Proton Magnetic Resonance Spectroscopy of Regional Metabolic Changes in Rat Brain during Pregnancy

Iris Y. Zhou[1,2], Russell W. Chan[1,2], Leon C. Ho[1,2], Patrick P. Gao[1,2], and Ed X. Wu[1,2]

[1]*Laboratory of Biomedical Imaging and Signal Processing, The University of Hong Kong, Hong Kong SAR, China, People's Republic of,* [2]*Department of Electrical and Electronic Engineering, The University of Hong Kong, Hong Kong SAR, China, People's Republic of*

INTRODUCTION

Pregnancy is associated with dramatic hormonal changes that remodel the female brain structurally and functionally. The affected regions are not limited to those involved in regulating maternal behaviors. Previous studies have reported that reproductive experience may facilitate spatial learning and memory [1] with attenuated stress and anxiety [2]. Therefore, it is believed that pregnancy also triggers changes in the brain regions that control learning, memory and responses to fear and stress. Proton MRS (^{1}H MRS) provides noninvasive assessment of metabolite levels in living brains and thus offers neurobiological information about neural processes such as developing [3] or brain disorders [4]. Previously, MRS investigation of pregnant subjects focused on studying eclampsia [5] or fetal development [6]. The regional neurochemical changes during normal pregnancy, especially in the regions related to learning and memory such as hippocampus, are still unclear. In this study, we aim to use in vivo ^{1}H MRS to investigate the metabolic changes in hippocampus and thalamus during pregnancy.

MATERIALS AND METHODS

Animal Preparation: Pregnant primiparous Sprague-Dawley rats (3.5 months, N=7) were MR scanned at day 17 of gestation. Age-matched nulliparous female rats (N=7) were served as non-pregnant controls. ***MRI Protocols:*** All MR measurements were performed on a 7 T Bruker MRI scanner using surface coil. Under inhaled isoflurane anaesthesia, the animal was kept warm under circulating water at 37 ^{o}C with respiratory monitoring. RARE T2-weighted anatomical images were acquired for voxel localization in ^{1}H MRS. After localized shimming with FieldMap, ^{1}H MRS was performed using a PRESS sequence combined with outer volume suppression (OVS) and with TR/TE=2500/20ms, 2048 data points and 256 averages. A 2×4×2 mm^3 voxel was placed over the left hippocampus and another 3×3×3 mm^3 voxel was centered at the left thalamus. ***Data Analysis:*** MR spectra were processed with jMRUIv4.0 software using simulated metabolites in NMR-SCOPE as prior knowledge. The raw data was apodized with a 15-Hz Gaussian filter and phase-corrected. The residual water signal was filtered out with HLSVD algorithm. Various ratios of metabolites, NAA:Cr, Cho:Cr, Glu:Cr, Lac:Cr, m-Ins:Cr and Tau:Cr were statistically evaluated using unpaired student's t-tests between the pregnant and non-pregnant rats with $p < 0.05$ considered as significant.

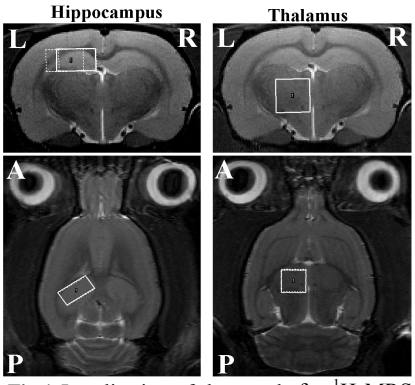

Fig.1 Localization of the voxels for ^{1}H MRS measurement in hippocampus and thalamus.

