Intracellular Studies of Thalamic Neurons Generating Sleep Delta Waves and Fast (40-Hz) Oscillations during Arousal

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Until quite recently it was generally thought that during quiet sleep the thalamus generates a single type of synchronized oscillation, known as spindle waves (7–14 Hz), and that the activated pattern of the electroencephalogram (EEG) upon arousal results from the suppression of synchronized oscillations in thalamic and cortical neurons (Steriade et al., 1990c). During the past two years we obtained intracellular evidence that (a) thalamocortical neurons also generate slow rhythms within the frequency range of sleep delta waves (1–4 Hz) when reaching high levels of membrane potential ($V_m$) polarization, and (b) states of increased alertness are associated in the thalamus and neocortex with fast (40-Hz) oscillations arising intrinsically or in afferent pathways. Here, we discuss these new findings of slow and fast oscillations, postulate the mechanisms accounting for the sequential occurrence of spindles and delta waves at different stages of EEG-synchronized sleep, and propose that brain stem–thalamic cholinergic systems exert a potentiating effect upon cortical 40-Hz waves.

Cellular Bases of Thalamic Delta Oscillations

Recently, a slow (1–2 Hz) rhythm has been recorded in vitro from dorsal lateral geniculate (dLG) neurons (McCormick and Pape, 1990; Leresche et al., 1991). The oscillation consisted of high-frequency spike bursts.
and involved the interplay of two intrinsic currents of thalamic cells: the hyperpolarization-activated cation current ($I_h$) and the transient Ca$^{2+}$ current ($I_t$) underlying the low-threshold spike (LTS).

Our in vivo studies have demonstrated that identified thalamocortical cells, recorded from a variety of thalamic nuclei, oscillate at delta frequency (1–4 Hz) either as a consequence of imposed hyperpolarization or following deafferentation procedures involving ablation or spreading depression of the related cortical areas (Curro Dossi et al., 1992). Decortication led to increased levels of $V_m$ polarization in thalamic cells due to removal of the depolarizing corticothalamic impingement. Figure 10-1 depicts the dramatic rhythmicity displayed by thalamic cells, consisting of LTSs followed by afterhyperpolarizing potentials (AHPs), after injection of hyperpolarizing current pulses or occurring spontaneously in decorticated preparations.

The relations between early sleep stages and prevailing EEG spindle oscillations, and between late sleep stages and prevailing EEG delta waves, led us to ask whether (a) spindles and delta EEG oscillations depend on various levels of $V_m$ hyperpolarization of thalamocortical cells; (b) individual thalamic elements can be synchronized and therefore contribute to the generation of delta oscillation as a macroscopic EEG event, as is known to be case for spindling; and (c) some incompatibility may exist between spindle and delta waves.

*Delta rhythm is generated with increasing hyperpolarization*

Cortical volleys represent a potentiating factor for sleep EEG rhythms in thalamic cells. Indeed, during EEG-synchronized sleep, the high-frequency spike bursts of identified corticothalamic neurons (Steriade, 1978) directly drive both gamma-aminobutyric acid (GABA)ergic cell types in the thalamus, reticular (RE), and local-circuit neurons. The engagement of thalamic inhibitory cells by cortical volleys has the consequence of (a) reinforcing the synaptically generated spindle oscillation at its very site of genesis, the RE nucleus (Steriade et al., 1985, 1987), and (b) bringing the $V_m$ of thalamocortical cells to more hyperpolarized levels where delta oscillation arises as an intrinsic event from the interplay of $I_h$ and $I_t$.

Spindle-like sequences in thalamocortical cells, consisting of long-lasting (100–200 msec) inhibitory postsynaptic potentials (IPSPs) followed by rebound LTSs, are induced by cortical stimuli, an effect that stands in contrast with the absence of similar oscillations by stimulating prethalamic pathways (Steriade, 1984). The difference between cortical