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# Age-Induced Adaptations to the Motor Unit

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Demographic data underscore the importance of our need to understand the physiologic adaptations associated with aging. Over the next 30 years, the projected number of Americans over age 65 will increase to nearly one quarter of the total population,<sup>1</sup> double what it was in 1986.<sup>2</sup> While a number of alterations are inherent throughout the body during normal aging (see reviews in Brookbank<sup>3</sup> and Timiras<sup>4</sup>), those changes that impact motor units at both the population and single unit levels are quite compelling. Because muscle force output is modulated by the number of motor units recruited, and the frequency at which those units discharge,<sup>5</sup> the study of motor unit behavior may offer valuable insights into understanding why some elderly clients have movement impairments.

## Changes in Motor Unit Behavior

There are two primary ways in which motor units alter their behavior with age. First, changes occur in the motor unit's *discharge characteristics*. The literature finds such adaptations to be equivocal. Both Nelson et al<sup>6</sup> and Galganski et al<sup>7</sup> examined inter-pulse intervals (IPIs) in human hand muscles during submaximal isometric contractions. IPIs measure the speed at which motor units discharge. Surprisingly, neither study found a difference in the mean IPI between young and aged subjects. However, Nelson and coworkers did find the IPI to be significantly more variable in its output for a given condition in the elderly group, while Galganski did not.

Motor unit contraction time, another discharge characteristic, shows similar variability between studies. Comparisons of electrically activated young and aged human first dorsal interosseus muscle<sup>7</sup> with rat plantaris muscle<sup>8</sup> revealed no age-related alterations in the twitch time-to-peak force. Kanda and Hashizume<sup>9</sup> found

no difference between elderly and "middle-aged" rat medial gastrocnemius muscle. In contrast, statistically significant increases in contraction time have been demonstrated in aged rat soleus, tibialis anterior,<sup>10,11</sup> and extensor digitorum longus muscles.<sup>12</sup> These differing results may be attributed to utilization of varied testing protocols (eg, whole muscle<sup>10</sup> vs single motor unit<sup>7</sup>), use of different muscles, and/or differences in relative age of subjects (eg, classifying 26-month-old rats as "aged" despite their lack of ATPase enzyme transformation, which does not occur until 30 months<sup>9</sup>).

Unlike mean IPI and contraction time, the motor unit discharge property of relaxation rate enjoys a clear consensus across studies—aged muscle relaxes more slowly than young muscle. Narici and colleagues<sup>13</sup> examined voluntary and electrically activated contractions of human adductor pollicis muscle in male subjects aged 10 to 91 years (10 subjects per decade). An impressive 48.7% drop in the maximum relaxation rate was seen between the second and eighth decade, becoming statistically significant at approximately 60 years. Others note similar results.<sup>8,10</sup> Such alterations in discharge properties may have a large impact on the muscle's ability to generate and maintain force.

A second way a motor unit's behavior may change with age is through its *force production capabilities*. Electrical stimulation is often used to artificially activate units and characterize their twitch and tetanic properties. Kanda and Hashizume<sup>9</sup> used this method to differentiate rat muscle motor units based on their physiologic properties (fast fatigable [FF], slow [S]). Elderly Type S units produced significantly more tetanic tension than younger Type S, while Types FF, FI, and FR showed significantly smaller tensions than their middle-aged counterparts. Others have shown similar results.<sup>11</sup> Even more intriguing, these same studies found no increases in elderly muscle specific tension (ie, the force generated per fiber cross-sectional area). How is it that stimulated elderly Type S units produce more tension, but their fibers do not have greater

