

Intramyocellular lipids mobilization in elderly: relationships with physical activity, maximal aerobic capacity and insulin sensitivity

D. M. Rouffet^{1,2}, R. Fissoune¹, C. Hautier³, D. Sappey-Marinier⁴, M. Laville⁵, D. Ibarolla⁴, M. Sothier⁵, M-F. Monnet⁶, M. Ovize⁶, M. Bonnefoy⁷, C. Boesch⁸, and E. Canet-Soulas¹

¹CREATIS LRMN, UMR CNRS #5220, INSERM U630, University of Lyon - Université Lyon 1, Lyon, Rhône-Alpes, France, ²Centre for Ageing, Rehabilitation Exercise & Sport, Victoria University, Melbourne, Victoria, Australia, ³CRIS EA647, University of Lyon - Université Lyon 1, France, ⁴CERMEP, University of Lyon - Université Lyon 1, France, ⁵CRNH, University of Lyon - Université Lyon 1, France, ⁶Unité de Rééducation Cardiaque, University of Lyon - Université Lyon 1, France, ⁷Service de Médecine Gériatrique, University of Lyon - Université Lyon 1, France, ⁸Dept.Clinical Research, University Bern, Switzerland

Introduction

In France, prevalence of diabetes was estimated to have increased by 5.7% per year between 2000 and 2005. Epidemiological studies have shown that impairments of the insulin-stimulated glucose metabolism in skeletal muscle are at the origin of the transition from a healthy state to type 2 diabetes' apparition in elderly subjects. It is commonly accepted that insulin sensitivity is altered by the combined effects of ageing process and reduced physical exercise. Repeating physical activities throughout entire life may positively affect insulin sensitivity by improving intracellular fat homeostasis in skeletal muscle. ¹H nuclear magnetic resonance spectroscopy (¹H-MRS) technique offers the possibility to study lipid metabolism by performing repeated and non invasive measurements of intramyocellular lipids (IMCL) content [1,2]. One can assume that regular exercise may positively affect lipid turnover and insulin sensitivity via an improvement of mitochondrial enzyme activity [3]. The first objective of this study was to analyze if inter-individual variations in physical activity and maximal aerobic capacities influence IMCL turnover. The second aim was to determine if variations in insulin sensitivity can be associated with inter-individual differences in IMCL turnover in physically active older adults.

Methods

Twelve active and healthy male adults (age > 65 years) were recruited through print advertisement in the Lyon area. First, all participants undertook a medical screening consisting in the following measurements. Insulin sensitivity was evaluated using homeostasis model assessment for insulin resistance (HOMA-IR). Body composition was determined by bioelectrical impedance analysis (STAR 50 - SPENGLER). Total energy expenditure due to physical activity (EE) was estimated using the Paffenbarger Physical Activity Questionnaire. Maximal oxygen uptake (VO_2 max) was measured during an incremental walking treadmill test specifically designed for older adults. Then, all participants performed an endurance exercise that consisted in walking for two hours on a treadmill at 10% surface incline at a standardized intensity (50-60 % VO_2 max). Dietary intake was controlled over the 72 h that preceded the completion of the endurance exercise. Participants undertook ¹H-MRS scans of the right *tibialis anterior* muscle immediately before and after the endurance exercise. Measurements were performed on a whole body 1.5 T Siemens Magnetom Sonata (Siemens medical solutions, Erlangen, Germany) with a 10-cm diameter surface coil (RAPID Biomedical GmbH, Würzburg, Germany) wrapped around the right lower leg. Image-guided, localized, single-voxel ¹H-MRS was performed in the right *tibialis anterior* muscle. T1-weighted coronal (11 slices), sagittal (13 slices) and axial (23 slices) images were acquired with a SE sequence (TR/TE = 471/13 ms, 4-mm thickness, 1 average). Images were carefully inspected to avoid any visible vascular structures and adipose tissue. A PRESS sequence with CHESS water suppression (TR/TE = 3000 ms/30 ms, 128 acquisitions, acquisition time 6min36s, voxel volume 11x12x18 mm) was employed to collect proton spectroscopy signals. Absolute concentrations of IMCL were calculated using the jMRUI software version 3.0 by quantifying signals in the time domain [1,4].

Results

Between-subjects differences in HOMA-IR values (0.95 to 4.48; CV= 45%), body fat (14.4 to 19.8%; CV=19%), total energy expenditure due to physical activity (1785 to 6375 kcal/week; CV= 50%) and VO_2 max (27.3 to 44.3 mL/min/kg; CV= 16%) were observed among the participants of this study. IMCL content measured at the end of the diet period equaled 3.12 ± 1.46 mmol.kg⁻¹ wet weight, with between-subjects differences (from 0.58 to 6.03 mmol/wet weight; CV= 52%). IMCL contents measured during the second ¹H-MRS scan after exercise were lower than those measured before the two-hours endurance exercise completion (Paired T test, p<0.05). IMCL content measured at the end of the endurance exercise equaled 2.47 ± 1.23 mmol.kg⁻¹ wet weight, also with between subjects differences (from 0.32 to 4.13 mmol/wet weight; CV= 53%).

Multiple linear regression models with VO_2 max, EE and age failed to predict the variable IMCL mobilization during endurance exercise (p=0.36). In stepwise regression analysis, % body fat explained 84% of the between-subjects variations in the HOMA-IR values, whereas IMCL content and mobilization were not included as predictors in the model.

Conclusion

The feasibility of measuring IMCL content in *tibialis anterior* muscle of nondiabetic elderly subjects using a standard clinical MR system was demonstrated. In the cohort of healthy elderly subjects investigated in this study, inter-individual variations in spontaneous physical activity and maximal aerobic capacities did not explain differences in IMCL mobilization during an endurance exercise. Our results suggest that neither IMCL content nor IMCL turnover in skeletal muscles of physically active elderly subjects are the major determinants of insulin sensitivity.

References

1. Boesch C et al. NMR Biomed 2006; 19: 968-988.
2. Petersen KF et al. Science 2003; 300: 1140-1142.
3. Short KR et al. Diabetes 2003; 52: 1888-1896.
4. <http://www.mrui.uab.es/mrui/>

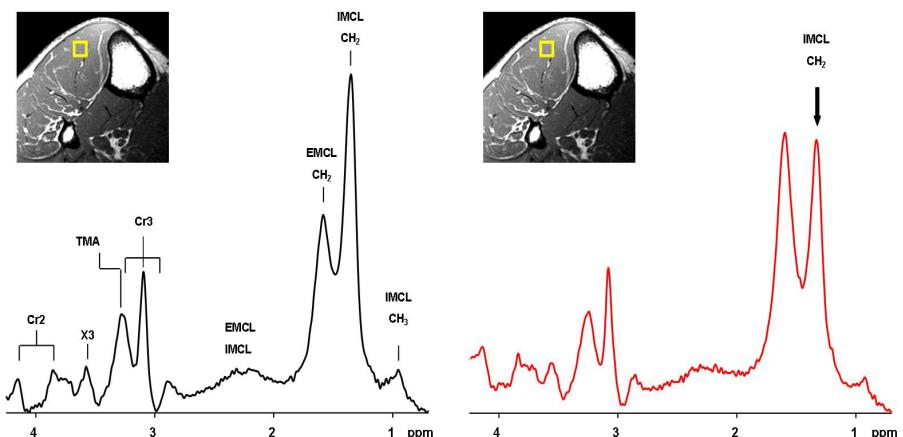


Figure 1: ¹H-MR spectra of the right *tibialis anterior* muscle before (left) and after (right) a 2-hours walking exercise at 55% VO_2 max.