

Different views on cerebral glycolysis by comparing hyperpolarized glucose and deuterated glucose MRS

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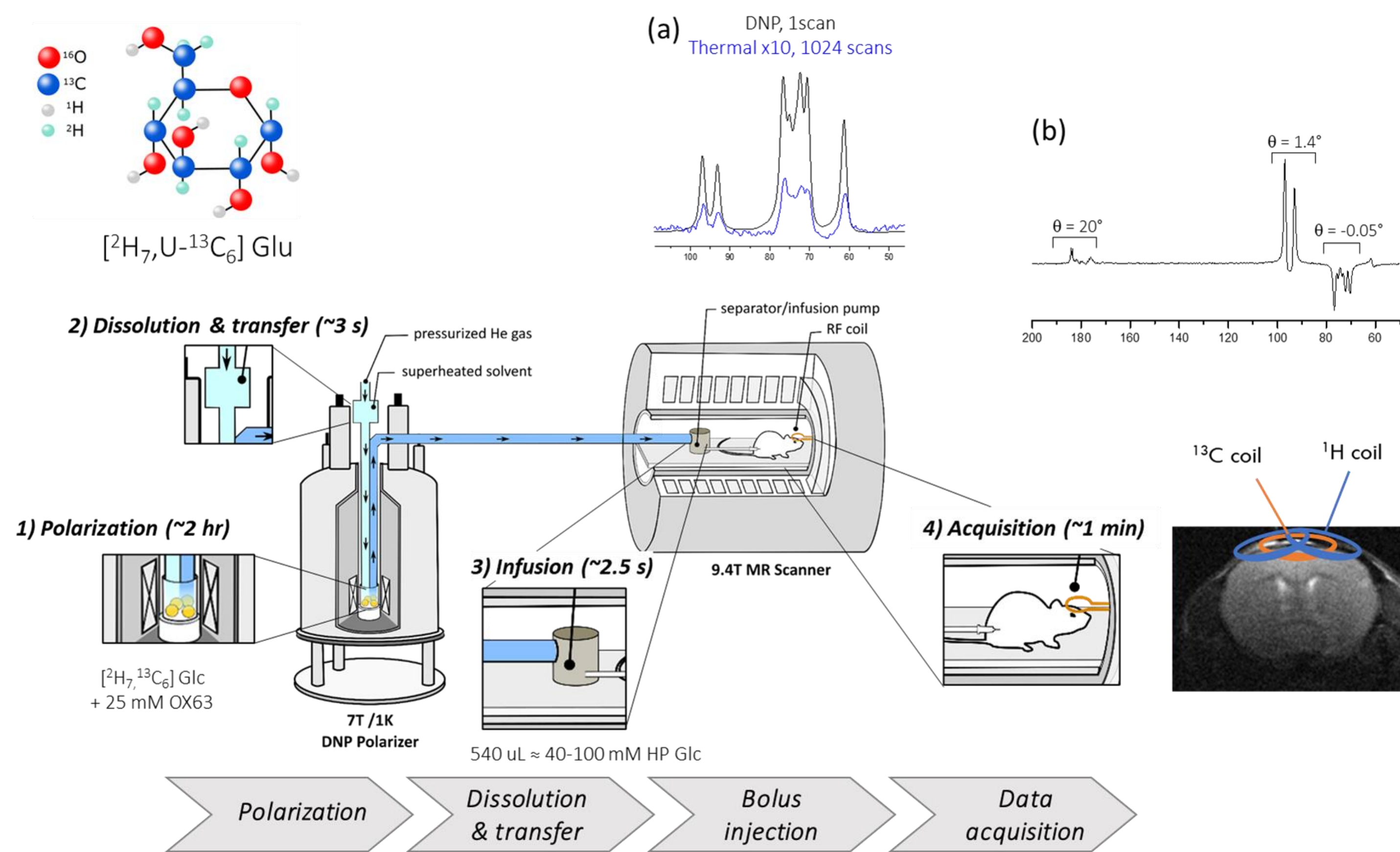
BACKGROUND AND AIMS

- Glucose is the primary fuel molecule for the brain.
- Hyperpolarization by dissolution dynamic nuclear polarization (dDNP) of metabolites boosts MR sensitivity^{1,2}.
- dDNP paves the way to a new class of real-time metabolic neuroimaging^{3,4}.
- Recent renewed interest in deuterium MRS⁵ emerged from the development of deuterium molecular imaging post intake of ²H-labelled⁶.
- **The aim of this study was to investigate brain glycolytic pathways while comparing the hyperpolarized glucose ¹³C MRS and thermally-polarized glucose ²H MRS. We compared these as methods to interrogate cerebral glucose metabolism under different anesthetic conditions.**

