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Maximal strength training increases muscle force generating capacity and the anaerobic ATP synthesis flux without altering the cost of contraction in elderly

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ABSTRACT

Aging is associated with a progressive decline in skeletal muscle function, then leading to impaired exercise tolerance. Maximal strength training (MST) appears to be a practical and effective intervention to increase both exercise capacity and efficiency. However, the underlying physiological mechanisms responsible for these functional improvements are still unclear. Accordingly, the purpose of this study was to examine the intramuscular and metabolic adaptations induced by 8 weeks of knee-extension MST in the quadriceps of 10 older individuals (75 ± 9 yrs) by employing a combination of molecular, magnetic resonance ^{1}H-imaging and ^{31}P-spectroscopy, muscle biopsies, motor nerve stimulation, and indirect calorimetry techniques. Dynamic and isometric muscle strength were both significantly increased by MST. The greater torque-time integral during sustained isometric maximal contraction post-MST ($P = 0.002$) was associated with increased rates of ATP synthesis from anaerobic glycolysis (PRE: 10 ± 7 mM·min^{-1}; POST: 14 ± 7 mM·min^{-1}, $P = 0.02$) and creatine kinase reaction (PRE: 31 ± 10 mM·min^{-1}; POST: 41 ± 10 mM·min^{-1}, $P = 0.006$) such that the ATP cost of contraction was not significantly altered. Expression of fast myosin heavy chain, quadriceps muscle volume, and submaximal cycling net efficiency were also increased with MST ($P = 0.005$; $P = 0.03$ and P = 0.03, respectively). Overall, MST induced a shift toward a more glycolytic muscle phenotype allowing for greater muscle force production during sustained maximal contraction. Consequently, some of the MST-induced improvements in exercise tolerance might stem from a greater anaerobic capacity to generate ATP, while the improvement in exercise efficiency appears to be independent from an alteration in the ATP cost of contraction.

1. Introduction

Sedentary aging is associated with a progressive decline in both exercise capacity and efficiency (the ratio of work generated to energy expended) during locomotion (McKinnon et al., 2015; Woo et al., 2006), which, ultimately, affect the ability to perform daily life activities, and lead to a loss of independence. This age-related functional impairment seems to be partly mediated by muscle weakness, a decline in the "anaerobic" work capacity above critical power (W′), and an exaggerated ATP cost of contraction in the locomotor muscles (Layec et al., 2015; Neder et al., 2000; Poole and Barstow, 2015; Zane et al., 2017).

With the rapid growth of the older population (Harper, 2014), it is becoming critically important to develop evidence-based and practical

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strategies targeting these hallmarks of aging to defer the decline in physical function. Interestingly, maximal strength training (MST), which is characterized by ~4 sets using few repetitions (4–5) at high loads (85–90% of 1 repetition maximum; 1RM) improve muscle strength, force development, efficiency and delay the time to exhaustion (Heggelund et al., 2013; Hoff et al., 2007; Wang et al., 2010, 2017). However, the underlying intramuscular mechanisms responsible for the improvement in muscle function with MST remain unclear. In the only study to date examining the morphometric adaptations induced by MST, Wang et al. (2017) documented a significant increase in the size and the percentage of type II fibers in the *vastus lateralis* of older subjects after MST. Such findings seem rather counter-intuitive as fast-twitch fibers are thought to exhibit a higher ATP cost of contraction compared to slow twitch fibers (Barclay and Weber, 2004; Reggiani et al., 1997), and MST has consistently been documented to improve exercise efficiency (Heggelund et al., 2013; Hoff et al., 2007; Wang et al., 2010, 2017).

Besides exercise efficiency, it has also recently been suggested that part of the beneficial effect of strength training on exercise tolerance may stem from an increase in anaerobic work capacity (Denadai and Greco, 2018). In accordance with this suggestion, elevated blood lactate has been reported at peak exercise following MST (Karlsen et al., 2009). However, this is not a consistent finding among studies (Hoff et al., 2007; Wang et al., 2010). Given the limitations associated with the use of blood lactate as a proxy for anaerobic metabolism, it is therefore still unclear whether MST can also alter the peak rates of ATP synthesis derived from anaerobic glycolysis and the creatine kinase reaction in the exercising muscle.

There is an apparent conundrum between the benefits of MST training on exercise capacity and the morphological adaptations occurring at the fiber level in older adults (shift toward type II fibers), which may have opposite effects on muscle efficiency and anaerobic metabolism. Therefore, the purpose of this study was to examine the mechanisms by which MST alters muscle metabolic fluxes and efficiency in the locomotor muscles of older individuals. We hypothesized that MST 1) will induce a shift toward a more glycolytic muscle phenotype (greater proportion of fast myosin heavy chain), 2) allowing for greater muscle force production during sustained maximal contraction associated with an enhanced capacity to generate ATP from glycolysis and high-energy phosphates, 3) whereas the ATP cost from both cross-bridge cycling and ion pumping will remain unchanged.

