What happens when we sleep

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Lack of sleep is a common complaint but for many, falling asleep involuntarily during the day poses a very real and dangerous problem. A new study from the Montreal Neurological Institute (MNI) at McGill University demonstrates interestingly, that sleep-wake states are regulated by two different types of nerve cells (neurons), melanin-concentrating hormone (MCH) neurons and orexin (Orx) neurons, which occupy the same region of the brain but perform opposite functions.

The MNI study is the first to discover that MCH neurons are activated during sleep and could thus be important in regulating the sleep state. The study, published in this week's issue of the journal *Proceedings of the National Academy of Sciences* (*PNAS*), provides deeper understanding of the sleep-wake cycle and vital insight into the basis of sleep disorders such as narcolepsy and possibly also other diseases such as depression and Parkinson's.

Sleep is regulated by processes in the brain in response to how long we are awake in addition to the light/dark cycle controlled by the circadian rhythm. With Drs. Oum Hassani and Maan Gee Lee, Dr. Barbara Jones at the MNI were studying a structure in the brain called the lateral hypothalamus (LH) known to be critical for maintaining wakefulness. MCH neurons, co-distributed with Orx neurons, constitute less than 10% of the LH.

Previous studies have shown that Orx neurons are essential for maintenance of the awake state. These neurons are active in the waking state and turn off during sleep and in their absence, animals and humans

experience narcolepsy with cataplexy or sudden loss of mucle tone. However, the role of MCH neurons was until now, unclear. Evidence from earlier knockout studies suggested that MCH neurons might play a different role than Orx neurons in regulating activity and sleep-wake states. Therefore the team at the MNI set up experiments to study the function of MCH neurons during the sleep-wake states.

"Remarkably, what we found is that MCH neurons are actually silent during waking, which is a surprising finding especially in this wake-promoting region of the brain. The neurons fire during sleep, and are most active during REM sleep," says Dr. Barbara Jones, neuroscientist at the MNI and principal investigator in the study. "Our study markedly demonstrates that MCH neurons discharge in a reciprocal manner to the Orx neurons across the sleep-wake cycle." Dr. Jones and colleagues used their expertise to apply and develop a difficult technique which allowed them to selectively record, label and thus identify a nerve cell containing a particular chemical. This allowed them to isolate the functions of the MCH and Orx cells even though they comprise less than 10% of the nerve cells in the LH.

The reciprocal profiles and roles of the Orx and MCH neurons could be significant in the manifestation of sleep disorders. It is possible that narcolepsy, which occurs with the loss of Orx neurons, is provoked in part by the MCH neurons that remain intact in the narcoleptic patients. A growing body of research shows that regular and normal sleep is necessary for overall health; regulating hormone levels, blood pressure, metabolism, alertness, mood, and consolidating memory. This study presents potential therapeutic avenues and targets for the treatment of various sleep disorders including the development of drugs that will act on receptors for Orx and MCH, to stimulate or block these receptors accordingly.

Source: McGill University