METHODS

- Brain metabolism of hyperpolarized or deuterated glucose was monitored in 12 hour-fasted male C57BL6/J mice (n = 26; age = 17 ± 2 weeks). Each animal received a single bolus
- Femoral vein was inserted to deliver the glucose bolus
- To monitor the effect of brain consciousness on cerebral metabolism two different anesthetic condition were tested: isoflurane (ISO group) or combination of medetomidine and low dose isoflurane (MED-ISO group).
- In mice that received hyperpolarized glucose, single voxel 1H MRS measurements were carried out in each mouse 10 min before the bolus.

SETUP FOR HYPERPOLARIZED IN VIVO MRS



Sketch of the setup for hyperpolarized ¹³C MRS @ LIFMET based on a 7T/1K polarizer coupled to the CIBM's 9.4T scanner: [²H₇, ¹³C₆] glucose is hyperpolarized with a polarizing agent. Then it dissolved and transferred to a separator infusion pump. A bolus is then automatically injected into the mouse and data acquisition commences. (a) glucose spectra acquired in the pump emphasizing the boost in sensitivity. (b) optimal in vivo acquisition scheme to minimize losses due to radiofrequency pulsing.

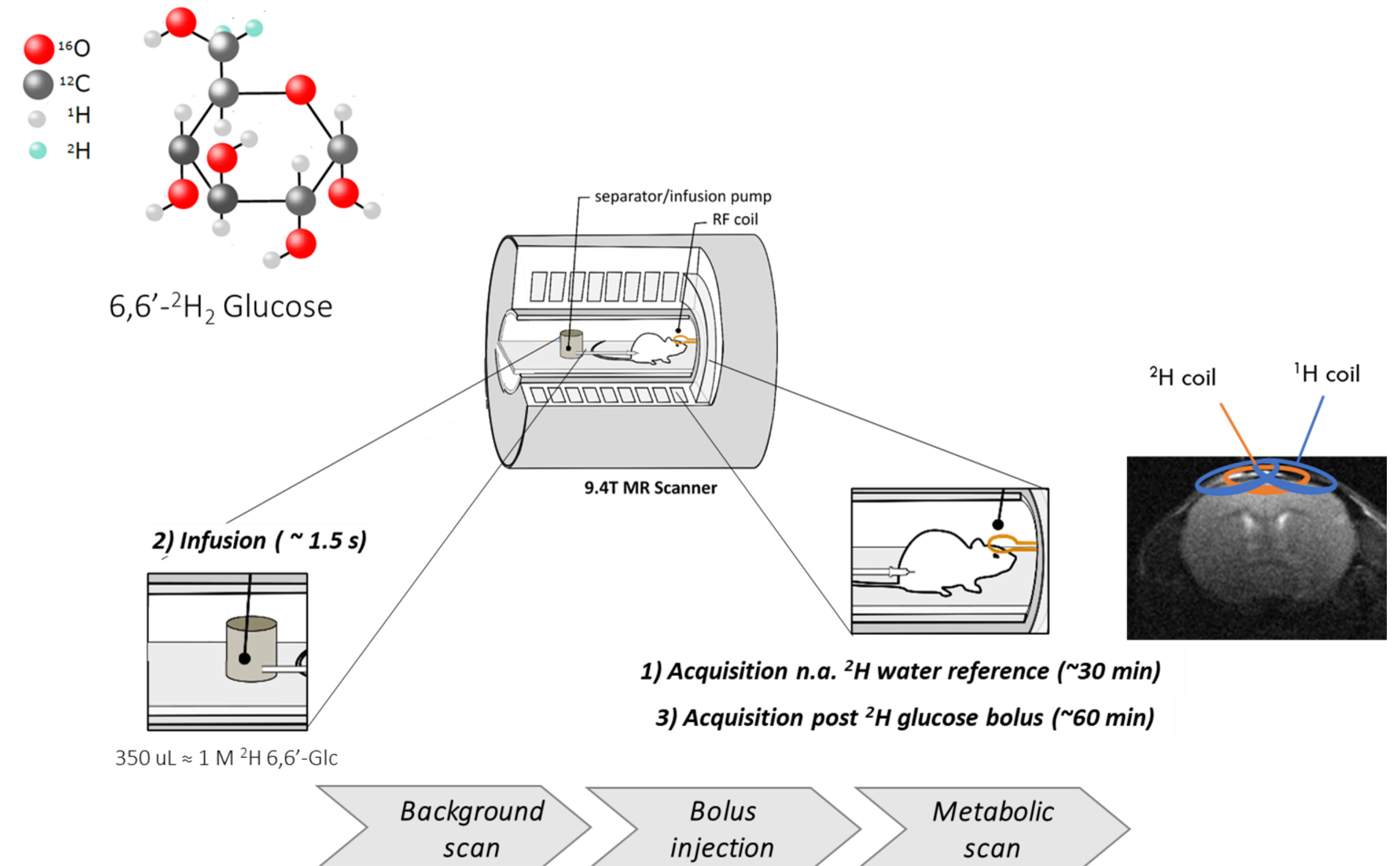
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ACKNOWLEDGEMENTS

