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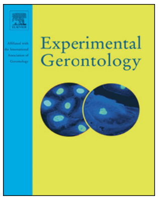

Age-related structural and functional changes of low back muscles

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ABSTRACT

During aging declining maximum force capacity with more or less unchanged fatigability is observed with the underlying mechanisms still not fully understood. Therefore, we compared morphology and function of skeletal muscles between different age groups. Changes in high-energy phosphate turnover (PCr, Pi and pH) and muscle functional MRI (mfMRI) parameters, including proton transverse relaxation time (T_2), diffusion (D) and vascular volume fraction (f), were investigated in moderately exercised low back muscles of young and late-middle-aged healthy subjects with ^{31}P-MR spectroscopy, T_2- and diffusion-weighted MRI at 3 T. In addition, T_1-weighted MRI data were acquired to determine muscle cross-sectional areas (CSA) and to assess fat infiltration into muscle tissue. Except for pH, both age groups showed similar load-induced MR changes and rates of perceived exertion (RPE), which indicates comparable behavior of muscle activation at moderate loads. Changes of mfMRI parameters were significantly associated with RPE in both cohorts. Age-related differences were observed, with lower pH and higher Pi/ATP ratios as well as lower D and f values in the late-middle-aged subjects. These findings are ascribed to age-related changes of fiber type composition, fiber size and vascularity. Interestingly, post exercise f was negatively associated with fat infiltration with the latter being significantly higher in late-middle-aged subjects. CSA of low back muscles remained unchanged, while CSA of inner back muscle as well as mean T_2 at rest were associated with maximum force capacity. Overall, applying the proposed MR approach provides evidence of age-related changes in several muscle tissue characteristics and gives new insights into the physiological processes that take place during aging.

1. Introduction

It is a widely accepted finding that the maximum voluntary contraction (MVC) force of skeletal muscles decreases with age as a result of loss of muscle mass that is caused by shrinking muscle fibers and degeneration of fast twitch (type II) fibers or conversion of type II to type I fibers (Goodpaster et al., 2006; Korhonen et al., 2006; Martel et al., 2006; Nilwik et al., 2013). Interestingly, endurance of moderately loaded muscles, such as trunk muscles, is preserved during healthy aging (Champagne et al., 2009; Yassierli et al., 2007), whereas patients suffering from non-specific low back pain (LBP) show increased fatigue of the lumbar extensor muscles during sub-maximal back extension independent of age (D'Hooge et al., 2013). Despite the great amount of work performed to date, the mechanisms causing muscle fatigue and their age- or disease-related characteristics are still incompletely understood and remain an intense area of research.

One approach to obtain objective measures of muscle activation and muscle fatigue is the application of non-invasive muscle functional MRI (mfMRI) (Damon and Gore, 2005), which has been increasingly used in recent years to resolve spatial patterns of muscular involvement in exercising human legs (Ababneh et al., 2008; Tawara et al., 2011; Vandenborne et al., 2000) and lower back muscles (D'Hooge et al., 2013; Dickx et al., 2010; Mayer et al., 2005). The mfMRI technique is based on the quantitation of transverse spin–spin relaxation times (T_2) before and after muscular loading. Changes of T_2 in exercised skeletal muscles are mainly ascribed to osmotically driven water shifts from the extra- to intra-cellular spaces in response to intra-cellular accumulation of small metabolic osmolites, such as inorganic phosphate and lactic acid (Bendahan et al., 2004; Damon and Gore, 2005; Damon et al., 2002; Saab et al., 2000; Schmid et al., 2014; Vandenborne et al., 2000). Changes of high-energy metabolism can be assessed by ^{31}P-MR spectroscopy (MRS) and spatially localized by ^{31}P-chemical shift imaging (CSI) (Bendahan et al., 2004; Boesch, 2007; Houtman et al., 2001; Layec et al., 2013; Rzanny et al., 2004, 2006). One further effect

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contributing to muscle T_2 is the vascular volume fraction (Ababneh et al., 2008; Morvan, 1995; Schewzow et al., 2014), which can be assessed by means of diffusion-weighted imaging (DWI) in combination with the intra-voxel incoherent motion (IVIM) model (Ababneh et al., 2008; Hiepe et al., 2014a; Karampinos et al., 2010; Le Bihan et al., 1986; Morvan, 1995; Yanagisawa et al., 2009).

Age-related changes of muscle perfusion have already been demonstrated for the human calf (Wray et al., 2009) and lower back muscles (Yanagisawa et al., 2009) during exercise with a steady decrease of muscle perfusion with age but only minimally affected muscle metabolism. Hence, muscle function is still widely preserved in contrast to LBP patients who show larger (D'Hooge et al., 2013) and more asymmetric T_2 changes between the left and right side muscles (Clark et al., 2009). Impaired muscle function is partly ascribed to increased infiltration of extra-cellular fat in muscle tissue with age (Buford et al., 2012), which has been also observed in low back muscles and is considered to be one potentially important biological contributor to the development of LBP (D'hooge et al., 2012; Hebert et al., 2014; Kjaer et al., 2007).

However, detailed analyses of age-related morphological (cross-sectional area, fat infiltration, fiber structure and composition) and functional (load-induced perfusion and metabolic changes) alterations in the back muscles of healthy volunteers have so far not been performed. In the present study we therefore examined the lower back muscles of young and late-middle-aged healthy subjects with an extensive MRI/MRS protocol, including anatomic imaging, mfMRI, DWI and dynamic ^{31}P-CSI in order to explore (i) age-related changes of vascular volume fraction and metabolic turnover, (ii) effects of these changes on load-induced alterations of T_2 relaxation as well as (iii) associations between age-related changes of structural and functional parameters. We hypothesized that muscle function at moderate loads is preserved during healthy aging and that structural changes, such as fat infiltration, are related to lower maximum force capacities.

