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Restoration of post-activation depression of the H-reflex by treadmill exercise in aged rats

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ABSTRACT

The purpose of this study was to evaluate the effects of aging and chronic physical activity on the post-activation depression of the Hoffman reflex (H-reflex). The maximal amplitude H wave/maximal amplitude M wave ratio was measured, and the rate-sensitive depression of the H-reflex was assessed. Measurements were performed on sedentary rats aged of 3, 6, 12, and 20 months and on animals aged of 12 and 20 months performing an incremental treadmill exercise protocol during the last eight weeks preceding the recordings. At the end of the experiment, the muscle mass and/or body mass ratio was calculated. Results indicated that the H-reflex depression of the tibialis anterior and soleus muscles were present until age of 6 and 12 months, respectively. For the tibialis anterior muscle, results also pointed out a decrease in the relative muscle mass with age and that the exercise allowed to restore the rate-sensitive depression of the H-reflex and to increase the relative muscle mass in comparison with sedentary animals. These findings clearly demonstrate that neural alteration of the spinal cord is prevented by activity in aged rats.

1. Introduction

Aging is associated with progressive decline in muscle function and mass leading to a decrease in mobility and metabolic disturbances (Lanza and Nair, 2009; Lindle et al., 1997; Macaluso and De Vito, 2004; Metter et al., 1997; Narici et al., 1991; Pasini et al., 2012; Reeves et al., 2006; Vandervoort and McComas, 1986). It was shown a muscle progressive weakness (force loss) generally attributed to change in muscle architecture, collagenous structures (including tendon), and neural drive (Enoka, 1997; Kjaer, 2004; Macaluso and De Vito, 2004; Narici et al., 2003; Roos et al., 1997; Scaglioni et al., 2002; Tuite et al., 1997; Unhjem et al., 2015; Yue et al., 1999). Muscle architecture alterations consist in a muscle fascicule shortening, change in pennation angles and a decrease number of type I (slow) and II (fast) muscle cells (muscle cell apoptosis), associated with type II cell atrophy (Lexell et al., 1988; Morse et al., 2004; Narici et al., 2003). Tendon alterations consist in cross-sectional area change with age leading to a thicker tendon which would be subject to smaller tensile stresses and would be less likely to rupture on tension (Magnusson et al., 2003). Neural alterations consist in a loss of motoneurons, a reduction of motor unit recruitment and firing frequency (Kamen et al., 1995; Lexell et al., 1988; Yue et al., 1999), and a decrease in motoneuron excitability and thus in nerve conduction velocity (deVries et al., 1985; Falco et al., 1994a; Huang et al., 2009; Sabbahi and Sedgwick, 1982; Vandervoort and Hayes, 1989). Because the muscle phenotype depends on its innervation (Lomo, 2003; Pette and Vrbova, 1985), the decrease of the number of actions potentials sent to the muscle could accelerate muscle phenotype changes with age and, then associated with a loss of motoneurons, could alter the sensorimotor loop (and motor and physiological adjustments). Indeed, in a recent article, we concluded that the response of metabosensitive muscle afferent fibers which is involved in the activation of the sensorimotor loop (and motor and physiological adjustments) depends on anatomic (mass, phenotype, vascularization, receptor, and afferent densityand so forth) and functional (flexor vs. extensor) characteristics of their originating muscles (Caron et al., 2015).

Muscle afferent activation in the exercising muscles is responsible of motoneuronal and cardiorespiratory adjustments (Decherchi and Dousset, 2003; Decherchi et al., 2004, 2007; Mitchell et al., 1977). Indeed, Golgi tendon organ (afferents Ib), muscle spindles (afferents Ia and II or Aβ; Rosales and Dressler, 2010), and muscle afferents from groups III (Aδ) and IV (C; Kniffki et al., 1978) send proprioceptive information to the spinal cord and supraspinal structures to adjust the neuron excitability.

Concerning the motor system, reflexes are involved in the control of posture and balance (Houk et al., 1981). The Hoffmann reflex

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(H-reflex) is a valuable tool to assess the modulation of monosynaptic reflex loop in the spinal cord (Hoffmann, 1910; Magladery and McDougal, 1950; Magladery et al., 1951a; Pierrot-Deseilligny and Mazevet, 2000). It is an estimate of α-motoneurons excitability when their intrinsic excitability (Capaday, 1997) and presynaptic inhibitions (Zehr, 2002) remain stable. The H-reflex, that is evoked by the direct activation of the Ia afferent nerve fibers, measures the efficacy of synaptic transmission through the α-motoneuron pool; that is, it is an indication of the number of motor units that are reflexively activated at a given stimulus intensity and any change in H-reflex amplitude reflects changes in the excitability of the sensorimotor loop. Thus, the H-reflex is used to study the sensorimotor integration (ascending peripheral and descending central influences) and plasticity of the central nervous system (Knikou, 2008).

The neuromuscular system of old subjects has been considered as less plastic and therefore less adaptive compared to young adults, and the integrity of the spinal stretch reflex system has been demonstrated to significantly degrade over time (Koceja et al., 1995; Mynark and Koceja, 2001).

