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

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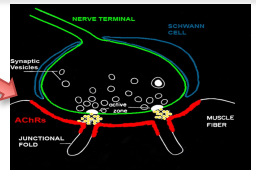
Background

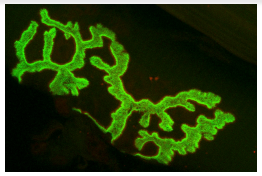
- **Obesity increases the risk of developing Obstructive Sleep Apnea (OSA).**
- **Obstructive sleep apnea** (OSA) is a frequent breathing disorder characterized by repeated relaxation of the tongue and soft palate during sleep[1,2].
- The **genioglossus (GG) muscle** is the largest extrinsic tongue muscle, 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[3]. 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$^{ob/ob}$*** mice is a great model to study OSA because they exhibit obesity, **pharyngeal collapsibility**, hypoventilation, and hypercapnia which can be alleviated by leptin replacement treatment[6].

Hypothesis:

- We hypothesize that obesity impacts GG muscle and specifically, the **neuromuscular junction (NMJ)** which is the site of communication between nerve and muscle and the best indicator of proper muscle function.
- By using the obesity mouse model *Lep$^{ob/ob}$* male and female mice, we analyze in detail the **neuromuscular junction (NMJ)** from GG muscle and other associated muscles of respiration such as diaphragm and sternomastoid muscles.

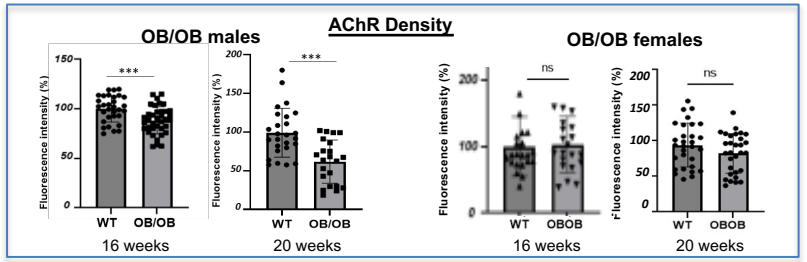


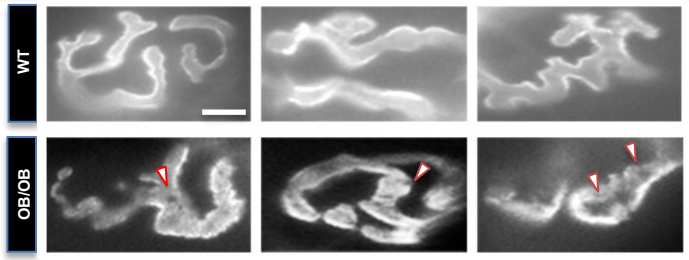
AChRs on the crest of muscle junctional folds at the NMJ



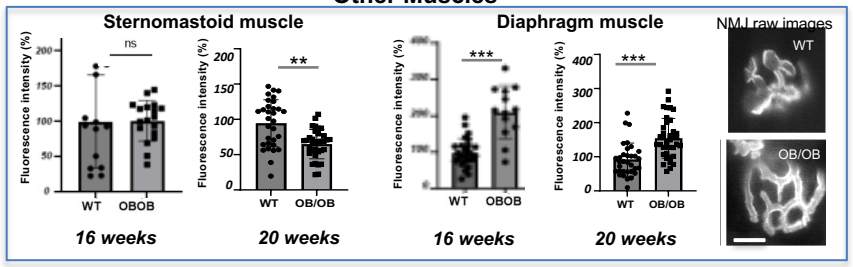
NMJ shows AChRs in the muscle labeled with fluorescent green α-bungarotoxin

Genioglossus Muscle (GG)

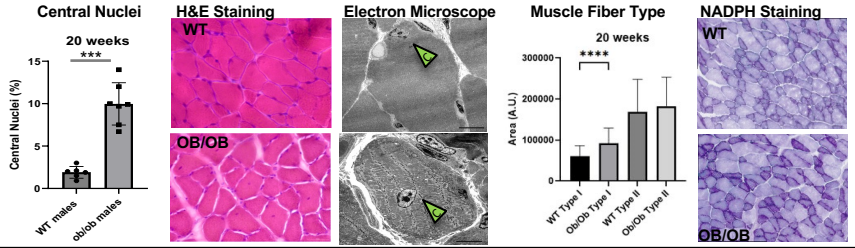




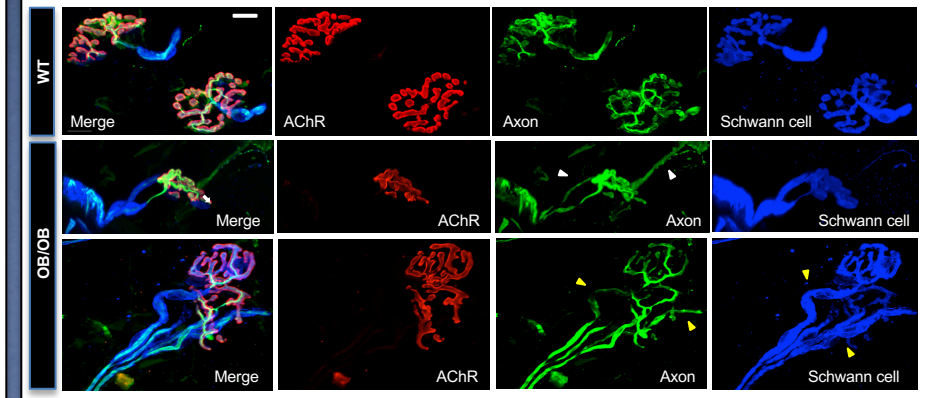
Other Muscles



Histology of GG of *Lep$^{ob/ob}$* male



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 male 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.

Citations

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