PET CMR$_\text{glic}$ mapping and $^1$H MRS show altered glucose uptake and neurometabolic profiles in a rat model of type C hepatic encephalopathy

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INTRODUCTION

- Type C hepatic encephalopathy (HE): severe neuropsychiatric decline following chronic liver disease
- Poor ammonia detoxification by the liver $\rightarrow$ toxin accumulation in the brain and a cascade of metabolic alterations$^{1-4}$

AIMS

A - Investigate brain energy metabolism in a rat model of type C HE using PET and MR spectroscopy (MRS)
B - Implement quantitative glucose cerebral metabolic rate (CMR$_\text{glic}$) map with an image-derived input function for minimal invasiveness and register the PET image to an atlas for ROI-based analysis

METHODS

- Bile duct-ligated (BDL) male Wistar rats, model of type C HE
- $^1$H MRS: 9.4 T Varian scanner, SPECIAL$^8$ sequence (TE=2.8ms), 2 brain regions (voxel sizes – cerebellum: 2.5$^3$ mm$,^3$, hippocampus: 2.8x2x2 mm$,^3$), 2 time points: week 0 as control (n$\in$3,4) and 6 post-surgery (n$\in$4,9)
- $^{18}$F-FDG PET: Avalanche photodiode LabPET 4 scanner (1)-Image derived input function (IDIF): 45min dynamic acquisition on the vena cava$^6$
  (2)-Quantitative 3D brain maps: 15min static acquisition on the brain (nominal resolution: 0.5x0.5x1.18 mm$^3$)
  CMR$_\text{glic}$$^7$ maps with LC 0.71, PET-atlas registration, 1 time point: week 6 post surgery (n$_\text{SHAM}=8$, n$_\text{BDL}=10$)

DISCUSSION

- IDIF (1) performs as well as manual blood samplings and external blood counters, is non-invasive, and allows for longitudinal studies
- 2-fold lower CMR$_\text{glic}$ in BDL rats $\rightarrow$ energy metabolism alterations in BDL rats

CONCLUSIONS

Pathophysiology in a rat model of type C HE: increased brain glutamine and decreased osmolytes in the cerebellum and the hippocampus measured by $^1$H MRS, 2-fold lower glucose cerebral metabolic rate measured by $^{18}$F-FDG PET

Methodology: minimally invasive, quantitative and spatial mapping of CMR$_\text{glic}$ using an image-derived IF and an atlas registration, limitations of the SUV when systemic metabolic effects occur

RESULTS - PET

- IDIF (1) performs as well as manual blood samplings and external blood counters, is non-invasive, and allows for longitudinal studies
- 2-fold lower CMR$_\text{glic}$ in BDL rats $\rightarrow$ energy metabolism alterations in BDL rats

RESULTS - MRS

Issues with the standardized uptake value (SUV):
- The dose does not reflect the tracer availability for the brain when systemic effects occur, but the IF does
- The weight does not inform on Glc/FDG competitive uptake and glycemia is not taken into account

CONCLUSIONS


In BDL rats:
- Increase in Gin (stronger in the cerebellum)
- Decrease in Glu, sum of osmolytes (Ins, Tau, tCr, tCho)
$\rightarrow$ Alterations in diverse brain functions: Gin metabolism and osmoregulation, neurotransmission, energy metabolism