

COMMENTARY ON: STRUCTURAL RECONSTRUCTION OF THE PERIVASCULAR SPACE IN THE ADULT MOUSE NEUROHYPOPHYSIS DURING AN OSMOTIC STIMULATION. NISHIKAWA K, FURUBE E, MORITA S, HORII-HAYASHI N, NISHI M, MIYATA S. *J NEUROENDOCRINOL.* 2017; 29.

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In a recent issue of *Journal of Neuroendocrinology*, Nishikawa and co-authors examined structural changes in the mouse neurohypophysis in response to chronic osmotic stimulation (1). The neurohypophysis (or posterior pituitary) is one of the brain's secretory circumventricular organs – a highly vascular structure lacking a complete blood brain barrier, thereby allowing neuropeptides to diffuse into peripheral circulation (2). The neurohypophysis harbors nerve terminals of magnocellular neurosecretory cells containing vasopressin, an antidiuretic hormone that is secreted in response to increased plasma osmolality to promote water reabsorption by the kidney (3). Chronic consumption of high dietary salt creates an increased demand for secretion of vasopressin to maintain body fluid homeostasis. Previous studies have established that the magnocellular hypothalamo-neurohypophysial system undergoes activity-dependent structural plasticity during chronic conditions demanding an increase in hormone release, such as dehydration and lactation; this plasticity includes synaptic and dendritic remodeling, increased direct neuronal apposition, glia retraction, as well as restructuring of the neurovascular contacts in the neurohypophysis (4, 5). In this study, the group of Miyata examined the organization of neuron-glia-vascular complexes in the mouse neurohypophysis and explored the hypothesis that these structures undergo structural plasticity during chronic salt loading to enable a more efficient secretion of vasopressin into the circulation. Using quantitative immunohistochemistry and electron microscopy examination of different cellular populations combined with the analysis of vascular permeability, the authors provided a detailed description of the perivascular space organization and remodeling in response to salt loading.

The authors discovered a major role for pericytes (6), contractile cells that wrap around endothelial cells of capillaries and contribute to the regulation of capillary blood flow, in the remodeling of the neurohypophyseal perivascular space in response to salt loading. The study revealed that pericytes are one of the main resident cells in the neurohypophysis. These cells are present in the perivascular space and extend their processes into the brain parenchyma, contacting nerve terminals. Remarkably, the authors revealed that pericytes undergo a robust restructuring in response to 5-day salt loading, showing a three-fold increase in the number of pericyte processes. In salt-loaded animals, these multiple ramified processes invade the space between nerve terminals, which according to the author's hypothesis increase the perivascular surface in direct contact with neuronal terminals and thereby can enhance the efficacy of diffusion of neurosecretory hormones into the circulation. This hypothesis was supported by measurements of vasculature permeability in the neurohypophysis, which was dramatically increased by more than 4 fold following salt loading. Importantly, this substantial structural plasticity displayed by pericytes in response to salt loading may indicate that this cellular population play an important role in the regulation of hormonal secretion by the neurohypophysis.

The authors proposed an intriguing hypothesis that this structural plasticity could be driven by factors secreted from local neuronal terminals in an activity-dependent fashion during hypertonicity-induced increase in the activity of magnocellular neurosecretory cells. Further studies are required to test this hypothesis and to determine the molecular and signalling mechanisms governing this structural plasticity.

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