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A Novel Function of the Ventral Lateral Preoptic Area of the Hypothalamus in Inducing Arousal

The ventral lateral preoptic area, situated in the hypothalamus of the brain, has traditionally been associated with its role in promoting sleep. Nevertheless, our recent breakthrough has unveiled a unique cluster of neurons within this region that project axons to the lateral hypothalamus and unexpectedly stimulate wakefulness. These findings strongly indicate that the ventral lateral preoptic area plays a crucial role in regulating both sleep and wakefulness.

Tsukuba, Japan—Deep within the intricate realms of the brain, a crucial component called the hypothalamus serves as a vital regulator of homeostasis. Within this remarkable structure, two distinct regions are found to be responsible for sleep and wakefulness: the preoptic area (POA) and the lateral hypothalamus (LHA), respectively. Specifically, the ventral lateral preoptic area (VLPO) in the preoptic area houses neurons known as VLPO^{GABA} and VLPO^{GAL} neurons, which produce gamma-aminobutyric acid and galanin (GAL) to promote sleep. Alternatively, the LHA harbors orexin neurons that play a crucial role in sustaining wakefulness. Together, these interconnected regions within the hypothalamus delicately balance restful slumber and vigilant wakefulness.

In our study using mice, we made the following intriguing discovery: VLPO^{GABA} and VLPO^{GAL} neurons form direct connections, or synapses, with orexin neurons in the LHA. Additionally, we identified numerous groups of neurons that project to VLPO^{GABA} and VLPO^{GAL} neurons and are thought to regulate their activity. Notably, these neuron groups were most prominent in the preoptic area and LHA. Furthermore, when we artificially stimulated only the neural circuits connecting VLPO^{GABA} neurons to the LHA, we observed the induction of arousal instead of sleep, challenging previous assumptions. Our study sheds light on the role of the coupling between VLPO and LHA in regulating sleep and wakefulness, unveiling a previously unknown function of the neural circuit connecting these two regions in controlling wakefulness.

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