Time-course of decline in the size of neuromuscular synaptic contacts with sedentary aging in mice

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Loss of connections between motor neurons and muscle fibres is thought to contribute to reduced motor function in old age but the process and mechanism by which neuromuscular junctions (NMJs) are lost remain to be defined. We investigated the time-course of age-associated changes to the structure of the NMJ and the impact of voluntary wheel running exercise.

Methods: C57BL/J female mice were separated into two groups, exercise and control. The exercise group were given access to a monitored running wheel in late middle age. Animals in the control groups were killed at 2, 8, 14, 19, 22, 25 and 28 months of age. Exercise group mice were killed at ages 25 and 28 months. Longitudinal cryosections of the *tibialis anterior* muscle were double labelled for postsynaptic acetylcholine receptors (AChR) with Alexa555-α-bungarotoxin, and for nerve terminals with synaptophysin antibody followed by FITC-secondary antibody. Confocal maximum projection images were used to measure the area of synaptophysin and AChR at endplates.

AChR area for the 14 and 28 month animals was 238±8 μm^2 and 149±19 μm^2 ($P<0.001$, one-way ANOVA). Over the same period the area of synaptophysin staining declined from 168±12 μm^2 to 75±9 μm^2 ($P<0.01$). The decline in nerve (synaptophysin) area occurred mainly between 19- and 28-months of age and preceded the fall in nerve terminal area. Endplates of mice with access to a running wheel preserved most of the nerve terminal area that was lost in old age in the sedentary group ($P<0.05$, unpaired t-test).