Neurochemical profile of the mouse hypothalamus using ^{1}H MRS at 14.1T

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INTRODUCTION ^{1}H MRS of murine brain mostly focused on striatum, hippocampus and cerebellum etc (1). ^{1}H MRS of small structures, such as hypothalamus has not been reported. High magnetic fields have been shown capabilities to sustain high SNRs and allow studying small volumes, such as in transgenic mouse (1, 2). To demonstrate the ability to study transgenic mice, we sought to investigate glucose transporter (GLUT) 8 knockout mice. GLUT8 has been shown heavily expressed in hippocampus and hypothalamus neurons (3, 4). Therefore, the aim of study is to estimate feasibilities of ^{1}H MRS of the hypothalamus in the GLUT8 knockout mice at 14.1T.

METHODS Six GLUT8 knockout (GLUT8-/-) animals were backcrossed in the C57BL/6 background and five C57BL/6 mice were in the control groups (GLUT8+/+) (3). Under the local authorities, all animals underwent MR studies at the age of 12-13 weeks in a horizontal 14.1T/26cm magnet (Varian/Magnex). A home-made quadrature coil was used as RF transceiver. Throughout the MR studies, the animals were anesthetized under 1-2% isoflurane well-mixed with oxygen to minimize potential motion with continuous monitoring of temperature and breathing (SA instruments). T_2-weighted images were acquired for localize the volume of interest (VOI), hippocampus ($1.7\times1.2\times1.5mm^3$, red square in Figure 1) and hypothalamus ($2\times1\times2mm^3$, yellow square in Figure 1) in this study, to minimize the partial volume effect. After automatic adjustment of field inhomogeneities, localized spectra were obtained using SPECIAL (2). Absolute quantification was achieved assuming 80% water as reference using LCModel (1 and reference therein). Regional difference was determined using two-way ANOVA analysis with P-value <0.05.

RESULTS AND DISCUSSION Shimming resulted in excellent linewidths of 17±3Hz in hippocampus and 16±2Hz in hypothalamus. In consequence, the high quality spectra of hippocampus and hypothalamus in mice have been obtained with satisfactory SNRs, 15±3 for hippocampus and 13±2 for hypothalamus, respectively, as shown in Figure 1. The obtained neurochemical profile of hippocampus (Figure 2, top row) is consistent with previous studies (1). Spectra of the hypothalamus presented apparent characteristics, such as low concentrated Tau and high GABA contents (arrows in Figure 1), which were observed in rodent brain biochemically (5). Interestedly, we observed higher GPC+PCho and *myo*-Ins contents in hypothalamus (arrows in Figure 1). Moreover, more than 20 metabolites except Scyllo, could be quantified with CRLB <35% in hypothalamus (Figure 2). The neurochemical profile of hypothalamus, such as Cr, Glu, GABA, PCr+Cr, *myo*-Ins and Tau were found different when comparing to that of hippocampus. To date, this is the first *in vivo* ^{1}H MRS measurements of the neurochemical profile in the hypothalamus. Moreover, there were some differences observed in GLUT8-/- animals, such as significantly increased total Cr and Tau in hippocampus, and lowered Gln in hypothalamus using student t-test (Figure 2). In conclusion, ^{1}H MRS of small structures such as hypothalamus is feasible in mouse brain, which opens the possibilities to study neurochemical profile alternations of this important brain region in transgenic mice as illustrated with GLUT8 knockout.

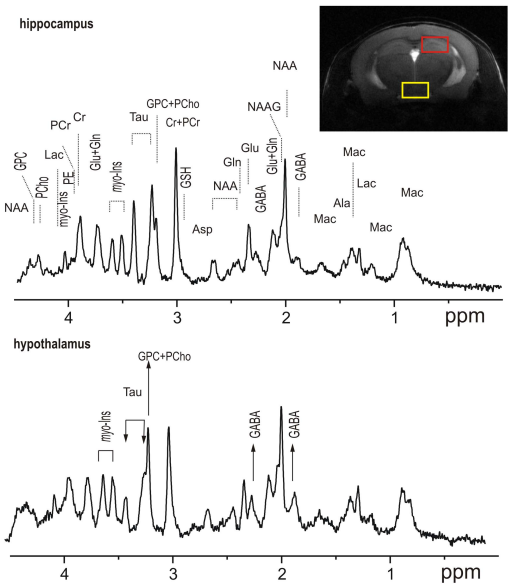

Figure 1 Typical spectra of the hippocampus (red square) and the hypothalamus (yellow square) were obtained from GLUT8+/+ animals and displayed (gf=0.015s) with the corresponding metabolites indicated, as in Tkac I et al. (1). The apparent characteristics of hypothalamus were marked with the oriented arrows.

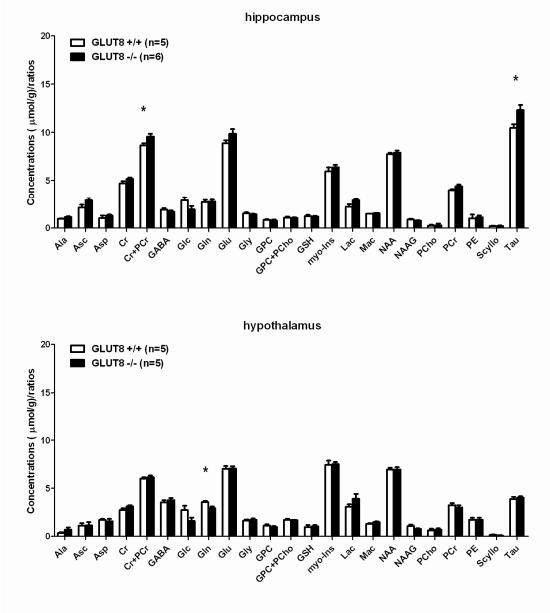

Figure 2.The neurochemical profiles of hippocampus and hypothalamus on GLUT8+/+ and GLUT8-/- mice (mean±SEMs). In parentheses, n represented the number of animals in individual group. "*" indicated the significant difference using student un-paired t-test.

References: 1) Tkac I et al. J Neurochem. 2007 100 :1397; 2) Mlynarik V et al. Mag Reson Med 2006 56:965; 3) Membrez M et al., Mol Cell Biol 2006 :4268-4276; 4) Schmidt S et al. Behav Genet 2008 38: 396-406; 5) Suda M et al. Industrial Health 2008:46, 348-359

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