

Acute Optogenetic Activation of Lateral Hypothalamic CRH Neurons Rapidly Promotes Wakefulness

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Objective: The lateral hypothalamus (LH) contains diverse neuronal populations involved in sleep–wake regulation, feeding, reward processing, and autonomic functions. Among these populations, the role of corticotropin-releasing hormone (CRH) neurons in rapid sleep–wake transitions remains unclear. This study aimed to investigate whether acute activation of LH–CRH neurons rapidly promotes wakefulness.

Methods: LH–CRH neurons expressing channelrhodopsin-2 (ChR2) were activated using blue light stimulation. Electroencephalogram (EEG) and accelerometer (ACC) recordings were used to monitor sleep–wake states. Two stimulation protocols were conducted: (1) open-loop stimulation, with blue light delivered at 10-minute intervals regardless of sleep–wake state, and (2) sleep state-dependent stimulation, with rapid eye movement (REM) and non-rapid eye movement (NREM) sleep tested in separate trials. Sleep–wake activity was recorded over 4 hours, and sleep state transitions following stimulation were analyzed.

Results: Acute optogenetic activation of LH–CRH neurons during sleep induced rapid EEG desynchronization, which is characteristic of wakefulness. Mice showed a rapid transition from sleep to wakefulness following blue light stimulation.

Conclusion: Acute optogenetic activation of LH–CRH neurons rapidly promotes sleep-to-wake transitions. These findings support the role of LH–CRH neurons in the immediate regulation of sleep–wake states and provide a basis for further investigation of neural circuits controlling arousal.