Skeletal muscle remodeling in response to alpine skiing training in older individuals

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This study investigated whether regular alpine skiing could reverse sarcopenia and muscle weakness in older individuals. Twenty-two older men and women (67 ± 4 years) underwent 12 weeks of recreational skiing, two to three times a week, each session lasting ~3.5 h. An age-matched, inactive group (n = 20, 67 ± 4 years) served as a control (CTRL).

Before and after the training period, knee extensors muscle thickness (T\textsubscript{exp}), pennation angle (θ) and fascicle length (L\textsubscript{f}) of the vastus lateralis muscle were measured by ultrasound. Maximum isokinetic knee extensor torque (MIT) at an angular velocity of 60°/s was measured by dynamometry.

After the training, T\textsubscript{exp} increased by 7.1% (P < 0.001), L\textsubscript{f} by 5.4% (P < 0.02) and θ by 3.4% (P < 0.05). The increase in T\textsubscript{exp} was matched by a significant gain in MIT (13.3%, P < 0.001). No significant changes, except for a decrease in L\textsubscript{f} (2.1%, P = 0.02), were found in the CTRL group. The gain in T\textsubscript{exp} in the training group correlated significantly with an increase in the focal adhesion kinase content, pointing to a primary role of this mechano-sensitive protein in sarcomere remodeling with muscle hypertrophy. Overall, the results show that alpine skiing is an effective intervention for combating sarcopenia and weakness in old age.

Sarcopenia and muscle weakness are the primary causes of the loss of mobility and independence in old age (Narici & Maffulli, 2010). From 20 to 80 years of age, men and women lose about 24–27% of locomotor muscle mass, with an even greater loss of muscle strength and power (Narici & Maffulli, 2010), indicating that skeletal muscle becomes intrinsically weaker with old age. Several factors contribute to this age-related loss of muscle mass (also known as “sarcopenia”), these involve neuropathic processes leading to a loss of motor units, inflammation, involving the release of cytokines (TNF-α, interleukin-1 and -6), hormonal changes (decreased levels of androgens, estrogens, growth hormone and growth factors, increased myostatin levels), nutritional status changes (anorexia of aging, vitamin D deficiency) and reduced physical activity, leading to disuse atrophy (Narici & Maffulli, 2010). Although little can be done to prevent the loss of muscle mass due to neuropathic processes, that due to disuse and to some extent also to inflammation, hormonal and nutritional changes may be mitigated/prevented through physical, pharmacological and nutritional interventions. With respect to pharmacological interventions, the use of non-steroidal selective androgen receptor modulators and anti-myostatin antibodies seem to be particularly promising for combating muscle wasting in sarcopenia and cachexia (Greig et al., 2009). Also, testosterone administration in testosterone-deficient frail elderly males has been found to reduce sarcopenia (Atkinson et al., 2010). As for protein supplementation alone, this seems ineffective in preventing sarcopenia because of anabolic resistance to amino acids in older individuals (Paddon-Jones et al., 2008). Instead, resistance training has been shown to be by far the most effective intervention for preventing muscle loss and weakness in old age and for reducing the risk of type-2 diabetes, cardiovascular disease and osteoporosis (Seguin & Nelson, 2003). A clear example of this is provided by the results of the Better Ageing study, in which 12 months of resistance training in septuagenarian males led to a 12% increase in calf muscle volume and a 20% increase in maximum isometric torque (Morse et al., 2005). The effectiveness of strength training in increasing muscle mass and strength, both in young and in older individuals, is mainly due to the mechanical stimuli that skeletal muscle is subjected to during the concentric and eccentric muscle actions against the training load.
Eccentric loading, in particular, because it induces muscle stretch and provides a greater possibility of overload, has been shown to produce greater gains in muscle size and strength than concentric loading (Hather et al., 1991; Higbie et al., 1996).

