Non-invasive Assessment of Fatty Acid Metabolism via PET/MRI

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Objective

Nutrient metabolism and its disorders in the liver are implicated in the pathogenesis of numerous diseases. Within the evolution of technology, medical imaging began to play an integral role in the assessment of metabolic disorders. The current development of magnet resonance imaging (MRI) and positron emission tomography (PET) techniques allows quantifying the metabolic rate under different conditions over time and to reveal crucial metabolic alterations. Further, this knowledge can be used to characterise models of metabolic associated fatty liver disease [1] and type 2 diabetes mellitus [2].

Methods

Male Sprague Dawley rats on standard or after 6-10 weeks on a high-fat diet were scanned with the long-chain fatty acid analog [^{18}F]FTHA that is taken up by tissues to enter mitochondria or be incorporated into complex lipids [3] using BioSpec 94/30 USR MRT with µPET insert after free access to food (SD: n=4, HFD: n=6) and after overnight (16-20h) fasting (SD: n=6, HFD: n=7). 60 min dynamic PET scans were recorded. Coronal T1-w FLASH MR images were simultaneously recorded with PET to verify anatomy (Fig. 1). For phenotyping, the fat content in the liver was assessed via localized MR spectroscopy (short TE STEAM). After delineating liver, standardized uptake values (SUVs) calculations were performed in PMOD 3.8. Significant differences were evaluated via the Student's T-test.

Results

Despite no significant difference in body mass (496.4±57g (SD) vs 544.7±55g (HFD)) and liver volume (11.51±0.64 cm^3 (SD) vs 11.19±1.00 cm^3(HFD)), MR liver spectroscopy confirmed (p=0.0001) the phenotypes by 2.9±1.2% (SD) vs 11.2±3.3% (HFD) fat in liver (Fig. 2). Mean SUV_{aver} normalized to body weight showed a near significant difference (p=0.07) between SD and HFD groups (7.066±1.08 g/ml vs 8.117±0.52 g/ml) with free access to food but no difference under fasting conditions (9.206±0.98 g/ml (SD) vs 9.644±0.79 g/ml (HFD)) was observed. However, the elimination constant (represented as slope) was significantly (p=0.0086) slower in the HFD group under non-fasting conditions compared to the SD group. Overnight fasting increased the elimination constant in the HFD group and no significant difference between both groups could be observed anymore (Fig. 3).

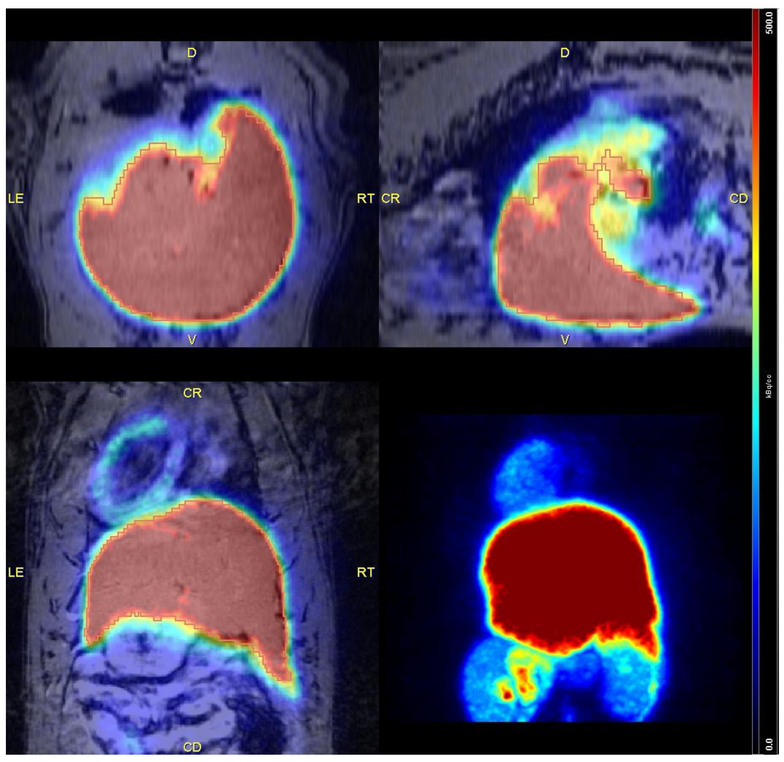

Figure 1. *Multimodal imaging of liver in rat by [^{18}F]FTHA PET imaging and fast low angle shot (FLASH) MRI-sequence. The PET scans were acquired on a Bruker µPET insert, the abdominal MR images were acquired simultaneously with PET on a 9,4 T BioSpec 94/30 small animal MR (Bruker Biospin MRI GmbH, Germany).*

Discussion and Conclusion

These findings clearly indicate alterations of fatty acid metabolism under HFD conditions. The slower elimination constant of [^{18}F]FTHA in the HFD group might be due to an increased lipogenesis and thereby an augmented storage of fatty acids into triglycerides in the liver [4]. Interestingly, overnight fasting regressed these metabolic alterations. Future assessment of [^{18}F]FTHA concentrations in lipoproteins should elucidate more the underlying mechanisms activated high-fat diet.

Moreover, the computer kinetic modelling and/or multiple-time graphical analysis of [^{18}F]FTHA liver phosphorylation might complement the observed effect or uncover differences in free fatty acids metabolism under different conditions.

