Monitoring neuroinflammation in vivo with MR spectroscopy and CEST imaging

Maria Yanez Lopez[1], Marie-Christine Pardon[2], Dorothee Auer[1], and Henryk Faas[1]

[1]Radiological and Imaging Sciences, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom, [2]School of Biomedical Sciences, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom

· **Purpose/Introduction–**Neuroinflammation plays an important role in a wide range of neurological disorders such as Alzheimer's disease and its detection through noninvasive imaging techniques could lead to improved diagnosis and a mechanistic understanding of these disease processes. The aim of this study is to assess the short term inflammatory response in the brain to a standard immune challenge, injection of lipopolysaccharide (LPS[1]), with serial magnetic resonance spectroscopy (MRS) and imaging using Chemical Exchange Saturation Transfer (CEST).

· **Methods–** Wild type adult B6D2F1 mice received either an iv LPS injection (100 µg/kg in PBS, n=2) or a PBS injection (n=2) . MRS and CEST recordings were performed before and after injection (at one, three and four hours post treatment). Spectra were acquired from a voxel placed in the right hippocampus (2.5x2.5x2.5 mm), using a Bruker 7T preclinical imaging system (volume transmitter-surface receiver coil, PRESS sequence: TR/TE/NS: 2.5s/13ms/512 with 21 min total scan time). CEST images were acquired using a gradient echo sequence (TR/TE=206ms/4ms, 20° flip angle, FOV=20x20mm, 2mm slice thickness, 128x128 matrix) with a pulse train of 4 gaussian prepulses (offset frequencies between ±3 ppm, 0.1 ppm steps, 20 min acquisition time). The WASSR method compensated for B0 field inhomogeneities[2] and MAPSHIM was used for shimming. Data were analysed using Matlab, TOPSPIN and LCModel (quantification of the metabolites expressed as a ratio to the sum of all metabolites, 10% Cranmer-Rao rejection limit).

· **Results–** LPS administration induced an increase in myo-inositol (Ins) and decrease in total choline (tCho) after three hours (Fig. 1, left). This effect was absent after administration of PBS during control experiments (Fig. 1, right). CEST images (Fig. 2) at offset frequencies of 0.5-1 ppm and 1.8-2.2 ppm in the z-spectrum asymmetry curve (Fig 3) showed a correlation with Ins and total creatine (tCr) MRS ratios (Fig. 4 and 5).

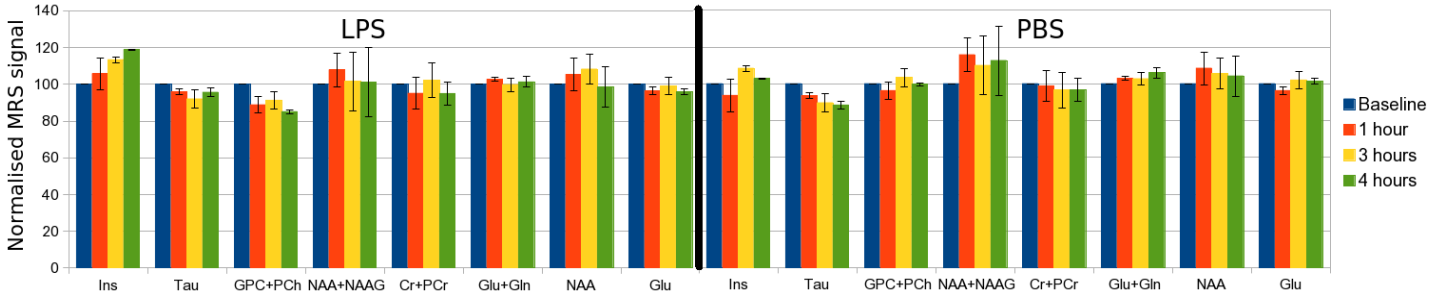

Figure 1 shows the averaged metabolic change from baseline.

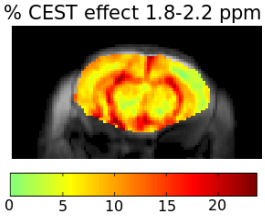

Figure 2: CEST map

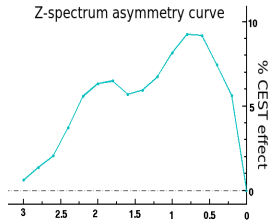

Figure 3: Z spectrum

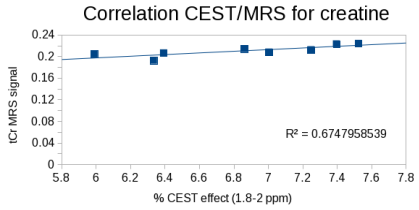

Figure 4: Correlation CEST/MRS tCr

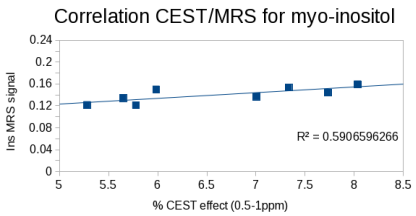

Figure 5: Correlation CEST/MRS Ins

· **Discussion/Conclusion-** These preliminary results of our ongoing study show in vivo MRS changes in the first four hours after LPS administration at levels low enough to avoid sickness syndrome, in particular, increase in the microglial marker Ins. The decrease in choline is consistent with the only other in vivo MRS study[3] after LPS administration that we are aware of. Our data also indicate that CEST can be used to assess, at high spatial resolution, metabolic changes following low dose LPS administration. These findings are currently being validated further in our study, and they could stablish CEST imaging as a new method to assess neuroinflammation.

· **References–** [1]Herber D.L. (2006), *Glia* 382-391. [2] Kim M. (2009), *MRM*, 1441-1450.

[3] Martin Recuero A.B. (2012) ESMRMB abstract.