Because of the need for overloading skeletal muscle, most strength training programs have been based on the use of commercial exercise machines. However, evidence exists that a recreational activity such as alpine skiing, which involves moderate to high eccentric and concentric loading (Tesch, 1995), provides sufficient mechanical stimuli to induce muscle fiber hypertrophy, particularly of fast fibers and increase muscle strength (Berg et al., 1995). This is because during the muscle-breaking action required to negotiate turns, motor unit recruitment often reaches near maximal levels (Berg & Eiken, 1999; Kroll et al., 2010).

Given that alpine skiing involves about 65% contribution from the anaerobic system in terms of the total energy requirement, it has been suggested that force production and neuromuscular coordination should be the main focus of training (Veicsteinas et al., 1984; Saibene et al., 1985). However, the use of alpine skiing as a form of training to increase muscle mass and strength in old age has never been tested before.

Therefore, the present study aimed to assess the effects of regular alpine skiing on muscle structure and function in a population of older medically stable (Greig et al., 1994) individuals. Furthermore, as muscle hypertrophy is the result of an increase in protein synthesis modulated by the stimulation of costameric mechanosensitive proteins, focal adhesion kinase (FAK) in particular (de Boer et al., 2007; Klossner et al., 2009), this study also investigated the possible role of FAK in skeletal muscle remodeling induced by overload.

Materials and methods
Subjects and skiing training protocol
Details regarding the subjects and the training protocol are presented in the companion paper by Müller et al. (2011a). Briefly, 22 older males and females (67 ± 2 years) were assigned to a guided skiing program and 20 age-matched (67 ± 4 years) volunteers served as controls. Alpine skiing training consisted of 12 weeks of guided skiing, 2–3 times/week, 3.5 h/session. Skiers were assigned into four subgroups of skiing expertise (A–D) according to predetermined skills criteria. However, the training content was monitored using individual GPS data and was matched across subjects for vertical and linear skiing distance. The study was approved by the Ethics Committee of the University of Salzburg and written informed consent to the investigation was obtained from all the participants.

Maximum isokinetic torque
Maximum isokinetic torque of the knee extensor muscles was measured in the dominant (right) limb in the seated position using an isokinetic dynamometer (IsoMed 2000, D&R GmbH, Hemau, Germany). Starting from a knee angle of 90° (0° corresponding to full extension), the subjects performed three consecutive maximum isokinetic contractions at the angular velocity of 60°/s; the highest torque generated in the three contractions was retained for data analysis.

Muscle architecture
Vastus lateralis (VL) muscle architecture was measured in vivo at rest. Measurements were performed in the anatomical position with the subject lying supine on a gurney, using a digital ultrasonographer (MyLab25, ESAOTE, Genoa, Italy), fitted with a 7–10 MHz linear-array probe. Scans were acquired at 60% of muscle length (previously estimated with ultrasound), mid-belly, in the mid-sagittal plane (Fig. 1). To ensure that all subsequent scanning measurements were taken in the same anatomical location, the ultrasound probe was positioned in the mid-sagittal plane, orthogonal to the mediolateral axis, and its positioning was marked on acetate paper using moles and small angiograms (which may be assumed to maintain a fixed position) as reference points. In each ultrasound image obtained at rest, the fascicular path was determined as the intervals between echos coming from the perimysial tissue surrounding the fascicle. Fascicle length (L), penetration angle (θ, °) and muscle thickness were measured using the public domain NIH software “ImageJ” (version 1.42q, National Institute of Health, USA, http://rsb.info.nih.gov/ij). Where the fascicle extended beyond the image, the non-visible part was estimated by extrapolating the fascicle and aponeurosis in a proximal direction (Reeves et al., 2004). Penetration angle was calculated as the angle between the fascicle and the deep aponeurosis of the muscle. In each scan, the average L and 8 of three fascicles was used for analysis. Muscle thickness (Tm) was defined as the distance between the deep and the superficial aponeuroses, and the average of three measurements along the aponeurosis was used as indicative of Tm.