2. Methods

2.1. Subjects

After obtaining written informed consent, 10 older subjects (7 males, 3 females) participated in this study (Table 1). The subjects were recruited based upon evidence of no regular physical activity above that required for activities of daily living (documented after recruitment by both questionnaire and accelerometry) and older than 65 yrs of age. All subjects were non-smokers, free of diabetes, known cardiovascular, neuromuscular, or pulmonary disease. Additionally, none of the subjects were taking medications recognized to affect muscle function. Women taking hormone replacement therapy were excluded from the study. The study was approved by the Institutional review board of both the University of Utah and the Salt Lake City Veterans Affairs Medical Center. All experimental trials were performed in a thermoneutral environment, with the subjects fasted overnight.

2.2. Testing procedures

2.2.1. Familiarization sessions

Prior to the main experiments, which were conducted on different days separated by at least 48 h, participants were familiarized with all testing procedures and blood samples were collected to perform a complete blood cell count, a fasting glucose and lipid panel. During a preliminary visit, subjects performed a maximal incremental exercise test [20 W + 25 W·min^{-1}] on a bicycle ergometer (Velotron, Elite Model, Racer Mate, Seattle, USA) for the determination of maximum workload (WR_{max}) and peak oxygen consumption (VO_{2peak}) using an open-circuit calorimetry system (Parvo Medics, True Max 2400, Salt Lake City, USA).

Table 1
Subjects characteristics.

Sample size	9	Normal range
Age (years)	75 ± 9	
Anthropometric characteristics		
Height (cm)	169 ± 9	
Weight (kg)	73 ± 16	
BMI (kg/m^2)	25 ± 4	
Functional characteristics		
Steps per day	5377 ± 2113	
Sedentary physical activity (min per day)	1237 ± 49	
Light physical activity (min per day)	113 ± 26	
Lifestyle physical activity (min per day)	57 ± 21	
Moderate physical activity (min per day)	23 ± 13	
Vigorous and very vigorous (min per day)	0 ± 0	
Cycling VO_2peak (mL·min^{-1}·kg^{-1})	24 ± 5	
Peak cycling work rate (W)	136 ± 37	
Blood characteristics		
Glucose (mg·dL^{-1})	87 ± 18	(74–106)
Cholesterol (mg·dL^{-1})	185 ± 29	(118–210)
Triglycerides (mg·dL^{-1})	101 ± 37	(30–150)
HDL (mg·dL^{-1})	58 ± 20	(35–72)
LDL (mg·dL^{-1})	108 ± 21	(0 – 100)
WBC (K·uL^{-1})	5.5 ± 0.8	(3.7–9.9)
RBC (M·uL^{-1})	4.7 ± 0.6	(4.0–5.6)
Haemoglobin (g·dL^{-1})	14 ± 1	(12.0–16.1)
Hematocrit (%)	43 ± 4	(37.0–47.1)
Neutrophil (K·uL^{-1})	3.3 ± 0.6	(1.9–8.0)
Lymphocyte (K·uL^{-1})	1.4 ± 0.5	(0.9–5.2)
Monocyte (K·uL^{-1})	0.5 ± 0.2	(0.16–1.50)

Data expressed as mean ± SD. Body mass index, BMI; high density lipoprotein, HDL; low density lipoprotein, LDL; white blood cells, WBC; red blood cells, RBC.

2.2.2. Whole-body cycling efficiency

After measuring resting energy expenditure, and following a 5 min warm-up with no resistance (0 W), subjects performed cycling exercise (Velotron, Elite Model, Racer Mate, Seattle, USA) at 30 and 50% of WR_{max} for 5 min followed by 3 min of passive recovery after each workload. At baseline and throughout the exercise, pulmonary gas exchanges were measured continuously using an open-circuit calorimetry system (Parvo Medics, True Max 2400, Salt Lake City, USA), with net efficiency calculated from the last minute of each exercise. Specifically, net efficiency was calculated from the ratio between the mechanical power and the energy expenditure (EE) above rest as previously described (Husby et al., 2010).

2.2.3. Isolated quadriceps ATP cost of contraction in vivo

To assess the ATP cost of contraction from the entire pool of muscle fibers, i.e. including both type I and II fibers, subjects performed two modes of isometric knee-extension exercise eliciting a maximal contraction of the quadriceps within the whole body MRI system. While supine, the knee was positioned at a ~45° knee joint angle over a custom-built knee support with the foot attached to a strain gauge (SSM-AJ-250, Interface Inc., Scottsdale, USA). To minimize hip movement and back extension during the contraction, participants were secured to the bed with a non-elastic strap placed over the hips and the thigh. The force signal was converted from analog-to-digital (MP150, Biopac Syst Inc., USA) and collected with a sample frequency of 200 Hz on a personal computer (Acknowledge, Biopac Syst Inc., USA). Utilizing