

## Diaphragm Muscle Fatigue Resistance Does Not Increase With Age

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**Introduction:** The diaphragm muscle (DIAM) contains a mixed motor units population, with FInt and FF units (comprising type IIx and/or IIb muscle fibers) vulnerable to sarcopenia - age-associated reductions of specific force and cross-sectional area (CSA). Fatigue-resistant S and FR units (comprising type I and IIa fibers) are relatively spared. There is controversy as to whether aging confers an enhanced resistance to DIAM fatigue, with interpretations relying on relative measurements of force.

**Objective:** To quantify differences in fatigue resistance between young (6-months) and old (24 months) Fischer 344 rats, taking into account maximum specific forces.

**Material and Methods:** We assessed the loss of DIAM force in young and old Fischer 344 rats of both sexes at 10, 40 and 75 Hz stimulation in 330 ms duration trains repeated each s (33% duty cycle) across a 2 min period.

**Results:** Although the initial specific force of the DIAM was lower in older rats across all stimulation frequencies, the final residual DIAM specific force after 2 min of stimulation was the same ( $\sim 5$  N/cm<sup>2</sup>) at all ages. These relative values gave the misconception of an improved fatigue resistance, especially at 40 and 75 Hz. We also found that aging is associated with an increase in the relative contributions of type I and IIa fiber CSA to DIAM mass with decreased contributions of type IIx and/or IIb fibers. When these changing contributions are factored into a fiber type-specific model of DIAM force generation, we found that ventilatory behaviors require activation of only type I and IIa fibers, regardless of age or fatigue. By contrast, the model predicts that aging impairs the ability of the DIAM to effectively perform expulsive manoeuvres, even in the non-fatigued condition.

**Conclusions:** Relative fatigue measurements are not indicative of improved fatigue resistance in aging and are an artifact of reduced initial specific force contributions from FIInt and FF units. These results are consistent with previous studies showing the relative vulnerability of FIInt and FF units and conserved ventilatory behaviors in aging DIAM.

**Keywords:** Diaphragm muscle, muscle fatigue resistance, age. rats, ventilatory behaviors,