ELECTRICAL STIMULATION REDUCES AGE RELATED ATROPHY AND WEAKNESS IN EDL MUSCLES OF RATS

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Abstract: **Skeletal muscles atrophy and weaken with old age. The number of motor-units decreases and the number of denervated fibres increases with age. Denervated fibres lack contractile activity, atrophy, and contribute to whole muscle atrophy and weakness. Electrical stimulation of denervated muscles suppresses the atrophy and weakness. We electrically stimulated EDL muscles of adult and old rats during a 2 month period of denervation. The control muscles of old rats had declines in muscle mass and maximum force compared with adult control muscles. Denervated muscles of either adult or old rats had even larger declines. Stimulated-denervated muscles of adult rats maintained mass and force at values not different from adult control values. Stimulated-denervated muscles of old rats maintained mass and force at values not lower than control muscles of old rats, and mass was even maintained not different from adult control values.**
Keywords: **sarcopenia, denervation, electrotherapy**

Introduction

As age extends beyond adulthood into the elderly years, the progressive atrophy and weakness of skeletal muscles impairs activities of daily living and increases the chance of falling. The age related decline in the total number of motor neurons [1] and motor units is only partially compensated for by an increase in innervation ratio [2]. Throughout life, muscle fibres spontaneously become denervated and reinnervated [3], but the ability of motor neurons (especially fast-type) to reinnervate denervated fibres declines with age [4]. Thus, the population of denervated fibres increases with age [5]. Denervated fibres undergo no contractile activity, atrophy and contribute to whole muscle atrophy and weakness [6]. Electrical stimulation that generates contractions in all muscle fibres would retard the atrophy and weakness of the denervated fibres [6]. Our hypothesis was that electrical stimulation generating tetanic contractions of denervated muscles of rats during a period of old age decline would maintain muscle mass and maximum force at values closer to adult control values compared with control muscles of same-age rats.

Materials and Methods

The extensor digitorum longus (EDL) muscles of adult (5 Mo) and old (26 ½ Mo) rats were divided into three treatment groups: control, denervated and stimulated-denervated. All operative procedures were performed on anesthetized rats. The left EDL muscles had no operative procedures, acting as controls for that age group. The right EDL muscles were randomly assigned into either the denervated or stimulated-denervated group for that age group. The sciatic nerve innervating each right EDL muscle was divided to permanently denervate the muscle. A battery powered, electrical stimulator that we developed and programmed (100 Hz, 0.4 ms pulse width, 20 pulses/contraction, 200 contractions/day) was implanted into rats having a muscle in the stimulated-denervated group.

We chose to electrically stimulate denervated rather than innervated muscles composed of mixed innervated and denervated fibres. Denervated fibres are much less excitable than innervated fibres [7]. A stimulation pulse with sufficient amplitude and duration to depolarize denervated fibres would have activated sensory neurons and the rats may have shown signs of pain.

The function of the stimulator and health of the rat were checked once per week. Lack of any movement in the foot or toes of the stimulated-denervated hindlimb during these test contractions indicated a defective stimulator. Data recorded from muscles having defective stimulators were not used in the analysis.

After a treatment period of two months, all EDL muscles were evaluated *in vitro*. Maximum force was measured for isometric, tetanic contractions [4]. A one-way ANOVA was used to compare differences between the experimental groups. The 0.05 level of probability was used to signify statistical significance.

Results

As indicated by the horizontal lines in Figure 1, control muscles of old rats had significantly lower mass and force compared with adult control muscles. Denervated muscles of either adult or old rats had an even larger decrease in mass and force. The stimulation of denervated muscles of adult rats maintained mass and force at values not different from values for adult control muscles (Figure 1). The stimulation of denervated muscles of old rats not only prevented the shift of mass and force to values of denervated muscles, but shifted the values away from the values of same-age control muscles of old rats to values of control muscles of adult rats.

Discussion

The decline in mass and force of control muscles of old rats is consistent with prior studies [4]. The declines

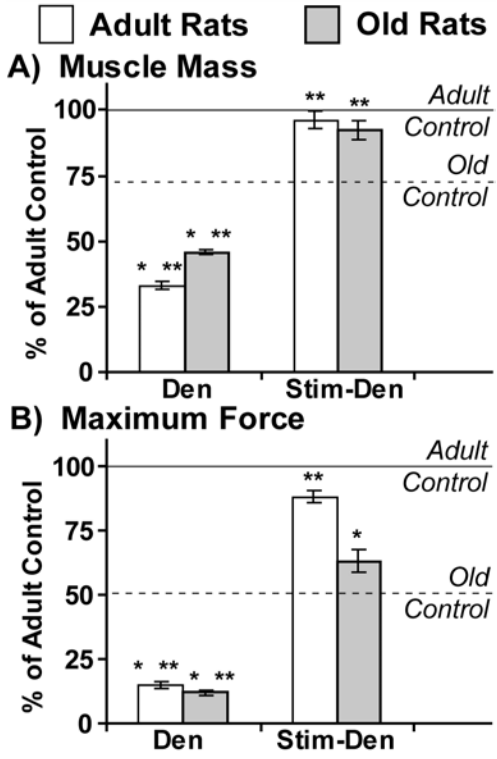

Figure 1: Muscle mass (A) and maximum force (B) for Adult (7 Mo) and Old (28 ½ Mo) rats. Den: muscles that were denervated for 2 months. Stim-Den: muscles that were denervated and electrically stimulated for 2 months. Control: unoperated, contralateral muscles for each age group. All values plotted as percent of Adult Control values. Error bars are standard error. The * indicates difference from Adult Control values, and ** indicates difference from Control values for Old rats.

in denervated muscles of either adult or old rats are consistent with prior studies [6]. For stimulated-denervated muscles of adult rats, the maintenance of muscle mass at control values has been reported [6] and in this study force was also maintained at values not different from adult control values.

Our hypothesis was supported by the observation that contractile activity generated by electrical stimulation of muscles of old rats maintained muscle mass at values different from control values of same-age old rats, but not different from adult control values. The mean value of force for stimulated-denervated muscles of old rats was also higher than the mean for control muscles of old rats, though the difference was not significant. In contrast, means for mass and force of stimulated-denervated muscles of adult rats have not been observed at higher levels than adult control values in this study or in prior reports [6]. These observations support the following mechanism as contributing to the atrophy and weakness of muscles observed in old age, that the lack of contractile activity in the population of denervated fibres results in atrophy and weakness in those fibres and the net effect contributes to the overall muscle atrophy and weakness [5].

Conclusions

Electrical stimulation reduced age-related atrophy and weakness by ensuring that all of the muscle fibres underwent tetanic contractions. Nevertheless, this form of electrotherapy would not retard the age related increase in the number of denervated fibres or decrease in motor units. Old age has similarities with stroke, neural diseases and spinal cord injury in that they all reduce motor function under voluntary control and thus, impair activities of daily living. Common strategies of neurorehabilitation may be beneficial.

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