Neuromuscular Junction Decline in Aging C57BL/6J Mice Model: Insights into Sarcopenia Progression

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Introduction

Sarcopenia is an age-related degenerative disease characterized by loss of muscle strength and loss of muscle mass. The neuromuscular junction (NMJ) is a synaptic connection formed between the motor nerve terminals and muscle fibers and is essential for the transmission of action potentials to induce muscle contraction. Degeneration of the function and structure of the NMJ is a pathological feature of sarcopenia and an important cause of accelerated muscle strength and muscle mass loss.

Purposes

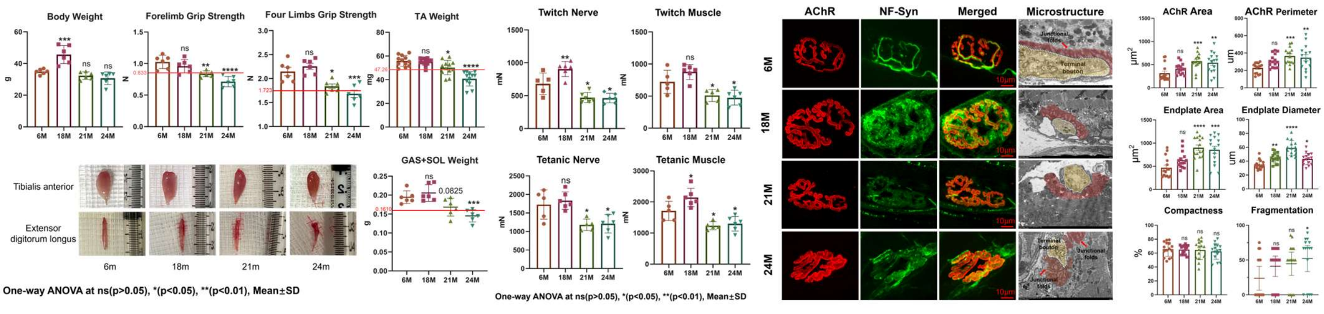
- To investigate the sequence of the NMJ functional and structural degeneration during sarcopenia in C57BL/6J mice.

Materials and Methods

- 6, 18, 21, 24-month-old C57BL/6J mice were selected to assess functional and structural degeneration of the NMJ during aging (n=6).
- Assessment: (1) Muscle strength: Forelimb grip strength, four limbs grip strength, Ex-vivo function test (by stimulating muscle); (2) Muscle mass: tibialis anterior muscle (TA) mass, Gastrocnemius (GTN) and soleus muscle mass; (3) NMJ structure: IF staining of AChR, neurofilament and neural synapse in EDL. (4) NMJ function: Ex-vivo function test (by stimulating sciatica nerve.

Results

- In the figures of forelimbs grip strength, four limbs grip strength, TA mass and GAS+SOL mass, muscle strength and mass values below the red line, representing the mean – 2SD of the values of 6-month-old mice, were considered indicative of muscle atrophy in sarcopenia.21-month-old and 24-month-old mice had lower forelimb grip strength, four limbs grip strength, TA weight, GAS+SOL weight, but larger AChR perimeters, AChR areas, endplate diameter and areas of NMJ compared with those of 6-month-old and 18-month-old mice.
- In aged mice (21- and 24-month-old), both twitch force and tetanic force, which are measures of muscle contractility, were significantly decreased following direct muscle stimulation and sciatic nerve activation.
- 24-month-old mice had a significantly higher proportion of fragmentation, which was statistically higher than 6-month-old mice. Synaptophysin degeneration and fragmentation of neurofilaments were observed in the NMJ of 21- and 24-month-old mice.



Discussion

- C57BL/6J mice showed a decline in lower limb skeletal muscle mass and strength starting at 21 months of age.
- Apparent morphological changes in motor neuron filament were observed in 18, 21, and 24-month-old C57BL6J mice. Significant degeneration of AChR structure was observed in mice at 24 months of age. It indicated that degeneration of motor neuron terminals precedes the post-membrane of the NMJ and muscle strength.
- To account for individual differences in the aging process, we need to use a larger sample size to ensure the robustness of the results.

Significance: Degeneration of motor nerve terminals in NMJs can help with early diagnosis and intervention of sarcopenia.

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