RESULTS

Fig. 1 illustrates the typical localization of the voxels for ^{1}H MRS measurement of rat hippocampus and thalamus. For each region of interest, averaged ^{1}H MRS spectra from the pregnant and non-pregnant rats, respectively, were shown in Fig.2. Higher N-acetylaspartate (NAA) can be observed in the hippocampal spectrum of pregnant rats compared to that of non-pregnant controls. In thalamus, choline (Cho) level appeared to be lower in pregnant rats. The statistical evaluation (Fig. 3) of the metabolite signal with respect to creatine (Cr) peak revealed that besides the distinct higher hippocampal NAA level ($p<0.01$) and lower Cho level ($p<0.05$) in thalamus, taurine (Tau) signal was significantly lower ($p<0.05$) in hippocampus of pregnant rats while lactate (Lac) level was found to be lower ($p<0.05$) in non-pregnant rats' thalamus.

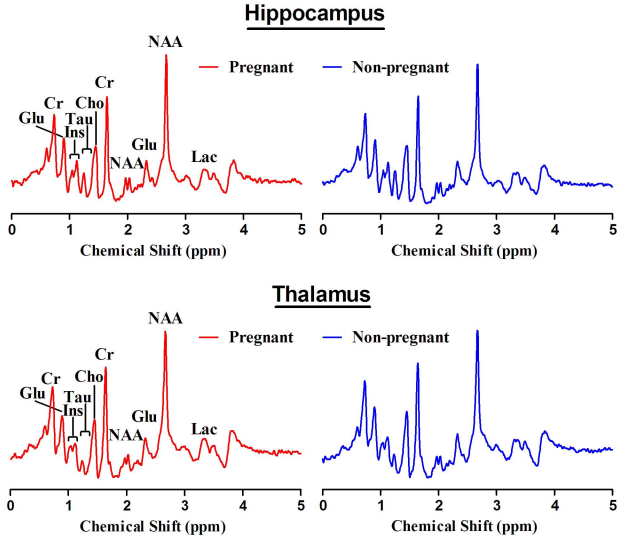

Fig.2 Averaged ^{1}H MRS spectra of pregnant (N=7) and non-pregnant (N=7) rats with the voxel of interest in hippocampus (top) and thalamus (bottom).

DISCUSSION AND CONCLUSION

Previously, it has been shown that the hormones of pregnancy can alter the hippocampal neurons, leading to significantly more neuronal dendrite spines in female rat [7]. NAA, as a marker of neuronal density, integrity and health [4], has significantly higher level in hippocampus of pregnant rats, indicating the increased density of neurons in this region. This neuronal modification in hippocampus of pregnant rats may therefore contribute to the better navigation skills involved in supporting behaviors such as foraging. A lower Tau:Cr in hippocampus of pregnant rats observed in this study is consistent with *ex vivo* measurements [8], resulting from an effect of steroid hormones. This difference was not detected in thalamus possibly due to the low concentration of Tau in this region compared to hippocampus. Reduced level of Cho in the maternal brain during pregnancy has also been observed in humans [9], reflecting high fetal demands. It has been reported that possible source of increased Lac concentrations is hyperventilation [10]. Therefore, the raised Lac level in thalamus might be related to the hyperventilation of pregnancy due to high oxygen consumption [11]. In conclusion, this study shows the metabolic differences between pregnant and non-pregnant rats using in vivo ^{1}H MRS, providing neurochemical evidence of the behavioral changes associated with pregnancy.

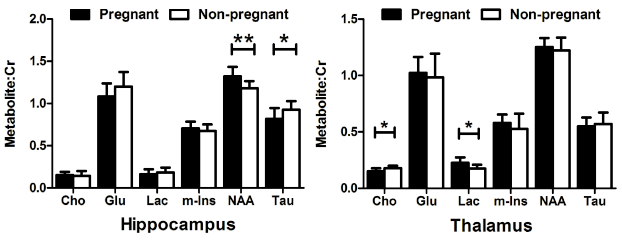

Fig.3 Comparisons of metabolite ratios between the pregnant and non-pregnant rats in hippocampus (left) and thalamus (right). Unpaired t-tests were performed with * $p<0.05$, ** $p<0.01$.

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