Optogenetic manipulation of the activity of orexin neurons controls sleep/wakefulness state in mice.

Orexin/hypocretin is a neuropeptide produced in the neurons, which are sparsely distributed in the lateral hypothalamic area. The mice lacking prepro-orexin gene or orexin-producing neurons (orexin neurons) show narcolepsy-like phenotypes, a fragmentation of sleep/wakefulness and sudden attack of muscle weakness, cataplexy. Although these facts suggest that the orexin neurons play critical role in the regulation of sleep/wakefulness, it is not clear that how the activity of orexin neurons maintain wakefulness. To study this *in vivo*, a hot technology optogenetics was incorporated. Optogenetics enables to control the activity of neurons by illuminating light. A light-activated neuronal silencer, halorhodopsin or arcaerhodopsin-3, is expressed in the orexin neurons in the transgenic mice. Slice patch clamp recordings of orexin neurons demonstrated that photic illumination silenced orexin neuron. In the light period, acute silencing of orexin neurons *in vivo* synchronized the electroencephalogram and reduced in amplitude of the electromyogram. These are characteristic in slow wave sleep (SWS). This result indicates that activation of orexin neurons is necessary for keeping wakefulness during the light period. Acute photic inhibition of orexin neurons reduced discharge rate of serotonergic neurons in the dorsal raphe (DR) nucleus. Taken together, this study revealed that optogenetics modulation of orexin neuronal activity enabled us to control the transition from wakefulness to SWS in mice. Furthermore, the silencing of orexin neurons and transition to SWS was accompanied by a reduction of the activity of serotonergic neurons in the DR.