

Auditory Processing in Wakefulness and Sleep: Subsecond Brain Dynamics

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Introduction: The realization of a unified perception relies on the functional integration of specialized brain regions. The transition from wakefulness to sleep is characterized by alterations of attention and sensory processing. At sleep onset, loss of perceptual awareness is paralleled by the appearance of sleep spindles and K-complexes in the electroencephalogram (EEG), indicating brain electrical synchronization. Several lines of evidence suggest, however, that the sleeping brain may still show signs of response to auditory stimuli. Thus a brief tone delivered during nonREM sleep elicits K-complexes. To investigate the physiological basis for the interaction of attention, perception and vigilance level new statistical and signal processing methods were applied to single-trial event-related EEG responses in a simple auditory discrimination task at sleep onset.

Methods: The EEG was recorded from ten healthy subjects at 29 scalp sites during task presentation. The experimental manipulation consisted in an auditory 'oddball' discrimination task performed repeatedly during sleep onset periods. A series of 1000 Hz 'standard' tone pip stimuli (96%) was presented, while a 1500 Hz 'target' stimulus was presented infrequently (4%). The subjects were asked to press a button upon detection of the 'target' stimulus. The EEG was decomposed into spatially fixed, temporally independent components with different patterns of projection to the scalp channels (component topography). Both the EEG data and the resulting independent components were analyzed with a variety of statistical and signal processing methods including spectral and time-frequency analyses, inter-trial coherence (ITC), event-related 'ERP images'. For each component scalp distribution, an equivalent sin-patterns of these mice are relatively normal. In contrast, orexin-/-;MCH-/- mice exhibited significant increases in direct transitions to REM sleep during both the light (2.4 ± 0.8 transitions, $p=0.003$) and dark (25.1 ± 7.3 transitions, $p=0.006$) phases.

Conclusions: Although loss of the MCH gene alone does not result in narcolepsy, inactivation of both orexin and MCH genes results in a phenotype that is much more severe than that observed with deficiency of orexin alone (genetic epistasis). These results suggest a compensatory role for MCH in the regulation of cataplexy and sleep-wake control. Further investigation of interactions between output pathways related to

energy homeostasis and arousal are warranted. Our findings may suggest that MCH neurons of the lateral hypothalamic area play a role in the presentation of human narcolepsy, a genetically complex disorder.