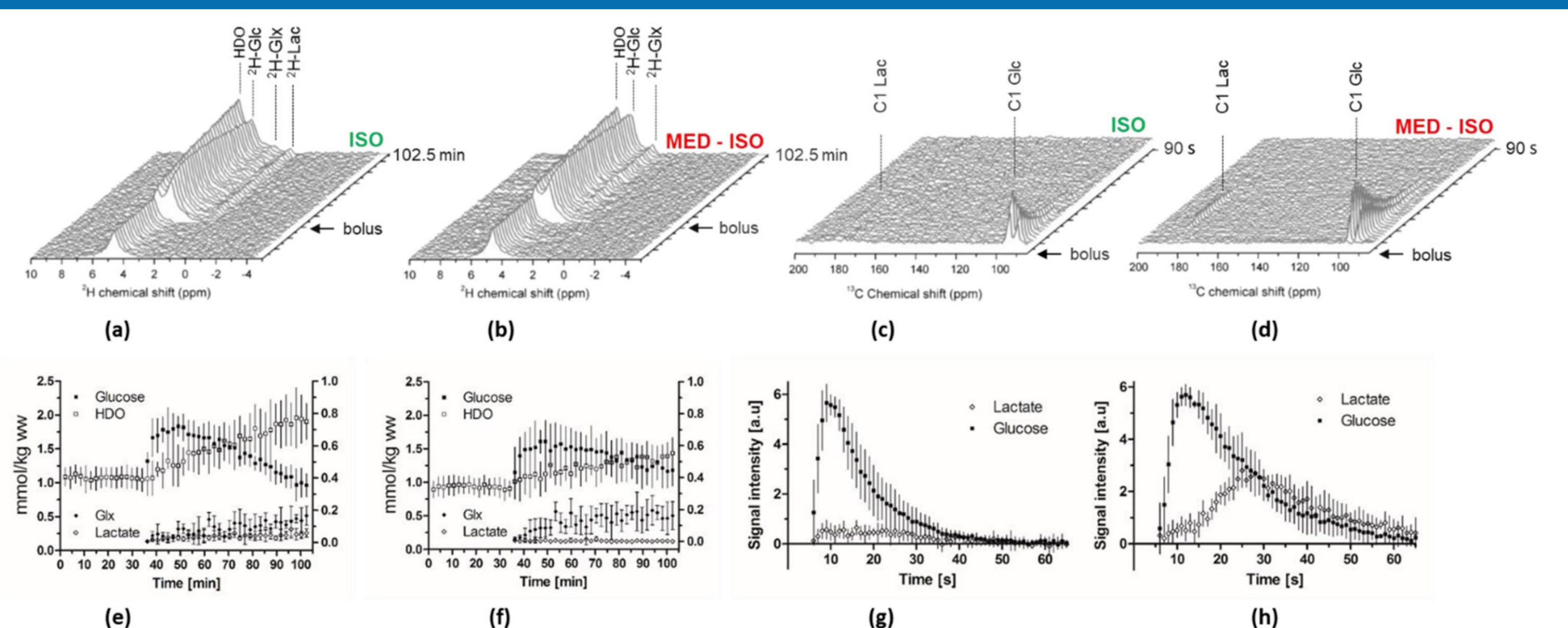
We thank Mr. Thnah Phong Lê for the fruitful discussion, and Drs. Analina Hausin, Mario Lepore and Stefan Mitrea for their assistance in animal preparation, as well as the CIBM Center for Biomedical Imaging, co-founded and supported by the CHUV, UNIL, EPFL, UNIGE and HUG.

