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# Markers of Mitochondrial Fusion and Mitophagy are Greater in Old versus Young Rat Skeletal Muscle

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Due to the mitochondria's essential role in energy production and regulation of metabolism, mitochondrial health is linked to skeletal muscle health. In healthy skeletal muscle, mitochondria exist in a dynamic reticulum that shares membrane potential and matrix contents. This reticulum is maintained by a balance of mitochondrial fusion, fission, and mitophagy which ensure adequate energy production is maintained. However, aging may cause detrimental alterations in skeletal muscle mitochondrial structure and function. **PURPOSE:** Determine whether there are age- and sex-related differences in the protein expression of markers of mitochondrial fusion (MFN2, OPA1), fission (Fis1), and mitophagy (Parkin, Pink1) in skeletal muscle. **METHODS:** Tibialis anterior muscles were excised from 16 young (≤6 months) and 16 old (≥18 months) male and female Sprague-Dawley rats after euthanasia. Western blotting was used to determine MFN2, OPA1, Fis1, Parkin, and Pink1 protein expression, normalized to total protein in each sample. Citrate synthase activity was measured as a surrogate for muscle mitochondrial content. ANOVAs were used to compare protein expression, with age and sex as factors. **RESULTS:** MFN2 expression was elevated 2.6-fold in old compared with young skeletal muscle (0.065±0.006 vs. 0.025±0.004 AU, respectively, $P<0.001$); however, OPA1 expression did not differ between young and old animals ($P=0.841$). There was an age*sex interaction for Fis1 expression ($P=0.049$), however there were no differences between any groups. Parkin expression was >4-fold higher in old compared with young skeletal muscle (0.120±0.020 vs. 0.029±0.006 AU, respectively, $P<0.001$); however, Pink 1 expression did not differ between young and old skeletal muscle. Citrate synthase activity did not differ with age ($P=0.440$). **CONCLUSION:** Specific markers of mitochondrial mitophagy (Parkin) and outer membrane fusion (MFN2) increase in skeletal muscle with age. However, a marker of inner mitochondrial membrane fusion (OPA1) does not change in skeletal muscle with age. While fusion can serve as a compensatory mechanism for dysfunctional mitochondria to preserve membrane potential and energy production, our results indicate the potential for incomplete fusion, with a resultant increase in mitophagy in older skeletal muscle. **SIGNIFICANCE/NOVELTY:** Abnormal mitochondrial fusion and mitophagy may serve as a contributing factor to age-associated detrimental changes in skeletal muscle. Altering these processes may improve mitochondrial health and subsequently skeletal muscle health with age.

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