Optogenetics reveals physiological role of orexin neurons in sleep/wakefulness regulation

National Institute for Physiological Sciences
Akihiro Yamanaka

We spend almost one third of our life time just to sleep. Sleep/wakefulness cycle is a very intriguing physiological phenomenon. We fall asleep at least once per day. After sleeping for a while, we can wake up naturally. However, the mechanism regulating sleep/wakefulness cycle has not been completely understood so far, while it appears to be regulated by neurons in the hypothalamus. Orexin/hypocretin neurons in the hypothalamus have a crucial role in the regulation of sleep and wakefulness. Although the afferent and efferent connections of these neurons have been determined, how orexin neuronal activity promotes wakefulness is incompletely understood. To further examine the role of orexin neuronal activity in sleep/wakefulness regulation, we generated transgenic mice in which orexin neurons expressed halorhodopsin, an orange light-activate d chloride ion pump. Slice patch clamp recordings of orexin/halorhodopsin neurons demonstrated that photic illumination produced an outward current, hyperpolarized, and reduced the discharge rate of orexin neurons in a wavelength- and intensity-dependent manner. Acute silencing of orexin neurons in vivo by orange light illumination decreased electromyography power and increased the delta frequency in the electroencephalogram, indicative of slow wave sleep (SWS), and was time-of-day dependent. These findings suggest that activation of orexin neurons is necessary to keep animals awake during the light period.