SETUP FOR IN VIVO DEUTERIUM MRS

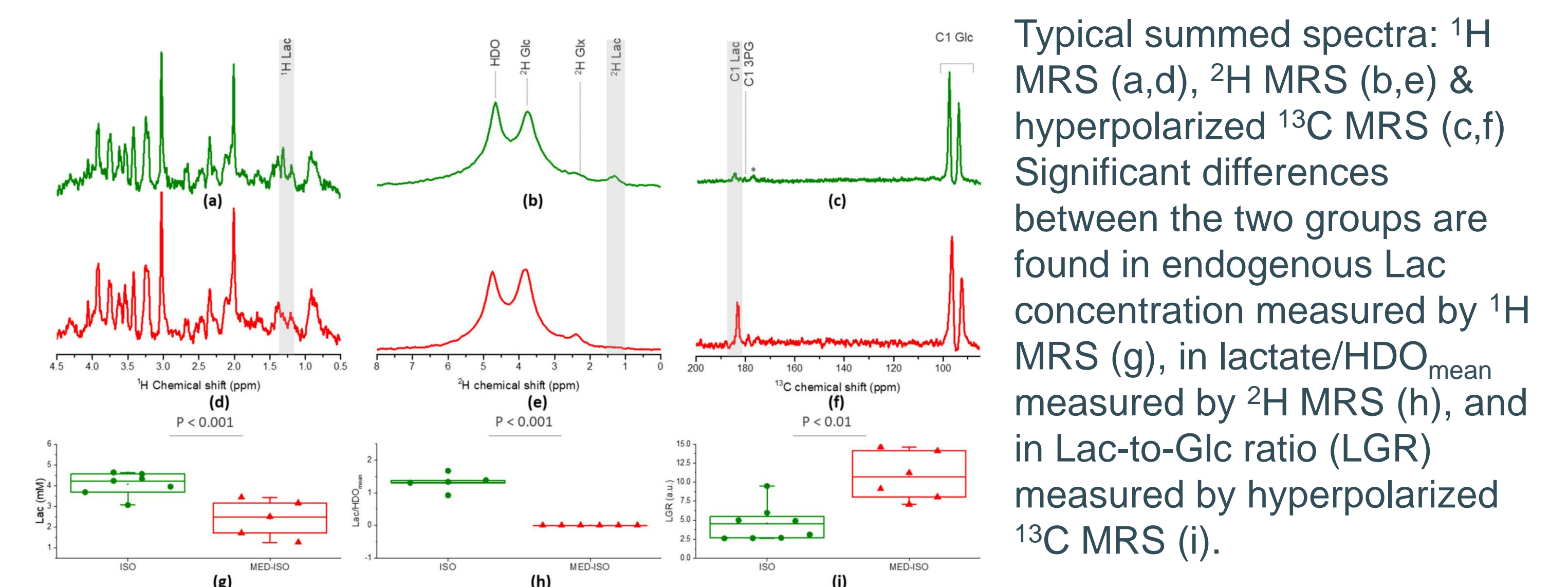


Sketch of the setup for deuterium MRS @ LIFMET based on a separator infusion pump: The [^{6,6'-2}H₂] glucose bolus is loaded into the pump. The endogenous water's reference scan is acquired before the deuterated glucose bolus. The detection of glucose metabolism is automatically triggered after the bolus injection.

RESULTS AND DISCUSSION



Characteristic dynamic spectra under the two anesthetic protocols following infusion of deuterated glucose (a,b) or hyperpolarized glucose (c,d). Corresponding time courses presented at the bottom. The water (HDO) and glucose (²H-Glc) refer to left y-axis. Glutamate–glutamine (²H-Glx) and lactate (²H-Lac) refer to the right y-axis (e, f). The corresponding time courses of hyperpolarized [¹⁻¹³C] Lactate and [¹⁻¹³C] glucose shown for each group (g,h). Values are mean ± SD; glucose signal normalized to 6, arbitrary units).



Typical summed spectra: ¹H MRS (a,d), ²H MRS (b,e) & hyperpolarized ¹³C MRS (c,f) Significant differences between the two groups are found in endogenous Lac concentration measured by ¹H MRS (g), in lactate/HDO_{mean} measured by ²H MRS (h), and in Lac-to-Glc ratio (LGR) measured by hyperpolarized ¹³C MRS (i).

SUMMARY

- Hyperpolarized glucose and deuterated glucose MRS enable highlighting different aspects in glycolytic metabolism.
- Lactate production from HP glucose does not reflect endogenous pool size.
- HP [²H₇, U-¹³C₆] glucose reports on de novo Lac synthesis and is sensitive to CMR_{Glc}.
- Lactate production in ²H glucose is reflecting the pool size.
- The level of brain consciousness manifested differently in HP and non-HP X-nuclei glucose MRS⁷.