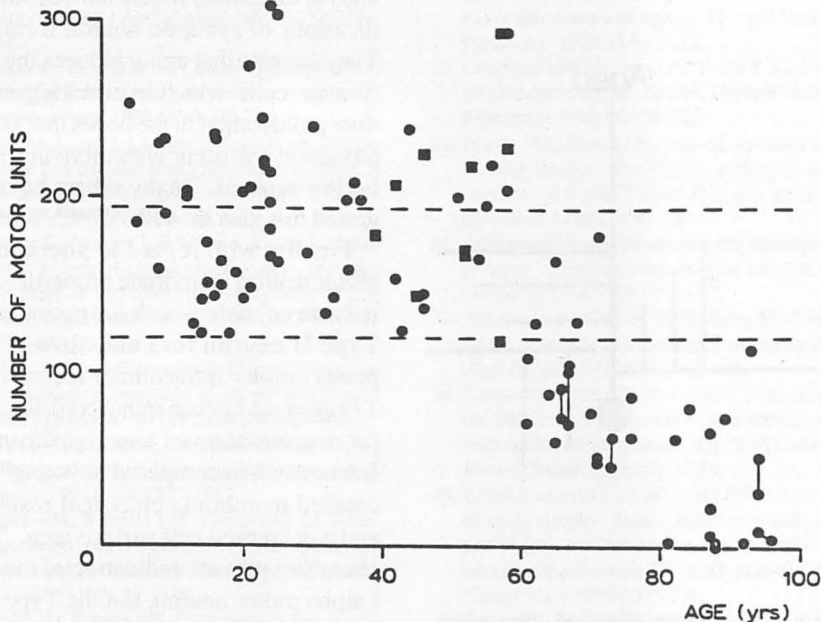
cross-sectional areas? An increase in the muscle's innervation ratio may explain this. Studies examining elderly voluntary contractions suggest this idea.

Although the elderly's stimulated muscle shows elevated force production, their ability to exert a maximal voluntary isometric contraction (MVC) is significantly diminished. In hand muscles, the impairment is as great as 57.6%<sup>13</sup> when compared with younger subjects.<sup>7</sup> Of more functional significance than maximal contractions, the aged have shown an inability to accurately control and grade submaximal forces. Investigators have examined submaximal isometric hand muscle contractions ranging from 5% MVC to 50% MVC, finding the lower forces to be the most variable for the elderly.<sup>7,14</sup> If a single Type S motor neuron increases the number of muscle fibers it innervates with aging (ie, an increase in innervation ratio), then it logically follows that the ability the grade low forces would be diminished. While these findings on force production may be clinically intuitive, the impact of aging on muscle's fatigability is not.

Artificially activated human adductor pollicis muscle has shown a linear *increase* in isometric endurance with age,<sup>13</sup> with animal models showing similar results.<sup>8</sup> How can aging be accompanied with improved muscular endurance? It may indicate that, while the elderly do show increased movement variability and inefficiency,<sup>15,16</sup> as well as altered muscle metabolism,<sup>17</sup> the *potential* for improved endurance of force may exist within the muscle itself. Studies examining motor unit fiber distribution/morphology confirm this.

## Changes in Motor Unit Morphology

The most basic finding in aged motor unit morphology is a loss in total unit number.<sup>9,18,19,20,21</sup> This loss is estimated to be approximately 1% of the total number per year, beginning in the third decade,<sup>21</sup> and dramatically increases in percentage at 60 years and greater (see Figure 1).<sup>20</sup> While caution should be used with the 1% estimate (due to variability seen between



**Figure 1.**

Numbers of functioning extensor digitorum brevis motor units in 94 subjects. Notice the rapid decline near 60 years. Reprinted with permission from: Campbell MJ, McComas AJ, Petito F. Physiological changes in ageing muscles. *J Neurol Neurosurg Psychiatry*. 1973;36:176.

subjects), the age of 60 has consistently proven to be a marker for radical changes.<sup>13,20,34</sup> But how can the loss of motor units at this age be compatible with the improved endurance demonstrated in electrical stimulation studies?