In a human study, it was shown that the maximal amplitude H wave/maximal amplitude M wave (H_{max}/M_{max}) ratio (proportion of the entire montoneuron pool capable of being recruited) decreased with age (Koceja and Mynark, 2000) and that the muscle tone increases (Marshall, 1982). Angulo-Kinzler et al. reported that the resting $H_{max/}M_{max}$ ratio of the soleus muscle increases in elderly subjects when standing compared with younger subjects in whom the ratio decrease, and no gain modulation of the reflex from prone to standing was noticed in elderly subjects (Angulo-Kinzler et al., 1998). Other study examining the modulation of the soleus H-reflex in response to the Jendrássik maneuver in standing positions showed some difference between young and elderly people (Tsuruike et al., 2003). It was also indicated that aging increases the between leg variability of H-reflex latency in individuals (Falco et al., 1994b). Other authors reported some difference in the soleus H-reflex postactivation depression between young and elderly (Robertson and Koceja, 2003). More recently, Raffalt et al. (2015) indicated that the H-reflex amplitude measured during walking was affected by aging, and Trompetto et al. (2013) assessing the postactivation depression, reported that the frequency-related depression of the flexor carpi radialis H-reflex is similar in young (28 ± 3 years) and elderly (69 ± 6 years) subjects at stimulation frequencies of 0.33, 0.5, and 1 Hz, with the exception of 2 Hz. In view of the scientific literature, it appears that no information has been reported concerning changes at rest in the postactivation depression of the H-reflex with age depending on the muscle phenotype.

It was suggested that physical activity retards alterations linked to aging by inducing neural adaptations, muscle mass increase, and muscle phenotype change from fast fatigable to more fatigue-resistant fibers (Cartee, 1994). Indeed, regular physical activity produces marked adaptations in both the muscular and nervous systems in young and elderly (Christie and Kamen, 2014; Mazzocchio et al., 2006; Piirainen et al., 2014). The excitability of the reflex arc could be modulated by physical training, even in old age. Thus, it was reported that physically active elderly preserved a faster reflex response compared with sedentary elderly (Hart, 1986). Furthermore, it was shown that strength gain observed in elderly was associated to changes in neural drive (distribution of the motor command to the muscles, modulation of neural excitability, and so forth; Enoka, 1997; Hakkinen et al., 2000). Finally, Lauber et al. (2011) observed that 12 weeks of alpine skiing increase the H-reflex excitability and maximal force and decrease the postural sway in elderly. However, other authors showed no modulation of the H-reflex (H_{max}/M_{max} ratio) of plantar flexor after 16 weeks of strengthening program in elderly men (Scaglioni et al., 2002). Likewise, Unhjem et al. (2015) reported, in elderly males, no change in H/M ratio of the triceps surae muscles after eight weeks of heavy resistance training despite an increase in maximal voluntary contraction, in rate of force development and in V wave/M wave ratio (reflecting the magnitude of efferent output to the muscle during maximal contraction). Nevertheless, as suggest by some authors, influences on the neuromuscular system are the result of the type and quantity of physical activity (Koceja et al., 2004). Furthermore, the rate-sensitive depression of the H-reflex that allows assessing the postactivation depression has never been studied in slow and fast muscles after a chronic training in older.

In light of these considerations, the present study was designed to compare the frequency-dependent depression of the H-reflex on predominantly glycolytic (tibialis anterior) and oxidative (soleus) muscles in sedentary rats aged of 3, 6, 12, and 20 months and in rats aged of 12 and 20 months performing a treadmill training during the eight weeks preceding the electrophysiological recordings. Thus, we explored the modulation of the H-reflex and changes in the homosynaptic depression in young and aged sedentary and active animals.

2. Materials and methods

2.1. Animals

A total of 70 male Sprague Dawley rats were used in the study (Janvier, Le Genest Saint Isle, France). Forty-eight were subdivided into four experimental groups depending to their age at the time of electrophysiological recordings: 3-month old (3M, n = 12), 6-month old (6M, n = 12), 12-month old (12M, n = 12), and 20-month old (20M, n = 12). The 22 other rats were divided into two experimental groups and performed a treadmill training during eight weeks before the electrophysiological session: 12-month old (12M-exercise [EXE], n = 10) and 20-month old (20M-EXE, n = 12). The comparison of exercise effects in the 12M-EXE and 20M-EXE groups were made against the 12M and 20M animals from the sedentary groups. Animals were housed in smooth-bottomed plastic cages at 22 °C with a 12-h light/dark cycle. Food (Safe, Augy, France) and water were available ad libitum.

2.2. Ethical approval

Anesthesia and surgical procedures were performed according to the French law on animal care guidelines and the Animal Care Committees of University Aix-Marseille (Aix-Marseille Université) and CNRS (Centre National de la Recherche Scientifique) approved our protocols (license n°A 13.013.06). Furthermore, experiments were performed following the recommendations provided in the Guide for Care and Use of Laboratory Animals (US Department of Health and Human Services, National Institutes of Health) and in accordance with the European Community's council directive of 24 November, 1986 (86/609/EEC).

2.3. Exercise-training protocol

Animals from the groups 12M-EXE and 20M-EXE were first familiarized with the treadmill for one week. Then, during the next eight weeks, animals performed an incremental treadmill exercise protocol adapted from Pasini et al. (2012). Physical exercise training was performed 3 days per week during eight weeks. Briefly, during the first week, the running speed was fixed at 13.5 m/min for 10 minutes. During the second week, the duration of the exercise was increased to 20 minutes, but the running speed was kept unchanged. From the third to the fifth week, the training time was progressively increases to reach 50 minutes, and the running speed