Sleep stage transitions in the network model of the thalamocortical system.

Giri P Krishnan[1], Eric Halgren[1], Maxim Bazhenov[1]
1. University of California, Riverside
2. University of California, San Diego

In the EEG, stage two of sleep is characterized by spindle activity (8-12 Hz) and the occasional K-Complex, while stage three or slow wave sleep is characterized by the slow oscillation (< 1 Hz). Activation of neuromodulatory systems controls transition between sleep states. An increase in the level of acetylcholine release associated with activation of nicotinic and muscarinic receptors depolarizes cortical pyramidal cells and thalamic relay cells both in awake states and during REM sleep. Furthermore, in states of arousal when forebrain activity is high, intracortical synapses are relatively depressed via presynaptic GABA-B and muscarinic receptors. In addition, there are is reduction of GABA levels during sleep. In this study, we show that the Acetylcholine mediated decrease in intracortical excitatory connections is sufficient for the transition from slow oscillation to stage two sleep. We demonstrate this using a computational model of the thalamocortical network which included reticular thalamic, thalamocortical and cortical neurons. The network displayed stage two sleep activity with intermittent spindles at 8 Hz in thalamic and cortical neurons similar to experimental studies. When the strength of excitatory intracortical connections increased, sleep slow oscillation like activity emerged in the network. The increase in excitatory connections was sufficient to induce active (Up) and silent (Down) cortical states which occurred synchronously across the network leading to the average activity around 1-1.5 Hz. The active states lasted for about 300-400 msec. The transition between sleep stages occurred abruptly in the model with a short period of mixed activity. We also demonstrate that reduction of GABA reduction or the increase in leak currents was not sufficient to induce the transition from stage two to stage three in this model. Overall, this study confirms that the change in synaptic connection strength which is produced by activation of neuromodulatory systems can act as a primary mechanism for the transition between stage two sleep and slow wave sleep.