# Muscle-type specific Intramyocellular Lipid Metabolism during Starvation in Wistar Rats

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**Introduction:** Intramyocellular lipids (IMCL) have been identified (i) as a major source of energy located within the muscle cell, which are elevated in endurance trained athletes [1, 2], and (ii) are correlated with insulin resistance [3]. Very little is known about the physiological dynamics of IMCL in different muscle fiber types. We therefore investigated the dynamics of IMCL in different muscles of normal Wistar rats *in vivo* during starvation and refeeding by $^1$H-spectroscopy. In parallel groups (n=8 per day, satellite groups) muscle malonyl-CoA as well as metabolic plasma parameters were studied.

**Materials & Methods:**

*Experimental protocols*. The study protocol ran for 5 days and consisted of the following study points: normal fed, 12h, 24h, 48h, 72h starvation, and refed. For each study point, body weight, metabolic serum and muscle malonyl-CoA as well as IMCL contents of the M. soleus (oxidative, SOL), M. tibialis ant. (glycolytic, TIB), and M. extensor digitorum longus (intermediary, EDL) were measured.

*NMR-groups:* 8 rats were used for normal fed, 24h, 48h, 72h starvation, and refed conditions to obtain intraindividually IMCL and tCr values by *in vivo* 1H-spectroscopy (7T Bruker Biospec, PRESS, TE/TR=17/1000ms) under isoflurane anesthesia. IMCL and tCr were expressed as ratio as described previously [4, 5]. Metabolic serum parameters were obtained daily. Because rats are night-active and take up food predominantly during the dark-phase, 8 additional rats were kept on a reverse light-dark cycle for one week prior to the NMR-study and were used for the measurements of their IMCL levels at the end of the light-phase after a 12h starvation period.

*Satellite-groups:* In parallel groups (n=8 for each point of the study protocol), blood samples for determination of metabolic serum parameters as well as defined tissue samples were collected during terminal isoflurane anesthesia. SOL, TIB, and EDL of both hind legs were isolated and immediately frozen in liquid nitrogen for later determination of malonyl-CoA (SOL, TIB, EDL).

**Results:** Metabolic plasma parameters were similar in the NMR- and satellite groups. During the transition from the fed to the fasted state there was a fall in blood glucose, insulin and triglycerides, and an elevation of FFA and ketone bodies, which is consistent with the metabolism during starvation. Refeeding after 3 days of starvation caused an opposite change of all parameters within 24h. Malonyl-CoA was relatively constant in SOL and increased slightly after refeeding, while in TIB its values decreased time-dependently during starvation. Despite significant elevations of FFA during starvation, IMCL in SOL remained relatively constant. However, in the TIB and EDL IMCL increased significantly by 170% and 450% after 72 h of starvation, respectively. Refeeding caused a fast drop of elevated IMCL in TIB and EDL.

| | fed | starvation | | | | refed |
|---|---|---|---|---|---|---|
| | | 12 h | 24 h | 48 h | 72 h | |
| Body weight (g) | 415 ± 22 | 384 ± 11 | 388 ± 21 | 375 ± 24 | 363 ± 22 | 379 ± 27 |
| Glucose (mmol/l) | 5.54 ± 0.37 | 4.21 ± 0.33 | 4.11 ± 0.48 | 4.11 ± 0.43 | 4.24 ± 0.48 | 6.55 ± 0.52 |
| Insulin (ng/ml) | 1.72 ± 0.69 | 1.38 ± 0.42 | 0.80 ± 0.40 | 0.79 ± 0.53 | 0.63 ± 0.23 | 1.41 ± 0.26 |
| FFA (mmol/l) | 0.18 ± 0.04 | 0.52 ± 0.13 | 0.47 ± 0.09 | 0.43 ± 0.09 | 0.42 ± 0.11 | 0.07 ± 0.02 |
| Triglyceride (mmol/l) | 1.33 ± 0.37 | 0.84 ± 0.27 | 0.43 ± 0.14 | 0.39 ± 0.06 | 0.41 ± 0.07 | 1.21 ± 0.12 |
| Ketone Bodies (µmol/l) | 261 ± 61 | 803 ± 204 | 1263 ± 408 | 1704 ± 364 | 1697 ± 516 | 139 ± 38 |

**Conclusion:** Our study resulted in several unexpected findings: (i) muscles with different fiber types coped with starvation differently, (ii) increased lipolysis in adipocytes during starvation appeared in parallel with increased FFA-reesterification in glycolytic (TIB) and intermediary (EDL) muscles but not in oxidative muscle (SOL), (iii) IMCL levels changed rapidly in TIB and EDL within hours. We conclude that there are muscle-type specific differences in lipid metabolism, and there is an increased reesterification of FFA in non-oxidative muscles in parallel to increased lipolysis in adipose tissue.

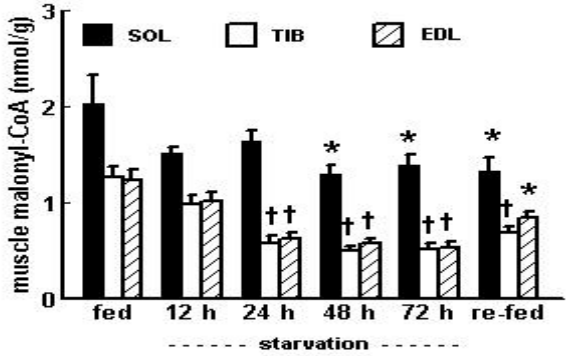


FIG. 1: Malonyl CoA contents of al three investigated muscles during fed, fasted and refed conditions. All values are from separate groups (satellite groups); the 12h values were from groups on a reverse light-dark cycle. Values are means +/- SE, n=8. *p<0.05 , †<0.001 vs. fed condition.

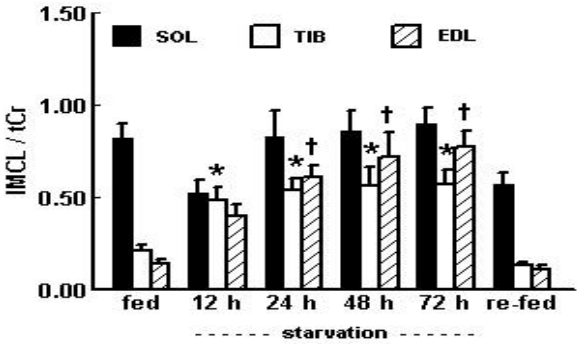


FIG. 2: IMCL contents of all three investigated muscles during fed, fasted and refed conditions. All values are from one group (NMR-group) except the 12h values; they were from a separate NMR-group on a reverse light-dark cycle. Values are means +/- SE, n=8. *p<0.05 , †<0.001 vs. fed condition.

References:
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3. Krssak M et al., Diabetologia 1999; 42(1).
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5. Neumann-Haefelin C et al., Magn Reson Med 2003; 50.