A biopsy was collected at baseline and after training using a Weil–Blakely conchotherme (Gebrueder Zenf Medizintechnik, Tuttingen, Germany) from VL muscle of the left leg, snap frozen during rapid shaking in liquid nitrogen and stored at –80°C for the analysis of expression of adhesion proteins (for details, see Fläck et al., 2011). Out of the adhesion protein analyzed, FAK was chosen to relate its changes to those in muscle thickness, as, in avian muscle, the FAK content has been shown to increase with overloading in correspondence with gains in muscle mass (Flick et al., 1999).

Fig. 1. Sagittal ultrasound image of the vastus lateralis muscle: Fascicle length (L) is measured as the length of the fascicle between the deep and the superficial aponeuroses (see “Material and methods”), penetration angle (θ) is measured as the angle of insertion of the fascicle into the deep aponeurosis and muscle thickness (Tm) is measured as the distance between the deep and superficial aponeuroses.
Details of the analysis of FAK content, and of other costameric proteins, are described in the manuscript of Flueck et al. (2011).

Statistics

Data were analyzed using two-way analysis of variances, with the following pairs of independent factors as appropriate: time (pre/post) × training (skiing/control), time (pre/post) × skiing level (A–D) and sex × training (skiing/control). In cases of significant interaction effects, differences were further analyzed at specific time points using a Bonferroni post hoc test. The relationships between variables of interest were tested using a Pearson’s product–moment correlation. The level of significance was set at \( P < 0.05 \). All data are presented as means ± SD and, for graphical purposes, as means ± SEM in bar charts.

Results

Muscle strength and architecture

After the 12-week alpine skiing program, significant changes in muscle architecture and isokinetic muscle torque were found in the training group (TG), while no significant changes, except for a decrease in the control group (CTRL) (Table 1). No significant differences were found between the two sexes before, except for \( T_m \), which was 15% smaller \( (P < 0.01) \) in the older women compared with the older men. No significant differences were found between the two sexes in terms of changes in muscle architecture and maximum isokinetic knee extensor torque (MIT) after training.

In the TG, \( T_m \) increased by 7.1% \( (P < 0.001) \), \( L_f \) by 5.4% \( (P < 0.02) \) and \( \theta \) by 3.4% \( (P < 0.05) \) [Fig. 2(a–c)]. No changes in muscle architecture were observed in the CTRL after the 12-month observation period, except for a 2.1% \( (P < 0.02) \) decrease in \( \theta \). These structural changes were accompanied by an increase in MIT of 13.3% \( (P < 0.001) \) in the TG group after training (Table 1), while no changes were found in the CTRL group (Table 1).

<table>
<thead>
<tr>
<th>Training group</th>
<th>Control group</th>
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<tbody>
<tr>
<td>( L_f ) (mm)</td>
<td>( \theta ) (deg.)</td>
</tr>
<tr>
<td>Before</td>
<td>71.7 ± 1.7</td>
</tr>
<tr>
<td>After</td>
<td>75.6 ± 1.6</td>
</tr>
<tr>
<td>Difference (%)</td>
<td>5.4</td>
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<tr>
<td>( P )-value</td>
<td>&lt;0.02</td>
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Skeletal muscle remodeling with overload

Muscle torque was found to correlate with muscle thickness both before \( (r = 0.50, P < 0.02) \) and after the skiing training period \( (r = 0.68, P < 0.001) \) (Fig. 3).

Muscle architecture and FAK content

After training, the FAK content was found to increase by 1.7-fold (see Flueck et al., 2011); the increase in muscle thickness was found to correlate with the increase in the FAK content \( (r = 0.59, P < 0.01) \) (Fig. 4).

