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PET CMR_{glc} 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 → 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_{glc}) map with an image-derived input function for minimal invasiveness and register the PET image to an atlas for ROI-based analysis

METHODS

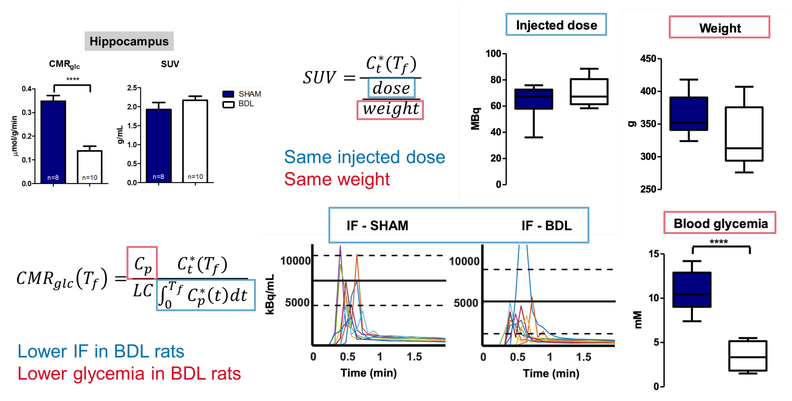
- Bile duct-ligated (BDL) male Wistar rats, model of type C HE
- ^{1}H MRS: 9.4 T Varian scanner, SPECIAL[5] sequence (TE=2.8ms), 2 brain regions (voxel sizes – cerebellum: 2.5^3 mm^3, hippocampus: 2.8x2x2 mm^3), 2 time points: week 0 as control (n∈{3,4}) and 6 post-surgery (n∈{4,9})
- ^{18}F-FDG PET: 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_{glc}[7] maps with LC 0.71[8], PET-atlas registration, 1 time point: week 6 post surgery (n_{SHAM}=8, n_{BDL}=10)

DISCUSSION



Issues with the standardized uptake value (SUV):

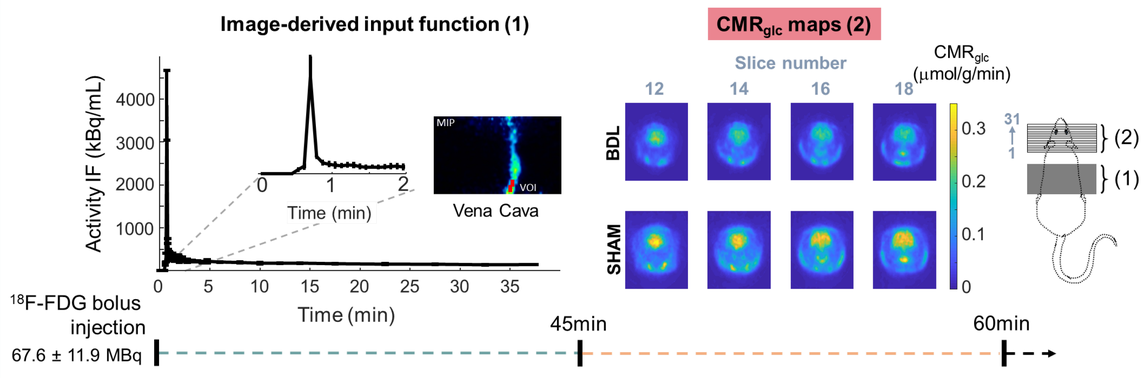
- The dose does not reflect the tracer availability for the brain when systemic effects occur, but the IF does
- The weight does not inform on Glc/FDG competitive uptake and glycemia is not taken into account

