Neuromuscular injuries and pharyngeal dysfunction in snorers and sleep apnea patients

A study on pathological changes in the human soft palate and its relationship with swallowing dysfunction

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Obstructive sleep apnea (OSA) is a prevalent progressive sleep disorder with serious negative health consequences. Although several risk factors such as obesity can make an individual vulnerable to develop OSA, the pathophysiological mechanism for the collapse of the upper airway is unclear. Moreover, the etiology of the commonly occurring swallowing dysfunction in snorers and sleep apnea patients is not understood. In the light of this, we aimed to investigate whether muscle and nerve changes in upper airway contributes to pharyngeal dysfunction in snorers and sleep apnea patients.

Twenty-two patients (1 female, 21 males, mean age 45 years) undergoing soft palate surgery because of snoring and sleep apnea were included in the study. Ten healthy non-snoring males, mean age 38 years, were recruited as controls. Biopsies from the uvula were obtained from both patients and voluntary controls. Control autopsies from both uvula and palatopharyngeus muscles were taken post mortem from 6 previously healthy adult subjects (3 males, 3 females, mean age 52 years) and two male infants (age 4 months and 1.4 years). Overnight sleep registration and videoradiographic examinations of pharyngeal swallowing function were performed in both patients and voluntary controls.

Enzyme and immunohistochemistry and morphometric techniques were used to investigate cytoskeletal and membrane proteins desmin and dystrophin and two neurotrophins, brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF). The nerve fascicles in the soft palate were explored for changes in axon and Schwann cell density and for signs of axon regeneration.

All patients were snorrers, and 14 patients had OSA with a mean apnea-hypopnea index 24, range 5-84. Sixteen of the 22 patients had swallowing dysfunction. None of the 10 voluntary controls had sleep apnea or swallowing dysfunction. In both controls and patients, a subgroup of muscle fibers in the soft palate lacked immunoreaction for desmin and the C-terminus of dystrophin, and these fibers were more common in patients than in controls (p<0.001). Moreover, muscle fibers with disorganized desmin were commonly observed in patients, but not in controls (p<0.001). Thus, overall, desmin abnormalities were significantly more frequent in patients (46 vs. 15%, p<0.001), and some of these fibers showed upregulation of BDNF. In addition, nerve fascicles from the soft palate of patients displayed lower density of axons (p<0.02) and a smaller area occupied by Schwann cells (p=0.001) compared to controls. The axon density within nerve fascicles as well as the cytoskeletal abnormalities in muscles correlated significantly with swallowing dysfunction (rₚ=0.50 and 0.76, respectively, p≤0.03).

To conclude, human soft palate muscles seem to be of a unique allotype. In the soft palate of snorers and sleep apnea patients, cytoskeletal myopathy and neuropathy were frequently observed, and these changes correlate significantly with pharyngeal swallowing dysfunction. The upregulation of BDNF in muscle fibers of patients may relate to a regenerative attempt after injury. Consequently, a disturbed sensorimotor function and muscle weakness may contribute to development and progression of swallowing dysfunction and OSA. Traumatic snoring vibrations and muscle overload are plausible causes of the neuromuscular injuries.

Keywords
Axons, BDNF, desmin, dystrophin, obstructive sleep apnea, OSA, pharyngeal function, muscle, myopathy, neuropathy, Schwann cells, swallowing dysfunction, upper airway