European Innovation Council

Grenoble Institut Neurosciences

Post-doc proposal - EIC Pathfinder PROMETEUS

Metabolic modeling of the nutrition effect on cerebral blood flow and oxygenation

Context

The brain of a baby born prematurely is highly susceptible to early neonatal injuries that, in turn, increase the risk for neurodevelopmental disability. Provision of adequate nutrients and oxygen is essential for proper brain development and growth. However, current nutritional strategies are unfit to target real-time brain necessities, and are driven by pre-specified (non personalised) nutritional charts, in the absence of contemporary cot-side monitoring of both brain "health" and metabolic supplies.

As a consequence, sudden changes of brain fuel-requirements cannot be promptly addressed by real-time adjustment of glucose and nutrients provision. PROMETEUS will develop a metabolic model of the interaction between the three key brain fuels [glucose, lactate and beta-hydroxybutyrate (BHB)] and their effect on regional cerebral blood flow (CBF), oxygen saturation (StO_2) and metabolism ($CMRO_2$). The model will serve to individualize brain nutrition targeting "brain health" according to the inputs derived from two novel minimally invasive metabolic sensing systems: a wearable cap measuring regional CBF, StO_2 and $CMRO_2$ and a subcutaneous miniaturized metabolic sensor for glucose, lactate and BHB. The system will create a metabolic "womb" to feed the brain of preterm neonates. We hope that PROMETEUS will dramatically reduce the risk for prematurity-associated disability in Europe and worldwide, with a consequent incalculable ethical, social and economic impact.

Roadmap

The goal is to develop the metabolic model of the effect of nutrition on brain StO_2, $CMRO_2$, CBF and metabolism, using a preclinical approach together with advanced MRI and blood readouts. The project includes the following items:

- **(i)** Measure the effects of different nutritional strategies (high and low fat, high and low protein) during hypoglycemia and hyperglycemia on brain StO_2, CBF and $CMRO_2$, using MRI readouts: Arterial Spin Labeling (ASL)[1] and multiparametric quantitative blood-oxygen level dependent MRI (mqBOLD)[2],
- **(ii)** Measure the effects of the same experimental conditions as above on the blood concentrations of glucose, lactate and BHB production and consumption, using ^{13}C or ^{2}H labeled molecules;
- **(iii)** Propose, in collaboration with the physiologists of the PROMETUS European consortium, a model of the relation between blood concentrations of glucose, lactate and BHB and brain StO_2, CBF and $CMRO_2$.

The successful candidate should have a Ph.D. in neuroimaging, neuroscience, or related field, and a strong interest for brain physiology and brain imaging. Experience in preclinical studies and/or MRI methods will be appreciated. The postdoc will focus on the MRI/MRS data acquisition and processing and on developing the model. He will also receive the help of an engineer recruited for the project to handle the animals.

Contact: send CV, motivation letter, and the contact details of at least two referees to Emmanuel Barbier (emmanuel.barbier@univ-grenoble-alpes.fr) and Florence Fauvelle (florence.fauvelle@univ-grenoble-alpes.fr), team 'Functional Neuroimaging and Brain Perfusion'

Location: Grenoble Institute Neurosciences (GIN), Grenoble, France, https://neurosciences.univ-grenoble-alpes.fr

Start date: First semester, 2023 – Contract duration: 1 year, renewable.

References:

(1) *L. Hirschler, C. S. Debacker, J. Voiron, S. Köhler, J. M. Warnking, E. L. Barbier. Inter-Pulse Phase Corrections for Unbalanced Pseudo-Continuous Arterial Spin Labeling at High Magnetic Field. Magnetic Resonance in Medicine. 79(3):1314-1324, 2018*

(2) *T. Christen, P. Bouzat, N. Pannetier, N. Coquery, A. Moisan, B. Lemasson, S. Thomas, E. Grillon, O. Detante, C. Rémy, J.-F. Payen, E.L. Barbier. Tissue oxygen saturation mapping with magnetic resonance imaging. Journal of Cerebral Blood Flow and Metabolism. 34(9):1550-1557, 2014*