PADUA DAYS ON MUSCLE AND MOBILITY MEDICINE 2026

International Conference

March 3rd to 6th Euganean Thermae and Padua, Italy

SLEEP AND ORAL FUNCTION, CLAUDIA DELLAVIA, RICCARDO ROSATI

MAGISTRAL LESSON: THE ROLE PLAYED BY SLEEP PHYSIOLOGY AND ITS DISRUPTION IN STOMATOGNATHIC AND SYSTEMIC DISORDERS

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Allan Hobson, a neurophysiologist and psychiatrist at Harvard, and one of the "founding fathers" of sleep medicine and physiology, rephrasing a passage from the famous Gettysburg speech by Abraham Lincoln, wrote that "sleep is of the brain, by the brain, for the brain" (1). But, at the very same time, sleep involves and affects our whole body. Both brain and body work in completely different ways when awake and when asleep: when awake, brain activity is highly differentiated, since different areas fulfill specific functions and body organs and systems subserve our continuously changing activities. When asleep, brain activity is simplified, as neurons are not required anymore to perform so many different functions. Activity of different body systems, since we are now at rest, slows down and becomes regular. But this is true for our sleep without rapid eye movement (NREM sleep), because during REM sleep (which follows NREM sleep) everything changes. Brain activity becomes paradoxically like that of wakefulness, while homeostatic control of vegetative functions seems to be suspended or reduced to a lower and less precise level of regulation: for instance, blood pressure and heart rate, reduced during NREM sleep, increase and their variability increases as well during REM sleep. This is a mystery within a mystery: although there is a consensus on some hypotheses, we still do not really know why we sleep, i. e. why we spend a third of our life in a condition during which consciousness is suspended or altered, we are unaware of what is happening in our surroundings and consequently of possible attacks by our predators. Within this mystery, there is the other mystery of REM sleep: why does the brain works similarly to when we are awake, and we lose the full control of our vegetative functions? Sleep exerts profound consequences on different disorders (1-5). We all experience the reduction of muscle tone when we fall asleep, and it is easy to understand how this reduction plays a role in the collapse of part of the upper airways in obstructive sleep apnea (OSA). But maybe it is less known that muscle tone is completely abolished during REM sleep, when we are paralyzed. Moreover, during REM sleep, as part of the derangement of vegetative functions that characterize this sleep phase, the sensitivity of brainstem breathing regulatory centers to changes in blood levels of oxygen and carbon dioxide (induced for example by OSA) is impaired in such a way that the awakening response and subsequent restoration of upper airways muscle tone and patency is delayed. As shown, two facets of REM sleep physiology are crucial for the development of a high prevalence disorder like OSA. Sleep and immune response are reciprocally linked (2). Specifically, it has also been proposed and shown that sleep, when it occurs at the correct circadian phase, potentiates the immune response, maybe because circadian rhythms and sleep, in coordination, produce during the night a pro-inflammatory, neuro-endocrine environment which boosts a correct and effective immune response (3). Sleep, a phase of lowered metabolic demand, would allow to use precious resources to mount the highly energetically demanding host defense, which would be ready for the immune challenges in the subsequent hours of wakefulness. But when sleep, for any reason, is disturbed and the pro-inflammatory activity is not contained into the night, but diffuses along the whole day, a correct immune response is compromised: for instance, it has been shown that antibody response to vaccination is reduced in sleep deprived healthy subjects as well as in OSA patients (4). Deranged sleep determines the condition of dis-immunity. Due to the link between immune response and inflammation, with its cardinal signs of redness (rubor), swelling (tumor), heat (calor) and pain (dolor), it is not surprising that insomnia is associated with chronic orofacial pain and that OSA treatment improves pain associated with temporomandibular disorder, showing how sleep disruption plays a role in pain pathophysiology

Keywords: *Vegetative control, obstructive sleep apnea (OSA), immune response, vaccination, orofacial pain.*