THE REORGANIZATION OF THE NEUROMUSCULAR SYSTEM DURING AGEING: INFLUENCE OF REGULAR PHYSICAL ACTIVITY

Duchateau Jacques

**Laboratory of Applied Biology and Neurophysiology,
Université Libre de Bruxelles, Brussels, Belgium**

Senescence is accompanied by various changes affecting the neuromuscular system that contribute to the decline in functional performances observed in elderly individuals. In addition to a profound remodelling of the neuromuscular system, several mechanisms located at both muscular and neural levels contribute to this lost of performances. Hopefully, regular physical activity may counteract or reverse some of the alterations encountered in old age. The purpose of this keynote lecture is to give an overview of the main age-related changes of the neuromuscular system and to evoke the potential influence of regular physical activity in limiting these alterations.

KEY WORDS: strength, motor control, motor unit, sarcopenia

INTRODUCTION: Among the age-related alterations of the neuromuscular system, one of the most visible changes is the decrease in muscle strength. Many studies have shown that the decline in maximal strength is relatively slow between the age of 20 and 50-60 years in active individuals but is clearly accentuated in the seventh decade of life (Vandervoort & McComas, 1986). At this stage, depending of the muscle type and the amount of physical activity performed by individuals, the drop in maximal strength may reach ~1.5% per year (Vandervoort, 2002). However, the decline in maximal strength is not uniform among the types of muscle contraction but is more pronounced for concentric (shortening) and isometric contractions than for eccentric (lengthening) contraction (Klass et al., 2005).

CHANGES AND REORGANISATION OF THE NEUROMUSCULAR SYSTEM: The decline in maximal strength is associated with a reduction in muscle mass (i.e. sarcopenia). Sarcopenia is due to a loss of muscle fibres and the atrophy of the remaining muscles fibres; the latter effect being more pronounced for fast than slow muscle fibres (Lexell, 1993; Hunter et al., 1999). In parallel, muscle architecture is often changed and a reduction in the pennation angle of muscle fascicles has been reported (Narici et al., 2005). By a better orientation of the force vector along the longitudinal orientation of the muscle, such change may partly counteract the reduction in the force produced by each muscle fibre. These muscular changes are further accompanied by a slowing of the intrinsic speed-related properties of the muscle as assessed by electrical stimulation (Vandervoort & McComas, 1986). The slower contractile kinetics is primarily caused by a reduced rate of cross-bridge cycling (D'Antona et al., 2003) and alteration in excitation-contraction coupling (Baudry et al., 2005). An enhanced tendon compliance with ageing (Narici et al., 2005) may further contribute to reduce the rate of force development.
The age-related changes recorded at the whole muscle level are also associated with a profound reorganization of the motor unit structure that comprises a motor neurone, its axon, and the muscle fibres that the axon innervates. The number of motor units in a muscle is reduced with ageing due to the death of some motor neurones. For example in the tibialis anterior, a muscle involved in locomotion, the average number estimate of motor unit declines from ~150 motor units in young adults (20-30 years) to about 90 and 60 motor units in elderly adults of ~65 and ~80 years, respectively. This means that at an age of 80 years more than 50% of our motor units are lost (McNeil et al., 2005). Although some of the denervated muscle fibres degenerate due the apoptosis of motor neurones and contribute to sarcopenia, other fibres are reinnervated by the surviving motor neurones. This leads to an increased innervation ratio (greater number of muscle fibres innervated per motor neurone) and thereby to the development of "giant" motor units (Galganski et al., 1993). This profound age-related

motor unit remodelling may have functional implications for the neural control of muscle contraction and in particular for fine motor tasks, as the performance will be affected by the reduced number of motor units and the greater force produced by each of them.
In addition to the profound reorganization of the motor system, part of the decrease in maximal force and rate of force development during fast contractions results in some but not all elderly adults in submaximal activation of the agonist muscles by the central nervous system (Klass et al., 2007). For example, it has been reported that voluntary activation is reduced in some aged individuals due to an incomplete recruitment of motor unit and a submaximal discharge frequency. Furthermore, the decline in maximal motor unit discharge frequency explains part of the reduced rate of force development during rapid contractions (Klass et al., 2008). In this context, the increased concurrent antagonist muscle activation (i.e. coactivation) during agonist contraction may further contribute to reduce force production in elderly adults (Klass et al., 2008). In addition, the control of movement and balance during upright standing in elderly adults is accompanied by a greater involvement of the supraspinal structures compared with young adults (Baudry & Duchateau, 2014). As the sensory feedback is also altered and/or down-regulated during motor tasks, these observations suggest that elderly adults rely more on central than peripheral mechanisms to control motor output. Together, these changes indicate that both muscular and nervous factors contribute to the age-related decline in performance.

BENEFITS OF PHYSICAL ACTIVITY: In the last few decades, experiments have shown that regular physical activity can counteract or reverse some of the age-related alterations encountered by the neuromuscular system. For example, maximal force and muscle hypertrophy are susceptible to re-augment even at an age above 70 years old (Frontera et al., 1988) providing that the chronic physical loading and the amount of daily amino acid intake are sufficient.
Neural adaptations to training are also observed. For example, it has been shown in very old adults (>80 years) presenting a large deficit in voluntary activation (≥ 20%), that only a few number of maximal isometric contractions are sufficient to regain part of their activation capacity (Jakobi & Rice, 2002). Depending of the extent of the initial deficit, this adaptation may be related to an increased ability to recruit a greater number of motor units and/or to discharge them at a greater frequency. Interestingly, we observed recently in elderly subjects that a combination of balance and moderate strength training was sufficient, at the beginning of a training programme, to increase maximal strength by an enhanced voluntary activation (Penzer et al., 2014). On a functional point of view, this observation is interesting because it indicates that even with low mechanical constraints on the muscular-skeletal system, limiting thereby the risk of injuries, training sessions containing mainly balance exercises are susceptible to improve steadiness during upright standing but also to increase the maximal strength of lower leg muscles. Similarly, a programme of strength training reduces antagonist activation, favouring thereby the activation of the agonist muscles and strength production (Hakkinen et al., 1998). It has also been shown that manual dexterity assessed by a functional test (pegboard test) and force steadiness during static, and concentric and eccentric contractions, can be improved in old age by a training programme combining light (10% max) and high (70% max) loads. Such improvement in manual dexterity is quite fast (2-4 weeks) and seems to be mainly related to a reduction in the variability of motor units discharge frequency (Laidlaw et al., 1999; Kornatz et al., 2005). However, the observation that the performances remained inferior in elderly than in young subjects after 12 weeks of training suggests that some of the changes related to motor unit remodelling are irreversible and cannot be completely counteracted by training.
More recently, it has been reported that long-term aerobic training might have a preventive effect on the loss of motor neurones (Power et al., 2010). Indeed, contrary to sedentary old adults (~65 years), that displayed a reduced number of motor units in the tibialis anterior compared with young adults, age-matched master runners (45-80 km/week) had a similar number of motor units than their younger counterparts. Interestingly, such observation differed in the biceps brachii for which the reduction in the number of motor units was present

and similar in both sedentary and active elderly adults (Power et al., 2012). These findings underscore that the denervation-reinnervation process may be minimized or counteracted by regular physical activity but that the protective benefits seem to be limited to the exercised muscles. Such encouraging findings confirm the conclusion of animal studies supporting a neuroprotective effect of lifelong physical activity. The next challenge will be to determine the most effective physical activity, its intensity and the training volume required to optimize this effect.

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