The elderly's loss of motor neurons may be *preferential*, as suggested by a decrease in the proportion of Type II ("fast") muscle fibers with aging.<sup>9,11,21,23</sup> That is, for a given muscle, there is an increase in the number of slow, high-endurance fibers with aging. For example, Tomonaga<sup>22</sup> biopsied muscle from 80 elderly subjects, finding the 60 to 79-year-old group to show preferential Type II atrophy, as well as sarcomeric ultrastructural changes, with the most distal limb muscles being most affected. Despite being cited widely in the literature,<sup>6,13,24,25</sup> a strong case could be made against the robustness of Tomonaga's findings based on choices in subject selection, data analysis, and electron microscopic technique. For example, Lexell and colleagues<sup>25</sup> autopsied whole human vastus lateralis muscle, rather than biopsies, and report no preferential fiber loss. They did suggest that a change in

the arrangement of muscle fiber types (ie, within fascicles) does occur with aging.

The random spatial arrangement of slow- and fast-twitch fibers seen in young muscle is not present in the elderly.<sup>9,10,26</sup> How does this occur? The notion of muscle-fiber-type grouping enjoys widespread support. A denervation-reinnervation process is thought to take place in which fast-type alpha motor neurons die and are reinnervated by slow-type motor neurons.<sup>9,10,11,13,14,18,26</sup> The exact mechanism behind this process is unclear; however, experiments with rat muscle<sup>8,10</sup> have suggested that a gradual transition in the fast-intermediate type muscle fibers occurs across the lifespan, with their myosin heavy chains gradually converting to the slow type. Hopp<sup>17</sup> reviews the literature surrounding the influence of resistance training on this fiber-type conversion.

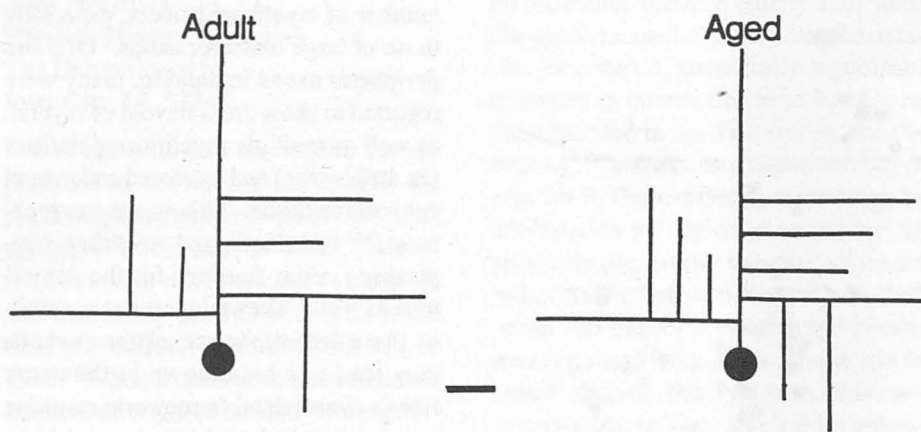
### Other Changes

Age-induced alterations occur with other parts of the motor unit, not just the muscle fiber. Modifications to the peripheral motor axon result in structural, trophic, and performance alterations.

Ansved and Larsson<sup>27</sup> compared young and old rat L5 ventral roots and distal peripheral nerves, finding decreases in the number of myelinated fibers, especially those of large diameter axons. Of those peripheral axons remaining, many were reported to show areas devoid of myelin, as well as multiple myelin irregularities (eg, ballooning) and increased endoneurial connective tissue. Others are in agreement,<sup>28,29</sup> with Knox and coworkers<sup>29</sup> reporting similar findings for the ventral root as well. They suggest the possibility that a decrease in axonal transport rate may lead to a breakdown in the nerve fiber's cytoskeletal framework, resulting in axonal atrophy. Investigators have found that slow-component axonal vesicle transport is, indeed, significantly slower in elderly versus young rat ventral roots.<sup>29,30</sup> It may be that the alterations in large-diameter nerve fibers, the myelin irregularities, and the trophic degeneration seen in animal models could collectively account for the well-documented slowing of nerve conduction velocity that occurs with aging.<sup>9,30,31</sup>

The neuromuscular junctions of a motor unit also change with age. Elderly human intercostal muscle endplates<sup>32</sup> were found to have increases in pre-terminal axon branching (ie, branches that enter the same endplate), and an increase in endplate length. Perijunctional acetylcholine receptors (ie, surrounding the junctions' perimeter) were found in the aged, but not the young. Interestingly, there were no extrajunctional acetylcholine receptors, which appear with denervation. Could this be because intercostal muscles, which are used for breathing, are spared from the intense denervation-reinnervation process seen in skeletal muscle? Kobayashi and colleagues<sup>33</sup> found a particular type of molecule (NCAM—which is indicative of this process) to be significantly elevated in aged rat soleus and sternomastoid, but not diaphragm and endplates. Selective adaptation does appear to be a motif of the aging process.

