Exploring the OVLT: insight into a critically important window into the brain

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Submitted 1 July 2015; accepted in final form 3 July 2015

OSMOSENSITIVE NEURONS IN THE subfornical organ (SFO) and organum vasculosum of the lamina terminalis (OVLT), two blood-brain barrier-free areas in the rostral forebrain, sense changes in plasma osmolality. While the integrative roles of the SFO in the regulation of body fluid and neuroendocrine regulation have been extensively studied, far less attention has been focused on the OVLT, in part, as a consequence of its poorly understood neuroanatomical composition and boundaries. Neurons in the OVLT clearly have been shown to monitor not only solute levels, but also detect unique changes in plasma sodium content (1, 5, 8), information that is then transmitted to multiple brain sites important in the behavioral and endocrine responses (vasopressin secretion, thirst, autonomic nervous system activation) required for the maintenance of fluid and electrolyte homeostasis (4, 7, 14, 17). However, the importance of the OVLT is not limited to osmoregulation, as this structure has also been demonstrated to play a role in reproduction (16), thermoregulation (10), and cardiovascular control (6, 17).

While a number of articles have used track tracing and electrophysiological techniques to identify neuronal projections from the OVLT, there has to date been no comprehensive systematic analysis of the anatomy of this structure. Prior studies have identified the presence of the fenestrated capillary endothelium, as well as the interdigitation of glial cells between local neuron populations, the capillary plexi, and the anterior extension of the third cerebroventricle. There has, in addition, been abundant speculation that the glial elements (tanyocytes, ependymocytes, and astrocytes) participate in the communication of blood-borne cues to the resident neurons and perhaps even serve as a conduit connecting the plasma with the cerebrospinal fluid of the third cerebroventricle (15). Additionally, numerous groups have described c-Fos activation in the OVLT following osmotic stimulation (e.g., 9), but to date, a detailed anatomic description of the cellular organization of the OVLT and the complete extent of the cellular activation to osmotic stimulation has been lacking. Not any more. Prager-Khoutorsky and Bourque (11) have now presented a detailed analysis of the topographical distribution of the various cellular elements of the OVLT and in a tour-de-force of multiple antigen detection labeling that has identified the previously unrecognized, pan-OVLT cellular activation that occurs upon osmotic stimulation. The images are not only visually pleasing, but also provide new insight into the cellular structure of several subregions of the OVLT, while at the same time identifying a unique septum in the midline of the structure whose function awaits discovery.

Those with a solely osmocentric view of the OVLT now must allow for a broader view of this unique structure, including the possibility of a transport function and a more expansive role in homeostasis, including being the sensor for circulating factors affecting a wide variety of physiological functions. This elegant anatomical study complements previous work from the Bourque lab describing the cellular mechanisms of osmosensation (2, 3, 12, 13, 18) and sets the stage for more detailed analysis of the important structure and its efferent connections with multiple brain regions behind the blood-brain barrier.

REFERENCES