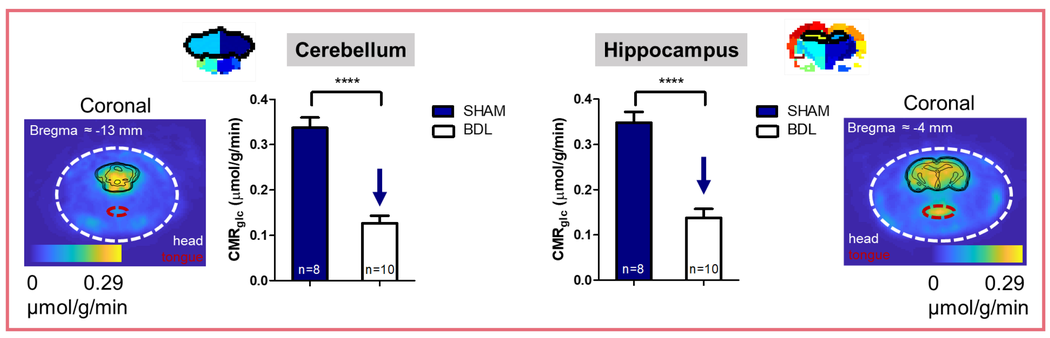
CONCLUSIONS

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_{glc} using an image-derived IF and an atlas registration, limitations of the SUV when systemic metabolic effects occur

RESULTS - PET

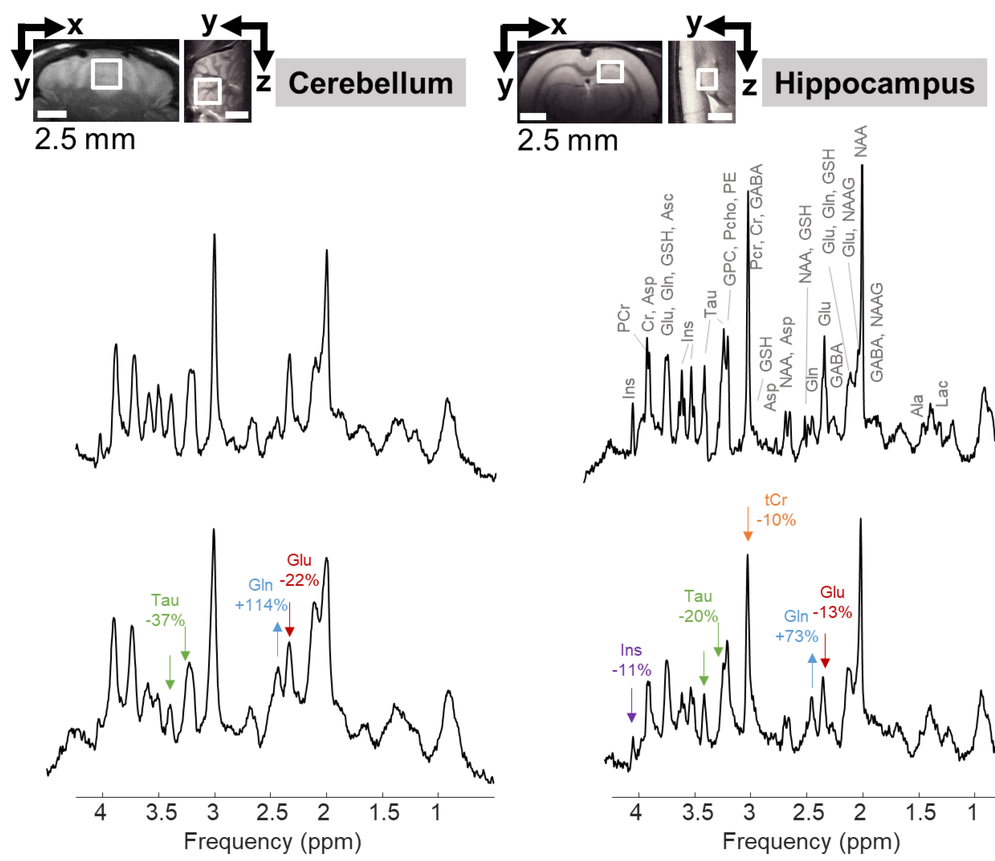




- IDIF (1) performs as well as manual blood samplings and external blood counters, is non-invasive, and allows for longitudinal studies
- 2-fold lower CMR_{glc} in BDL rats

→ energy metabolism alterations in BDL rats

RESULTS - MRS



In BDL rats:

- Increase in Gln (stronger in the cerebellum)
- Decrease in Glu, sum of osmolytes (Ins, Tau, tCr, tCho)

→ Alterations in diverse brain functions: Gln metabolism and osmoregulation, neurotransmission, energy metabolism

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