The motor neuron itself is altered in three dramatic ways with aging: 1) loss of anterior horn cells; 2) changes in segmental dendritic branching; and 3) modifications of cell membrane electrical properties. After examining serial sections of lumbosacral spinal cords from 47 human



**Figure 2.**

Schematic to illustrate dendritic branching patterns/frequency in young adult and aged motor neurons. Scale = 200 microns. Reprinted with permission from: Ramirez V, Ulfhake B. Anatomy of dendrites in motoneurons supplying the intrinsic muscles of the foot sole in the aged cat: evidence for dendritic growth and neo-synaptogenesis. *J Comp Neurol.* 1992;316:7.

**Table 1. Selected adaptations of the aging motor unit, summarized.**

- Axon and ventral root:
  - irregularities in myelin
  - diminished slow axonal transport
  - decreased conduction velocity
- Alpha motor neuron:
  - decreased number past 60 years (selective to Type II)
  - increased dendritic branch complexity (selective to Type I)
- Motor endplate:
  - significant remodeling
- Muscle:
  - increased action potential amplitude, duration, and complexity
  - elevated contraction and relaxation times
  - elevated twitch and twitch-tetanus forces (selective to Type I)
  - variable control of force production
  - decreased fatigability
  - increased muscle-fiber grouping
  - elevated innervation ratio (selective to Type I)

subjects, Tomlinson and Irving<sup>34</sup> concluded that a subtle loss of ventral horn motor neurons occurs throughout adulthood. Then, at age 60, a very dramatic increase in the rate of loss occurs. The striking feature of this finding is how well it correlates with the results of electromyographic and force data from human hand muscle.<sup>20</sup>

Considering this motor neuron loss, it is not surprising that surviving segmental neu-

rons of the elderly increase in their branching complexity. Ramirez and Ulfhake<sup>31</sup> found young and old cat spinal cord motor neurons to be similar in many aspects: mean number of dendrites per neuron, dendrite path distance, length of terminal branches, and dendrite diameter. The aged cats, however, revealed two unique findings: 1) a significantly more complex branching pattern of dendrites with additional collateral growth (see Figure 2) and

2) "growth cone-like" extensions on the ends of dendrites, which showed some indications of synaptic bouton formation. They suggest that aging induces the death of some cells, which in turn triggers dendrite proliferation in the hopes that synapse formation will occur with surviving, neighboring neurons. Many others have suggested this idea as well.<sup>7,8,9,10,14,18,19,20,21,24,27</sup>

Finally, with regard to alterations in motor neuron membrane properties, findings are consistent with the notion of fast, Type II neuron loss and slow, Type I preservation. Intracellular recordings of 179 aged cat lumbar spinal cord alpha motor neurons showed two significant differences when compared to young<sup>35</sup>—increased membrane electrical resistance and a decreased cell surface area. These characteristics are indicative of the Type I alpha motor neuron, not the Type II.<sup>5</sup>

## Limitations and Conclusions

Although it occurs in basic science, as well as in the clinic, making extrapolations and inferences between morphology and physiology, between animal and human models, between different muscles, and between volitional/purposeful movement and artificially activated single motor units is inherently dangerous. This act becomes even more hazardous when one also considers the age-related adaptations to suprasegmental,<sup>36,37</sup> metabolic,<sup>17</sup> and biomechanical<sup>38</sup> components of movement. But, as physical therapists, our clients compel us to understand such "microscopic" changes (see Table 1) and consider how they may apply to our "macroscopic," increasingly elderly, patient population.

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