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Aging impairs the recovery in mechanical muscle function following 4 days of disuse

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ABSTRACT

As aged individuals are frequently exposed to short-term disuse caused by disease or musculoskeletal injury, it is important to understand how short-term disuse and subsequent retraining affect lower limb mechanical muscle function. The purpose of the present study was, therefore, to investigate the effect of 4 days of lower limb disuse followed by 7 days of active recovery on mechanical muscle function of the knee extensors in young (24.3 ± 0.9 years, $n = 11$) and old (67.2 ± 1.0 years, $n = 11$) recreationally active healthy males. Slow and moderate dynamic muscle strength were assessed using isokinetic dynamometry (60 and 180° s^{-1}, respectively) along with isometric muscle strength and rapid muscle force capacity examined as contractile rate of force development (RFD), Impulse, and relative RFD (rRFD) during the initial phase of contraction (100 ms time interval relative to onset of contraction). Prior to disuse, marked age-related differences ($p < 0.05$) were observed in isometric and dynamic muscle strength (~35%) as well as in RFD and Impulse (~39%). Following disuse, young and old individuals experienced comparable decrements ($p < 0.05$) in isometric strength (~9%), slow dynamic strength (~13%), and RFD and Impulse (~19%), whereas old individuals only experienced decrements ($p < 0.05$) in moderate dynamic strength (12%) and rRFD (~17%). Following recovery, all measures of mechanical muscle function were restored in young individuals compared to pre-disuse values, while isometric, slow and moderate dynamic muscle strength remained suppressed ($p < 0.05$) in old individuals (~8%) along with a tendency to suppressed RFD_{100} ($p = 0.068$). In conclusion, 4 days of lower limb disuse led to marked decrements in knee extensor mechanical muscle function in both young and old individuals, yet with greater decrements observed in moderate dynamic strength and rapid muscle force capacity in old individuals. While 7 days of recovery – including free ambulation, one test session and a single session of strength training – was sufficient to restore mechanical muscle function in young individuals, old individuals appeared to have an impaired ability to fully recover as evidenced by suppressed values of isometric and dynamic muscle strength and rapid muscle force capacity.

1. Introduction

Disuse has been shown to induce marked impairments in lower limb mechanical muscle function of both young and old individuals, characterized by decrements in isometric and dynamic muscle strength as well as in rapid muscle force capacity (e.g. rate of force development (RFD) and contractile Impulse) (Deschenes et al., 2008; Hvid et al., 2010; Kortebein et al., 2008; LeBlanc et al., 1992; Narici and de Boer, 2011; Suetta et al., 2009). As these specific measures of muscle function have been shown to be strong predictors of general functional status, quality of life, and risk of mortality in aged individuals (Buchman et al., 2007; Cesari et al., 2009; Newman et al., 2006; Pijnappels et al., 2008; Wyszomierski et al., 2009), even short periods of disuse may lead to severe consequences for a single individual. Specifically, rapid muscle force capacity (i.e. the ability to produce as much force as possible within fractions of a second, e.g. 100 ms) has been advocated to be highly important for the ability to counteract unexpected perturbations during walking and thus avoiding falling (Aagaard et al., 2002; Caserotti et al., 2008; Wyszomierski et al., 2009). In support, having a low vs. a high rate of force development (RFD) has been shown to discriminate older fallers from non-fallers, respectively (Pijnappels et al., 2008).

Based on existing data, impairments in lower limb mechanical muscle function appear to occur very fast within the initial phase (days) of disuse followed by an attenuated rate of decline as time progresses (Deschenes et al., 2008; Deutz et al., 2013; Hvid et al., 2010, 2013; Kortebein et al., 2008; LeBlanc et al., 1992; Narici and de Boer, 2011; Suetta et al., 2009, 2012). Moreover, the subsequent recovery in mechanical muscle function following cessation of disuse appears to be compromised in older compared to younger individuals, at least after more prolonged periods (14 days) of disuse (Hvid et al., 2010;

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Suetta et al., 2009), altogether contributing to an increased risk of functional impairments and disability.

Yet, no previous studies have comprehensively investigated lower limb mechanical muscle function in response to disuse lasting less than 7 days and subsequent recovery in aged individuals. As aged individuals are frequently exposed to short periods of disuse due to disease or musculoskeletal injury occasionally involving hospitalization (Cookson and Laudicella, 2011; Covinsky et al., 2003; Saczynski et al., 2010), knowledge of the potential disuse-induced impairments in mechanical muscle function as well as of the responsible underlying mechanisms is of major importance.

The purpose of the present study was, therefore, to investigate the effect of 4 days of lower limb disuse followed by 7 days of recovery on mechanical muscle function of the knee extensors (isometric and dynamic strength as well as rapid muscle force capacity) in young and old healthy men. It was hypothesized that young and old individuals would show a comparable decline in mechanical muscle function with disuse, and that old individuals would have an impaired ability to recover compared to young individuals.