Discussion

This study, an integral part of the SASES, is the first to show the efficacy of ski training as an intervention to combat the loss of muscle mass and strength in old age. The results obtained clearly demonstrate an increase in muscle size and strength of the main locomotor muscles (quadriceps) as a result of 12-week alpine skiing. The results also show, for the first time in humans, that skeletal muscle remodeling in response to resistive loading is closely associated with an increase in FAK. This mechano-sensitive protein tyrosine kinase is associated with the lamin receptor proteins integrin and dystrophin that connect the Z-disk of muscle fibers via the cytoskeleton and the extracellular matrix to adjacent muscle bers (Fluck et al., 1999; Durieux et al., 2007). FAK is essential for sarcomerogenesis (Quach & Rando, 2006) and has been shown in culture to be involved in the transduction of mechanical forces into the intracellular signaling that regulate gene and protein expression (Ingber, 2006). Phosphotransfer activation of FAK and of its downstream signaling molecules occurs within minutes of mechanical perturbation of integrins (Ingber, 2006) and has been found to be localized to the myotendinous junction and to the focal adhesion complexes of the sarcolemma. In rat muscle, a fourfold increase in FAK tyrosine phosphorylation occurs within 1 day of functional overload and, as FAK modulates the activity of the regulator of protein synthesis 70kDa ribosomal S6 kinase (p70S6K), this results in an elevation in protein synthesis.
Fig. 2. (a) Fascicle length of the training and control groups before and after training (means ± SEM), **P<0.02. (b) Pennation angle of the training and control groups before and after training (means ± SEM), *P<0.05. (c) Muscle thickness of the training and control groups before and after training (means ± SEM), ***P<0.001.

Fig. 3. Maximum isometric torque vs muscle thickness before (empty circles, dotted line) and after training (filled circles, full line).

Fig. 4. Change in focal adhesion kinase content vs change in muscle thickness, expressed as the ratio of the post/pre-value.
Skeletal muscle remodeling with overload

neurosis (Gans & Bock, 1965). Instead, an increase in fascicle length suggests the addition of sarcomeres in series. An increase in muscle thickness suggests an increase in both types of sarcomeres. We and others have reported previously an increase in all three parameters as a result of strength training (Kawakami et al., 1993; Aagaard et al., 2001; Reeves et al., 2004; Seynnes et al., 2007). However, an unprecedented finding of this study is that the increase in muscle thickness was positively correlated with the increase in the FAK content. This observation provides evidence of a major role of quantitative changes in the FAK content in sarcomere remodeling in response to muscle overloading. This pivotal role of FAK is also confirmed by our earlier observations of a decrease in the FAK content and activity with skeletal muscle atrophy, in the presence of architectural changes, induced by unilateral lower limb unloading in humans (de Boer et al., 2007).

While fascicle length and muscle thickness did not change in the CTRL after the 12-week observation period, pennation angle did show a decrease (2.1%). Although frank atrophy normally entails a decrease in both pennation angle and in thickness (or size) (Narici et al., 2003), a decrease in the pennation angle may be interpreted as a sign of atrophy, which, over a period longer than 12 weeks, would become more relevant.

In conclusion, this study has shown that alpine skiing is an effective intervention for increasing muscle mass and strength in older individuals. The mechanical loading provided by alpine skiing was sufficient to reverse the changes in muscle architecture typically associated with sarcopenia. The observed remodeling of muscle architecture was closely related to an increase in FAK, pointing to a primary role of this costameric protein in regulating muscle mass.

Perspectives

Alpine skiing provides sufficient mechanical loading to the lower limb muscles to combat sarcopenia and weakness. The results obtained with this type of intervention seem to be of the same order of magnitude as those obtained by conventional strength training protocols. Considering that alpine skiing also promotes social inclusion and interaction of elderly individuals, it does seem a very recommendable type of intervention for preventing musculoskeletal frailty in old age in countries with easy access to mountainous zones.

Key words: costamere, focal adhesion kinase, human, muscle architecture, muscle hypertrophy, skeletal muscle, training.
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References


