The paraventricular thalamus is a critical thalamic area for wakefulness

With the support by the National Natural Science Foundation of China, the research group directed by Prof. Hu ZhiAn (胡志安) at the Department of Physiology & Collaborative Innovation Center for Brain Science, Third Military Medical University, recently reported that the paraventricular thalamus is a critical thalamic area for wakefulness, which was published in *Science* (2018, 362: 429—434).

Wakefulness is a fundamental and universal biological process essential to survival. The thalamus gates sensory and neuromodulatory inputs to the cortex and has long been thought to be important for wakefulness control. Several lines of clinical observations indicate that the paramedian thalamus is a critical node for controlling wakefulness. However, nuclei in the paramedian thalamus have different input-output organizations and participate in different brain functions. the specific nucleus and circuitry controlling wakefulness has not yet been identified.

They first mapped c-fos expression in the paramedian thalamus during different sleep-wake states and found that the paraventricular thalamus (PVT) exhibited highest level c-fos expression during wakefulness. Fiber photometry and multichannel recordings revealed that the activity of the PVT was tightly coupled with wakefulness. They next demonstrated that temporal inhibition of the PVT using chemogenetics decreased wakefulness, whereas lesion of the PVT using diphtheria toxin A or ibotenic acid caused damage to wakefulness. Further optogenetic experiments showed that activation of the PVT not only induced fast transitions from sleep to wakefulness but also accelerated the emergence from isoflurane-induced unconsciousness. Importantly, they also confirmed that the PVT to nucleus accumbens (NAc) projections was the downstream neural circuit mediating the wakefulness-controlling function. Moreover, the PVT was received and regulated by inputs from hypocretin (Hcrt) neurons in the lateral hypothalamus (LH), indicating the LH_{Hcrt}→PVT pathway was important for wakefulness control.

These results provide experimental evidence supporting the role of the PVT as a critical thalamic node in the wakefulness-promoting neural network. More importantly, their results may reveal a potential pathological mechanism of decreasing or fluctuating the level of wakefulness observed in paramedian thalamus stroke patients.

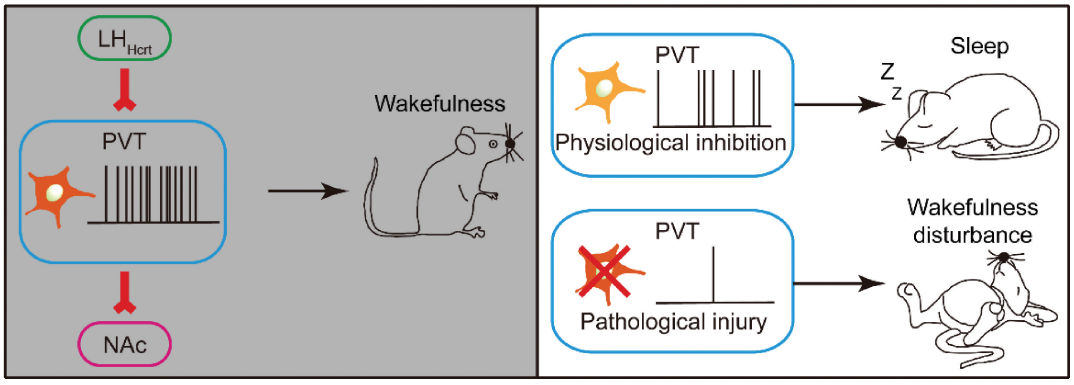

Figure Working model of the PVT control of wakefulness. Increased activity of the PVT is both necessary and sufficient for wakefulness. Physiological inhibition of the PVT leads to sleep, whereas pathological injury may be associated with wakefulness disturbance.