COMMENTARY ON: **EFFECTS OF LATERAL OLFACTORY TRACT STIMULATION ON FOS IMMUNOREACTIVITY IN VASOPRESSIN NEURONES OF THE RAT PIRIFORM CORTEX. TSUJI C, TSUJI T, ALLCHORNE A, LENG G, LUDWIG M. *J NEUROENDOCRINOL* 2017;29:e12531.**

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Vasopressin (VP) is well-known as an anti-diuretic hormone that is produced and secreted in the hypothalamus. However, VP is also synthesized in the medial amygdala, bed nuclei of the stria terminalis and throughout the olfactory system.[1,2] These extrahypothalamic VP populations have been implicated in a wide range of social behaviors, including aggression, parental and play behaviors.[3,4] In this study, Tsuji et al. (2017) characterized a novel population of VP-expressing neurons in the piriform cortex (PC) and tested their role in the processing of olfactory information.

Tsuji et al. used a well-characterized transgenic rat line where the VP promoter drives the expression of enhanced green fluorescent protein. In effect, they are able to determine the distribution and chemical phenotype of fluorescently-labelled VP cells in the PC. VP neurons were abundant throughout the entire PC but largely restricted to the cell-dense layer II. In contrast to what is known about the VP system,[1,4] the expression of VP in the PC is not sexually dimorphic as the number of VP neurons in the PC of male and female rats were similar. In the PC, double-label immunohistochemistry revealed that the largest proportion of VP neurons (63%) were glutamatergic pyramidal cells. A subset of VP neurons in the PC also stained positively for markers of cortical interneurons as they may coexpress GABA (20%) or calbindin (10.5%). Interestingly, no VP neurons in the PC colocalized with prominent interneuron groups (i.e. parvalbumin, vasoactive intestinal peptide or cholecystokinin). Only a few VP neurons in the PC expressed VP receptors, making it unlikely that they autoregulate or respond to VP released from other regions.

The PC forms part of the olfactory system to process and relay sensory odor information to higher cognitive centers.[6] Olfactory information is first processed in the main olfactory bulb, the anterior olfactory nucleus and then the PC. Furthermore, it is known that the olfactory bulb and PC are reciprocally innervated.[7-9] Tsuji et al. investigated if VP plays a role in olfaction by stimulating the lateral olfactory tract and determining if this activates VP cells in brain regions that respond to olfactory stimuli. Using Fos as a marker for neuronal activation, the authors found that high-frequency stimulation (50 Hz) significantly increased the activation of neurons in the olfactory bulb (i.e. main olfactory bulb, accessory olfactory bulb, anterior olfactory nucleus), supraoptic nucleus and PC. Interestingly, there was a specific increase in Fos expression in VP neurons of the supraoptic nucleus and PC. VP neurons may mediate social odor cues in the supraoptic nucleus,[5] but their role in the PC may be more complex based on the reciprocal connectivity between the PC and olfactory bulb. In aggregate, these findings are

consistent with a role for VP to integrate olfactory input.

These experiments provided the first characterization of a newly identified VP population in the PC. Tsuji et al. showed that VP neurons in the PC comprised of mostly pyramidal cells although a small subset was identified to be GABAergic interneurons. If the majority of VP neurons in this region were glutamatergic projection cells, then it would be of great interest to identify their efferent and afferent connections. Since VP neurons in the PC are sensitive to olfactory information, their dynamic interplay with the olfactory system and their contributions to social behaviors become important for future investigations.

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