

Five distinct neuronal types inhabit the ventrolateral preoptic nucleus

The ventrolateral preoptic nucleus (VLPO) is considered as the main brain region inducing slow-wave sleep (SWS). Despite its physiological importance, the neuronal composition of the VLPO still remained incompletely described. Yet, the characterization of neuronal properties within a brain structure is a necessary first step toward the understanding of its function.

To assess the neuronal diversity within the VLPO, we performed in our paper an exhaustive electrophysiological, morphological and pharmacological characterization of the VLPO neurons in brain slices of juvenile mice. First, we performed patch-clamp recordings of 289 VLPO neurons and analyzed their passive membrane properties and their firing modes of discharge. Then, we used an unsupervised clustering analysis called the Ward's method to group cells with large similarities without a personal bias of interpretation. We performed the Ward's clustering on 18 electrophysiological parameters. This analysis revealed 3 clusters of neurons subdivided into 5 classes of VLPO neurons (Fig. 1).

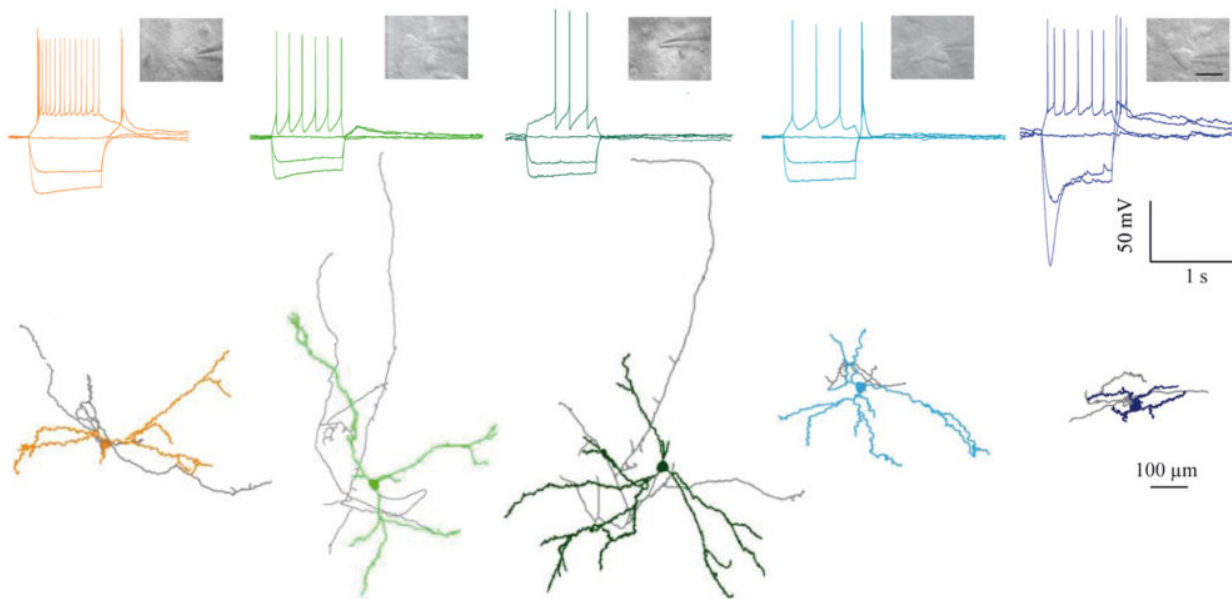


Fig. 1. VLPO neurons segregate into 5 different classes. Typical electrophysiological behavior and morphological aspect of VLPO neurons from each class are represented. Neurons were recorded using whole-cell patch-clamp recordings in response to the application of current pulses (-100, -50, 0 mV and at action potential threshold). Top inserts, infrared pictures of the recorded neuron (scale bar: 20 µm). Recorded neurons were subsequently reconstructed in 3 dimensions using the Neurolucida software. Axons are represented in gray whereas their somata and dendrites are color coded according to their cluster. Pial surface is downward.

Diffusion of a neuronal tracer (biocytin) contained in the patch pipette during electrophysiological recordings allowed, after the fixation of slices and diaminobenzidine (DAB)-based processing to visualize the recorded neurons. Somatodendritic morphologies were successfully revealed for 110 out of the 289 recorded neurons. Their morphological variables were next extracted from 3D Neurolucida reconstructions.

In our article, we found that the cluster 1 essentially contained intrinsic bursting neurons. These neurons were also characterized by their short lasting and low amplitude of after-hyperpolarizing potential (AHP) after a spike compared to neurons from the other clusters. Neurons from Cluster 1 frequently displayed a low-threshold calcium spike (LTS) and 40% of these neurons were inhibited by noradrenaline (NA) application that are two features of sleep-promoting neurons. These two hallmarks suggest that at least some neurons from the cluster 1 could correspond to sleep-promoting neurons.

The two following neuronal clusters exhibited a high proportion of NA-excited (74 and 81.9%) with a low occurrence of LTS. Thus, they could correspond to local interneurons. Indeed, NA-excited VLPO neurons have previously been reported to mediate some pharmacological effect to NA-inhibited neurons. This suggests that VLPO network processing could involve a local control of NA-inhibited neuron by NA-excited neurons.

Finally, the last two neuronal populations frequently exhibited an LTS (84%) and were in majority inhibited by NA application (61%) strongly suggesting that could correspond to sleep-promoting neurons. In particular, we demonstrated that neurons from the last group had the smallest membrane resistance and the largest voltage sags. Moreover, they displayed a particularly small somato-dendritic tree.

Altogether, our results undisclosed 5 distinct neuronal populations in the VLPO, expressing specific electrophysiological, morphological and pharmacological properties. These different neuronal types might be involved in diverse functions of sleep regulation. For example, the role of some VLPO neurons in the thermoregulation has previously been reported. One of the clusters identified in our study could therefore be involved in this function. Future studies are thus now needed to investigate the physiological roles of these 5 neuronal subpopulations and how they are interconnected within the VLPO network to regulate SWS.

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