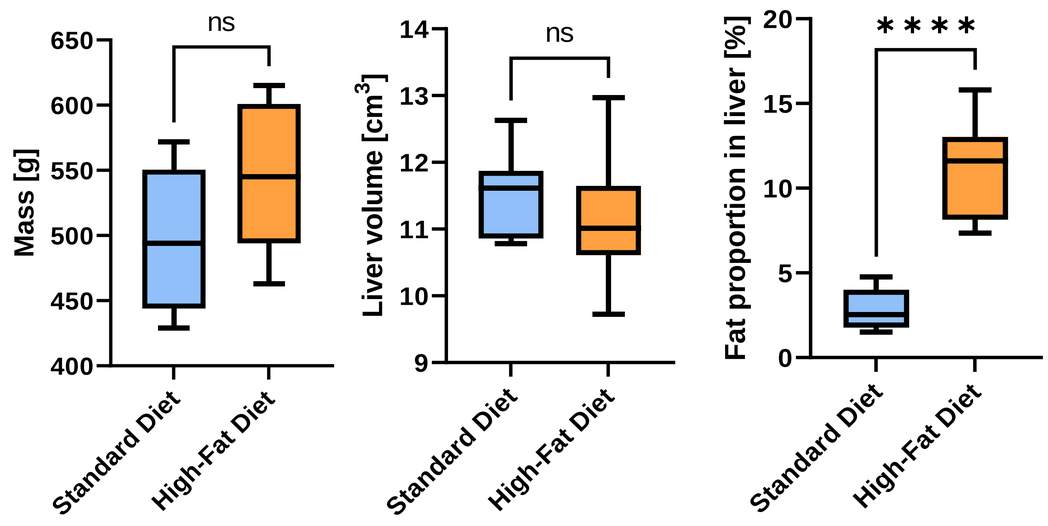

Figure 2: *Column boxplots for comparison of animal mass before imaging, liver volume and the fat percentage in the liver.*

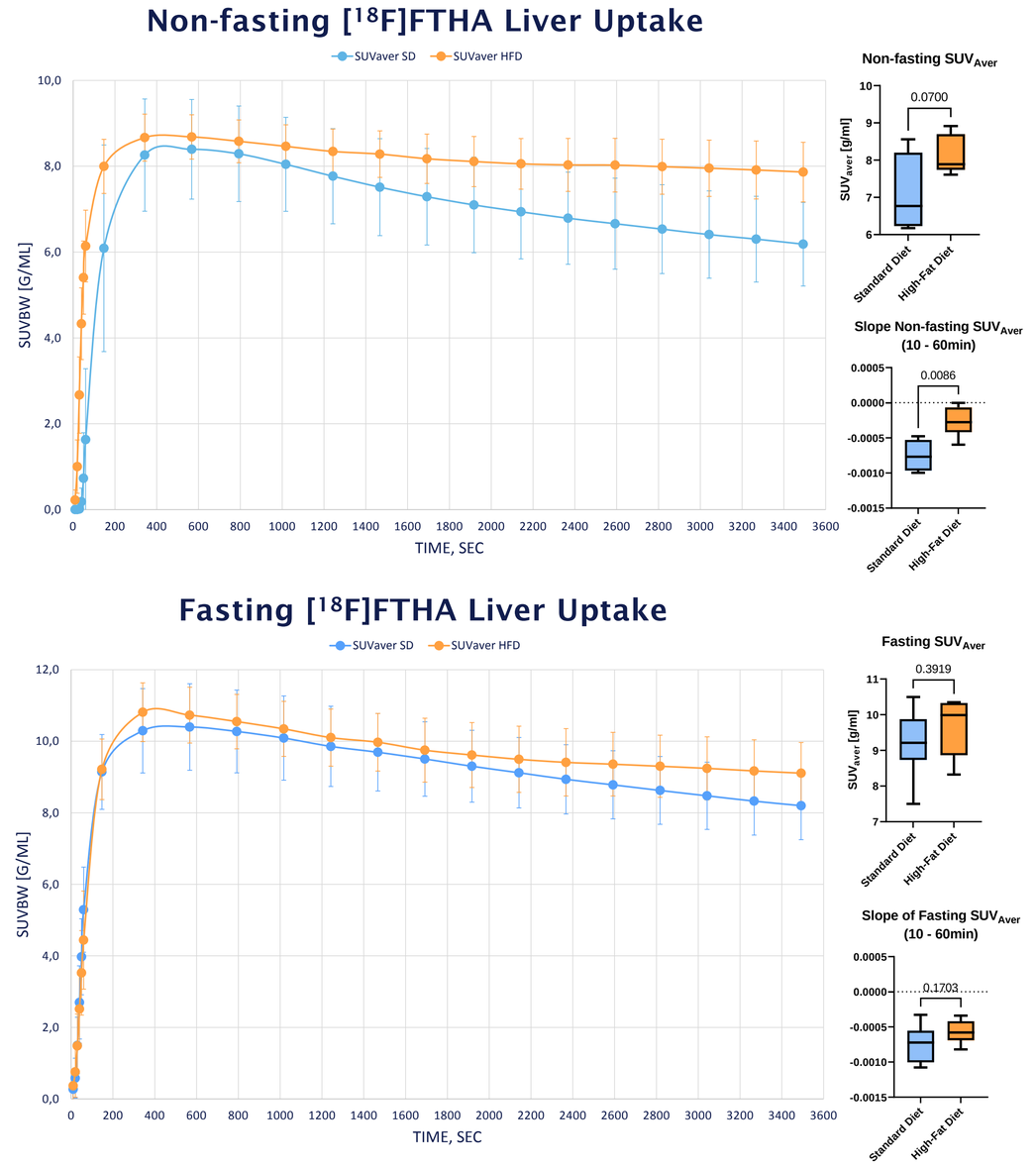

Figure 3: *Time activity curves of SUV_{aver} of [^{18}F]FTHA PET measurements with free food access and overnight fasting and corresponding column boxplot of 1h mean liver uptake.*

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References

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