

## Cardiac lipid content as determined by Magnetic Resonance Spectroscopy increases after exercise protocol in the fasted state

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**Background:** Excessive lipid accumulation in cardiac tissue might hamper cardiac function, predisposing to cardiomyopathy and heart failure (1). Elevated levels of plasma (free) fatty acids (FA) might be a risk factor for cardiac lipid accumulation. For skeletal muscle, we have shown that elevated levels of FA lead to increased levels of intramyocellular lipids (IMCL), however it is unknown whether the heart is responding similarly (3). A physiological way to increase circulating FA levels is by performing exercise in the fasted state, whereas glucose ingestion during exercise can blunt this exercise-induced increase in plasma FA.

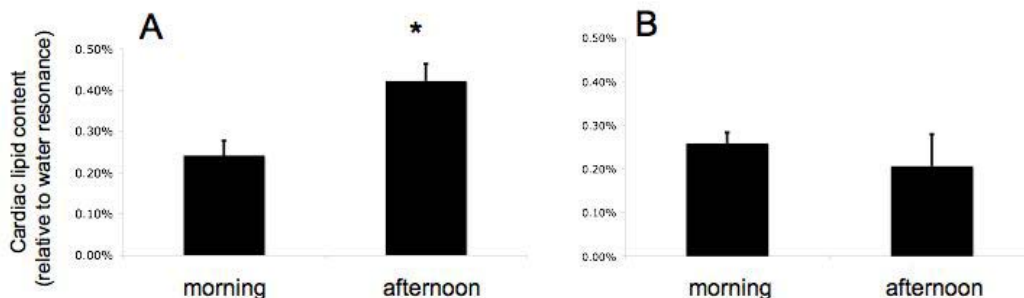
**Aim:** To investigate whether elevating plasma FA (by a validated protocol of cycling and resting in the fasted state (2)) results in an increased cardiac lipid content.

**Methods:** Seven male subjects (age:  $26 \pm 1.3$  y, BMI:  $24.0 \pm 1.0$  kg/m<sup>2</sup>) underwent a <sup>1</sup>H-MRS scan on a whole body MRI-scanner (Intera, 1.5T, Philips Healthcare) in the morning in the fasted state to determine cardiac lipid content. Subsequently, subjects performed cycling exercise for 2 hours at 50% of maximal performance and rested for three hours, after which cardiac lipid content was measured again. All subjects underwent this procedure twice (in a randomized manner), once while they stayed fasted, once while ingesting glucose (1 x 1.4g/kg, 8 x 0.35 g/kg). This protocol has been shown to produce very pronounced differences in plasma FA levels (3). Indirect calorimetry was used to determine whole body fat- and carbohydrate oxidation. Blood plasma samples were collected repeatedly for later analysis. For cardiac <sup>1</sup>H-MRS a PRESS sequence was used with the VOI placed in the septum of the heart (VOI = 10x20x30 mm, TR = 4s, TE = 26ms). Signal acquisition was ECG-triggered to end-systole and respiratory-gated with a pencil beam navigator placed on the diaphragm. High efficiency of the navigator-gated acquisition was achieved by instructing subjects to breath in the 4s-rhythm of the measurement. Chemical shift selective (CHESS) water suppression was performed. A spectrum of the lipid metabolites was acquired using a series of 64 spectra. To acquire a reference spectrum of the unsuppressed water peak in the same volume of interest, the acquisition was repeated while the CHESS pulse was defocused by 10000 Hz acquiring a series of 32 spectra. The acquisition of the lipid metabolites was then repeated, spectra were separately phase corrected and averaged (resulting in a lipid spectrum with 128 averages and a reference spectrum with 32 averages). The residual water peak was removed with a HLSVD filter and spectra were fitted in the jMRUI software ([www.mrui.uab.es](http://www.mrui.uab.es)). The ratio of signal intensity of the CH<sub>2</sub> peak of cardiac lipids and the water (in percentage) is given.

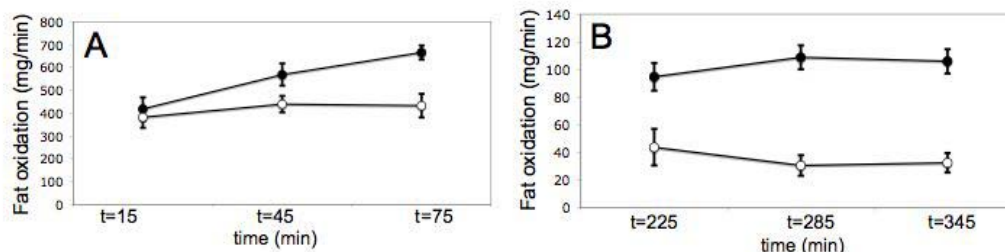
**Results:** Cardiac lipid content was elevated at the end of the fasted test day (from  $0.24 \pm 0.04$  to  $0.42 \pm 0.04$  %,  $p < 0.01$ , fig 1A), while it did not change when glucose supplementation was given to keep FA concentrations low (from  $0.26 \pm 0.03$  % to  $0.21 \pm 0.07$  %,  $p = 0.5$ , fig 1B). Fat oxidation was significantly higher in the fasted condition than in the glucose supplemented condition (fig 2A, 2B). Plasma concentrations of FA and glucose are presently being analyzed.

**Discussion:** The strongly increased cardiac lipid content in the fasted condition suggests that FA plasma concentrations play an important role in determining cardiac lipid content. Cardiac lipid accumulation occurred even in the context of very high rates of (whole-body) fat oxidation, suggesting that FA supply to the heart is much higher than oxidative needs.

**Figure1:** Cardiac lipid content increased (A) after exercise/rest protocol in the fasted state (high levels of FA) and did not change when FA-response is blunted by glucose supplementation (B)



**Figure2:** Whole body fat oxidation (by indirect calorimetry) during exercise (A) and recovery (B). Filled icons: fasted condition (high FA), open icons: glucose supplementation (low FA)



- References:**
1. McGavock JM et al., 2006, Ann Intern Med 144:517-524
  2. Schrauwen P et al., 2002, Am J Physiol Endocrinol Metab 282:E11-17
  3. Schrauwen-Hinderling VB et al., 2003, J Appl Physiol 95:2328-2332