Effects of Obesity on the Neuromuscular Junction of Genioglossus Muscle and Other Associated Muscles of Respiration

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Hypothesis

- Obesity increases the risk of developing Obstructive Sleep Apnea (OSA).
- Obstructive sleep apnea (OSA) is a frequent breathing disorder characterized by repeated relaxation of the tongue and soft palate during sleep.¹²
- The genioglossus (GG) muscle is the largest extrinsic tongue muscle, crucial for maintaining the patency of the upper airway while sleeping, and responsible for tongue depression and protrusion.
- OSA patients have decreased muscular tone in the GG muscle.¹ Due to this, the tongue pulls back into the throat while the patient sleeps, obstructing the airway, preventing airflow, and lowering the oxygen levels of the body.
- Lep⁻/− mice is a great model to study OSA because they exhibit obesity, pharyngeal collapsibility, hyperventilation, and hypercapnia which can be alleviated by leptin replacement treatment.²

Background

Muscle of the tongue is affected in male ob/ob mice. The density of nAChRs at the NMJs is decreased in ob/ob mice compared to controls. NMJs from male ob/ob mice show perforations and areas with low nAChRs density while control synapses exhibit high density and a uniform nAChRs distribution.³

Nerve Terminal and Schwann Cells in GG

Conclusions

- GG muscle is affected in male ob/ob mice. The density of nAChRs at the NMJs is decreased in ob/ob mice compared to controls. NMJs from male ob/ob mice show perforations and areas with low nAChRs density while control synapses exhibit high density and a uniform nAChRs distribution.
- A higher prevalence of central nuclei are observed in male ob/ob GG fibers than in WT GG fibers.
- Cross-sectional areas of male ob/ob Type I fibers are significantly larger than male WT Type I fibers. Male WT and male ob/ob Type II fibers display no differences in size.
- Lipid rafts density is decreased in GG of male ob/ob mice which might affect the clustering of nAChRs in their postsynaptic membrane (data not shown).
- Both Schwann cell and axon terminal morphologies are altered in GG muscles of male ob/ob mice.
- Diaphragm muscle is affected in male ob/ob mice. In contrast, their sternomastoid muscle is altered at 20 weeks only.
- Female ob/ob mice did not show nAChRs density alterations in GG or other muscles.

Histology of GG of Lep⁻/− male

Central Nuclei

H&E Staining

Electron Microscope

Muscle Fiber Type

NADPH Staining

WT

OB/OB

20 weeks

26 weeks

WT

OB/OB

Muscle Fiber Type

AChRs on the crest of muscle junctional folds at the NMJ

NMJ shows AChRs in the muscle labeled with fluorescent green- 

bungarotoxin

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Citations