedback through a BDNF–TRKB-mediated reduction in Cl^- transport

High dietary salt can cause hypertension, but the underlying mechanism is not well understood. A new study by Choe *et al.* now shows that excess sodium in the bloodstream alters synaptic transmission in a class of hypothalamic neurons that are involved in blood pressure regulation.

Increases in plasma sodium levels cause excitation of magnocellular neurosecretory cells (MNCs) in the supraoptic nucleus (SON), which in turn release vasopressin (VP), a hormone that causes peripheral vasoconstriction and hypertension. Under normal conditions, hypertension triggers the activation of arterial baroreceptors, which reduces VP secretion through GABAergic inhibition of MNCs and thus reduces blood pressure. The authors set out to determine whether high dietary salt can induce hypertension by causing dysregulation of this feedback mechanism.



Jennie Vallis/NPG

GABAergic inhibition requires maintenance of a Cl^- gradient across the cell membrane, and this gradient is maintained by the K^+–Cl^- cotransporter 2 (KCC2). Chronic salt loading causes collapse of this gradient and a weakening of baroreceptor-mediated GABAergic inhibition of MNCs. Reduced GABAergic inhibition in other conditions often results from a decrease in KCC2 activity, which is caused by receptor tyrosine kinase TRKB activation. The authors investigated the effects of salt loading on rats by giving them 2% NaCl in water as the only source of fluid for 7 days. Western blot analysis of SON lysates from salt-loaded rats showed increased levels of activated TRKB. Furthermore, scavenging of activated TRKB or knockdown of brain-derived neurotrophic factor (*Bdnf*) during salt-loading treatment corrected dysregulated GABAergic signalling in MNCs almost to control levels, suggesting that BDNF–TRKB signalling is required to mediate the loss of GABA-mediated inhibition of MNCs.

Administration of α-adrenoceptor agonists activates the baroreceptors that inhibit VP-expressing MNCs, and the effect of these drugs was attenuated in salt-loaded rats. Moreover, in freely moving salt-loaded rats, hypertension was accompanied by increases in firing of MNCs. Blocking system VP receptors also significantly reduced the hypertension that was induced by high dietary salt.

Together, these results suggest that high dietary salt induces hypertension by disrupting baroreceptor feedback through a BDNF–TRKB-mediated reduction in Cl^- transport. This allowsVP-mediated vasoconstriction — and consequent hypertension — to continue unregulated despite an ongoing hypertensive state.

Sian Lewis

ORIGINAL RESEARCH PAPER Choe, K. Y. *et al.* High salt intake increases blood pressure via BDNF-mediated downregulation of KCC2 and impaired baroreflex inhibition of vasopressin neurons. *Neuron* http://dx.doi.org/10.1016/j.neuron.2014.12.048 (2015)