2. Methods

2.1. Subjects and exercise protocol

Fourteen healthy young and fourteen healthy late-middle-aged male subjects participated in the study (Table 1) after informed written consent was obtained. The examination protocol was approved by the Ethics Committee of the University Hospital Jena. The subjects were interviewed for their physical activity on a scale ranging from "1" (no physical activity at all) to "5" (high physical activity during training or work with daily duration > 1 h). For both groups a median physical activity of "3" was observed (Table 1), which corresponds to normal physical activity including 2–4 physical exertions per week ("2": low, "4": high physical activity). Values of mean body mass index (BMI) and body fat fraction (measured via an impedance scale) were significantly higher in the late-middle-age group ($p < 0.05$). The volunteers' upper body mass (UBM) and the isometric maximum voluntary contraction (MVC) force during back extension were both determined in a separate experiment by using the computer-supported test and training device Centaur®, BfMC, Leipzig, Germany (Anders et al., 2008). Mean UBM and MVC values were lower in the late-middle-aged subjects as was the upper body torque ratio (UBTR), which corresponds to the anthropometrically normalized MVC (Kurz et al., 2014). The age-related reduction of UBTR ($p = 0.8$) is in line with previously reported studies of back muscles (Champagne et al., 2009; Yassierli et al., 2007).

A detailed description of the applied methodology together with initial results in young subjects has already been presented recently (Hiepe et al., 2014a). As exercise, we chose a modified Biering-Sørensen test (Biering-Sorensen, 1984) — a sustained isometric back extension exercise that can be performed inside the bore of an MR scanner. Supported by a self-built wooden rocker frame, which enables freely selectable, specific load removals by means of adjustable counterweights, the volunteer contracts the lower back muscles to maintain his upper body part in a horizontal position (Fig. 1). In the present study, moderate exercise intensity was adjusted by applying load removals of 50% of the UBM. The ergometer was equipped with an angle sensor to monitor the upper body position and this information was visually fed back to the volunteer via a self-written GUI (MATLAB, The Mathworks, Inc., USA) and an MR-compatible video system (Virtual Stim Digital, Resonance Technologies Inc., USA).

The exercise was performed over a time period of 10 min and was repeated in two separate sessions on different days with an inter-session interval of 1–2 weeks (Fig. 1): During the first MRI session, T_2-weighted and diffusion-weighted data were collected before and after the exercise with subjects lying in supine position to reduce breathing motion artifacts that typically occur in prone position. The exercise was performed outside the scanner but in the scanner room. To exclude subjects with pathological findings, e.g., disk degeneration diseases, a T_1-weighted anatomic scan was acquired prior to the exercise. Post-exercise data acquisition started 1.5 min after the end of the exercise providing sufficient time to position the subject again in the scanner and to select the volume to be imaged.

Table 1
Subject characteristics (mean ± SD).

	Young ($n = 14$)	Late-middle-age ($n = 14$)	
Age [yr]	22.5 ± 1.4	55.3 ± 3.6	
Height [cm]	179.2 ± 5.8	174.0 ± 7.3	*
Weight [kg]	74.7 ± 7.5	76.6 ± 10.1	
Phys. activity	3 (IQR: 1)	3 (IQR: 1)	
BMI [kg m^{-2}]	23.2 ± 1.8	25.3 ± 2.8*	*
Body fat [%]	17.6 ± 4.6	21.5 ± 6.8	*
UBM [kg]	34.1 ± 2.6	35.7 ± 4.7	
MVC [Nm]	270.1 ± 44.0	230.7 ± 77.0	
UBTR [a.u.]	2.45 ± 0.39	2.07 ± 0.68	†

* Statistical difference with $p < .05$.
† Statistical difference with $p < .10$.

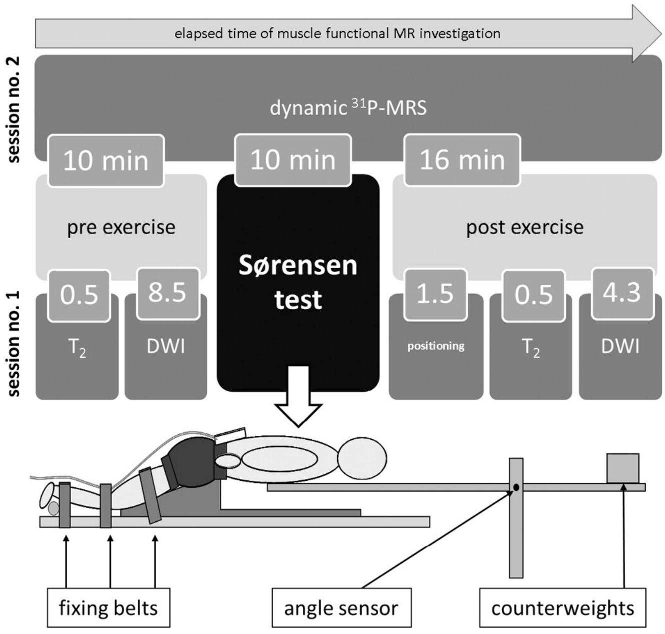

Fig. 1. MR examination protocol including an MR spectroscopy session (top row) during which ^{31}P-MR spectra were continuously acquired during rest (10 min), exercise (10 min) and post exercise (16 min), and an MR imaging session (middle row) during which T_2-weighted and DW data were collected before and after the exercise. The exercise was arranged as a modified Biering-Sørensen test using a MR compatible ergometer (bottom row) equipped with an angle sensor on the ergometer stilt for interactive self-adjustment of the upper body position during the exercise.

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