2. Material and methods

2.1. Study design

While the present study focuses on the effects of short-term disuse and subsequent recovery on lower limb muscle mechanical function in old individuals vs. young individuals, detailed information on the disuse design and additional data comprising disuse-induced effects on single fiber contractile function and molecular signaling pathways have previously been published (Hvid et al., 2013; Suetta et al., 2012). In brief, young and old healthy men underwent 4 days of unilateral lower limb disuse followed by 7 days of active recovery. In addition to a familiarization session ~2 weeks prior to the start of the study (Fam), tests of knee extensor mechanical muscle function as well as body weight and height were performed ~1 week before (Pre) and 24 hrs after disuse (Post), as well as 7 days after recovery (Rec) (Fig. 1). Tests of mechanical muscle function were performed in both limbs, thus with the contra-lateral "non-disused" leg serving as an internal control. Muscle biopsies were obtained from the *vastus lateralis* muscle at Pre, Post, and Rec, in order to examine myosin heavy chain (MHC) isoform composition as and muscle fiber cross-sectional area (CSA) of the disused leg. To minimize the influence of discomfort from the biopsy and particularly the risk of severe muscle damage in the older subjects, tests of mechanical muscle function were performed the day following the muscle biopsy (Fig. 1) according to previous procedures (Hvid et al., 2010; Suetta et al., 2009). Subjects were instructed not to engage in any vigorous activities 48 hrs prior to all test sessions. To minimize the influence from diurnal variation, each subject was tested at the same time of day (±2 hrs).

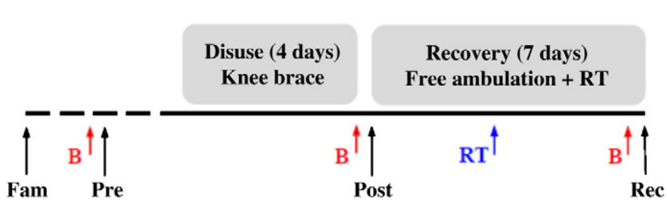

Fig. 1. Study overview. In addition to a familiarization session (Fam), various tests of mechanical muscle function of the knee extensors were carried out prior to (Pre) and following disuse (Post), as well as after recovery (Rec). Muscle biopsy sampling (B) was performed at Pre, Post, and Rec, always 1 day preceding tests of mechanical muscle function. In addition to free ambulation and the activities during post testing, the period of recovery included one session of high-intense unilateral resistance training (RT).

2.2. Subjects

While twenty-three healthy men were initially recruited for the study, one subject did not adhere to the disuse protocol for which reason his data was excluded from the analysis. Altogether, 11 young men (24.3 ± 0.9 yrs, 180.4 ± 2.7 cm, 74.3 ± 2.4 kg) and 11 old men (67.2 ± 1.0 yrs, 178.8 ± 1.7 cm, 87.7 ± 3.0 kg) participated in the study, with body mass differing between young and old individuals ($p < 0.05$). Care was taken to include young and old individuals with comparable levels of physical activity. This was done by using a questionnaire to estimate the amount (hours per week) of occupational (groups I–IV, ranging from *predominantly sedentary work* to *heavy manual work*) and recreational activities (groups I–IV, ranging from *almost completely inactive* to *regular high-intense physically active*, including description of the activities) on a general basis (Saltin and Grimby, 1968). Based on the questionnaire data, physical activity levels were similar in young and old individuals (4.3 ± 0.6 vs. 4.4 ± 0.6 hrs wk^{-1}, respectively) with no differences in low-to-moderate intensity occupational (group II *sitting or standing, some walking*) and recreational activities (group II *some physical activity during at least 4 h per week*). None of the subjects had previous experience with systematic resistance training.

Sample size was calculated based on findings from previous short-term disuse studies (Deschenes et al., 2008; Hvid et al., 2010; Suetta et al., 2009) using a statistical power (β) of 0.80, level of significance (α) = 0.05, and an expected range of change of ~10% in maximal knee extensor isometric strength.

All subjects were thoroughly informed of the details of the study and gave written, informed consent prior to participation. The study was approved by the Ethical Committee of Copenhagen and Frederiksberg in accordance with the Helsinki declaration (KF01-322606).

2.3. Disuse protocol

Details of the disuse protocol have been described elsewhere (Hvid et al., 2013). Briefly, 4 days of randomized unilateral lower limb disuse was conducted using a knee brace (DonJoy, DJO Global Inc., USA) fixed in a 30° knee angle (0° = full extension), with plastic strips applied to ensure that the brace was not removed during the disuse period. All ambulatory activities were carried out on the contralateral limb using crutches. Subjects were carefully instructed to refrain from weight-bearing activities (~ground contact) using the disused leg, but were encouraged to perform unloaded ankle flexion–extension on a daily basis in order to reduce the potential risk of venous thrombosis. Daily contact was kept with all subjects to ensure optimal compliance and to avoid health implications.

2.4. Recovery protocol

Immediately after the removal of the knee brace, subjects were biopsied and subsequently received manual mobilization of the disused leg to ensure that minimal pain was present and that normal range of motion could be obtained at the knee joint. In addition to returning to free ambulation and the test session of mechanical muscle function the day after the removal of the knee brace, subjects performed one session of supervised unilateral resistance training (including 5RM testing) of the disused leg three days after the removal of the brace (Fig. 1). Exercises included knee extension, leg press, and knee flexion using load adjustable machines (Technogym International, Italy). Following a brief warm-up (cycle ergometer, 5 min, 50–150 W) and determination of loading intensity of the chosen exercises by use of the 5RM testing, subjects performed 3 sets × 12 reps (at 15RM) using moderate (~1–2 s) and slow movement speeds (~3–4 s) in the concentric and eccentric contraction phases, respectively.