PhD student position

Location : EPFL AVP-CP CIBM-AIT, Bâtiment CH F.
Dates: 1st of October 2021 to 30 September 2025
Duration: 4 years

Enhanced MR Spectroscopic mapping of brain regional changes in type C hepatic encephalopathy

Dr Cristina Cudalbu from the CIBM MRI EPFL Animal Imaging and Technology Section is looking for a highly motivated PhD candidate in the area of **fast magnetic resonance spectroscopic imaging (^{1}H and ^{31}P MRSI)** (Fig 1**)**: advanced methodological developments (i.e. pulse sequence development and implementation, reconstruction, post-processing, denoising techniques) and applications in type C hepatic encephalopathy.

Background

Type C hepatic encephalopathy (HE) is a complication of chronic liver disease (CLD) and its underlying pathophysiology is incompletely understood. We know that the neurological consequences of elevated ammonium (NH_4^+) on the brain leave devastating long-term sequelae, especially in the developing brain. We showed that preclinical models having acquired CLD during brain development display more profound neurometabolic disturbances, suggesting that the developing brain is exquisitely sensitive to the systemic effects of CLD [1]. What more, different anatomical brain regions seem to be more or less vulnerable to these effects, as suggested by different long-term neurocognitive and neuromotor deficits observed in pediatric patients with CLD and by our preliminary results in preclinical models [2], [3]. Still, very little is known about the neurological consequences of CLD in children and juvenile preclinical models of cholestatic liver disease.

Project description

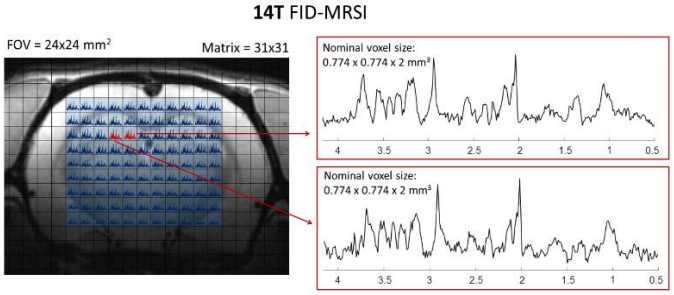

Figure 1: Preliminary results for single slice FID-MRSI @ 14.1T in the healthy rat brain. Acquisition time 13min for metabolites, TR=800ms, flip angle 52°

The current project will build on the work performed by our group in which we combined magnetic resonance spectroscopy (MRS), behavioral assessment and histology to show compelling evidence that longitudinal changes in the adult brain with type C HE are seemingly driven by increases in plasma NH_4^+ and brain glutamine (Gln) in turn leading to decreases in antioxidants (ascorbate/Asc) and creatine (Cr), metabolites previously unknown indicating new opportunities to be targeted by therapy [1], [4]. What more, these changes differ according to age at disease onset [1], while they also differ according to brain region [2], [3]. Importantly, we showed that the neurometabolic changes in type C HE were significantly less pronounced when treating with either a Cr enriched diet or with probiotics [5].

Therefore, *we aim to build on these findings and on MRSI methodological advancements implemented during this project to answer the following questions in vivo in the developing brain: is there differential regional response to the metabolic insults of CLD? If so, is this amenable to treatment? Given the limited therapeutic options for HE in adults and children, might a combinatorial approach be more beneficial to mitigate the neurometabolic changes seen in HE?*

The PhD candidate will first familiarize himself/herself with the MRS/MRSI part of the project. Working directly on the preclinical 14.1T magnet, she/he **will develop a fast, highly spatially resolved MRSI acquisition sequence with full brain coverage.** Furthermore, she/he **will implement advanced reconstruction/denoising methods and will analyze the brain regional differences in a preclinical model of type C HE. Finally, a combinatorial (neuro) protection using Cr, Asc and probiotics will be tested.**

References

[1] V. Rackayova *et al.*, "Longitudinal osmotic and neurometabolic changes in young rats with chronic cholestatic liver disease," *Sci. Rep.*, vol. 10, no. 1, p. 7536, 2020, doi: 10.1038/s41598-020-64416-3.

[2] D. Simicic *et al.*, "In Vivo Longitudinal 1H MRS Study of Hippocampal, Cereberal and Striatal Metabolic Changes in the Adult Brain Using an Animal Model of Chronic Hepatic Encephalopathy," *Am. J. Gastroenterol.*, vol. 114, no. S17, 2019.

[3] K. Pierzchala *et al.*, "Brain regional susceptibility to Oxidative Stress in a rat model of Chronic Hepatic Encephalopathy: in-vivo 1H MRS, ex-vivo ESR spectroscopy and histology findings," *Am. J. Gastroenterol.*, vol. 114, no. S33-36, 2019.

[4] O. Braissant, V. Rackayová, K. Pierzchala, J. Grosse, V. A. McLin, and C. Cudalbu, "Longitudinal neurometabolic changes in the hippocampus of a rat model of chronic hepatic encephalopathy," *J. Hepatol.*, vol. 71, no. 3, pp. 505–515, 2019, doi: 10.1016/j.jhep.2019.05.022.

[5] V. Rackayová *et al.*, "Probiotics improve the neurometabolic profile of rats with chronic cholestatic liver disease," *Sci. Rep.*, vol. 11, no. 1, p. 2269, 2021, doi: 10.1038/s41598-021-81871-8.

Supervisors:

- Dr. Cristina Cudalbu, CIBM MRI EPFL-AIT, https://cibm.ch/people/, cristina.cudalbu@epfl.ch
- Prof. Dimitri Van De Ville, CIBM MRI EPFL AIT, dimitri.vandeville@epfl.ch

Collaborators:

- Prof. Valérie Anne McLin, HUG-UNIGE Département de pédiatrie, gynécologie et obstétrique
- Prof. Olivier Braissant, CHUV-UNIL Département médecine de laboratoire et pathologie

Skills: Master's degree in (biomedical) physics, bioengineering, computer science or a similar degree. Experience in programming (i.e. Matlab) is desirable. Proficient in English, both verbal and in writing.

We offer:

- A dynamic, interdisciplinary, and international team of very motivated people.
- A stimulating working environment based at CIBM in Lausanne, Switzerland.
- Participation in one of the world's leading transitional brain ultra-high field MRS efforts.
- Access to cutting-edge technology and state-of-the-art resources.
- Salary in compliance with Swiss National Science Foundation guidelines.

How to apply: Applications will be considered until the position is filled, so interested candidates are encouraged to apply early. Please send your CV and motivation letter to cristina.cudalbu@epfl.ch

About CIBM

The CIBM Center for Biomedical Imaging was founded in 2004 and is the result of a major research and teaching initiative of the partners in the Science-Vie-Société (SVS) project between the Ecole Polytechnique Fédérale de Lausanne (EPFL), the Université de Lausanne (UNIL), Université de Genève (UNIGE), the Hôpitaux Universitaires de Genève (HUG) and the Centre Hospitalier Universitaire Vaudois (CHUV), with the generous support from the Fondation Leenaards and Fondation Louis-Jeantet.
CIBM brings together highly qualified, diverse, complementary and multidisciplinary groups of people with common interest in biomedical imaging.
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