'Evaluation of the taurine treatment effects in a APP/PS1 double transgenic model of Alzheimer's Disease using MRS'

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I. Introduction

Recovery from dementia is the key clinical benefit to the patients of Alzheimer's disease (AD). Taurine, 2-aminoethanesulfonic acid, is the second most abundant endogenous amino acid in the central nervous system (CNS) and plays multiple roles in our body. Recently, taurine has shown a positive effect in preventing cognitive impairment in AD-like mouse model [1]. ^{1}H-MR spectroscopy (^{1}H-MRS) is a non-invasive technique that has been used to characterize AD and evaluate to better understand treatment effects. The aim of this study was designed to characterize the neurochemical profile to monitoring taurine treatment effect in APP/PS1 mice, compared with that of wild-type mice, using ^{1}H-MRS.

II. Materials and Methods

Animals: APP/PS1 double transgenic mice as non-taurine treated group (AD), APP/PS1 double transgenic mice orally administered with taurine dissolved water containing 1kg/kg/day as taurine treated group (AD_t) and wild-type mice (WT) age of 20 months (n=6).

MRI: ^{1}H-MRS was performed using a 9.4 T MR system with Point-resolved spectroscopy (PRESS) sequence : TR = 5000 ms, TE1 = 7.66 ms, TE2 = 6.01 ms, 384 averages, scan time = 32min. A 1.2 mm × 1.5 mm × 2 mm voxel was positioned around the hippocampus (Fig. 1). Signal could be reliably quantified (CRLB < 5%) for NAA, total creatine (tCr), γ-aminobutyric acid (GABA), glutamate (Glu), Glutamine (Gln), taurine (Tau). The concentrations of the metabolites relative to tCr was estimated by LCModel. Due to the excellent spectral resolution, Cr and PCr were well resolves at 4.2 ppm and could be separately quantified (CRLB < 5% at all b for PCr).

III. Results and Discussion

Fig. 2 presents *in vivo* spectra from the hippocampus of WT, AD and AD_t groups. In the AD, the levels of GABA, NAA and Glu are lower, and the level of mIns is higher than that of the WT. In the AD_t, the levels of GABA, NAA and mIns is higher than that of the AD-water. Fig. 2(d) shows the concentration of metabolite to tCr. NAA/tCr, was observed to be reduced in AD, but increased in AD_t, compared to WT. GABA/tCr in AD-water was estimated to be significantly decrease than in WT($P<0.008$), but GABA/tCr in AD_t was higher than AD ($P=0.01$). mIns/tCr was observed to be increased in AD ($P<0.035$), and more increased in AD_t, compared to WT. Glu/tCr was observed to be similar between AD and AD_t. Further studies are warranted about the metabolite change results of the taurine treatment effect, that might be helpful to monitor of AD.

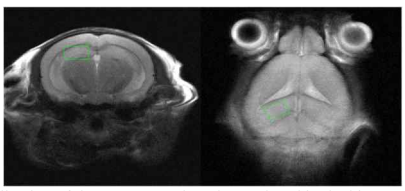

Fig. 1. Localization of the spectroscopic volume placed in the hippocampus.

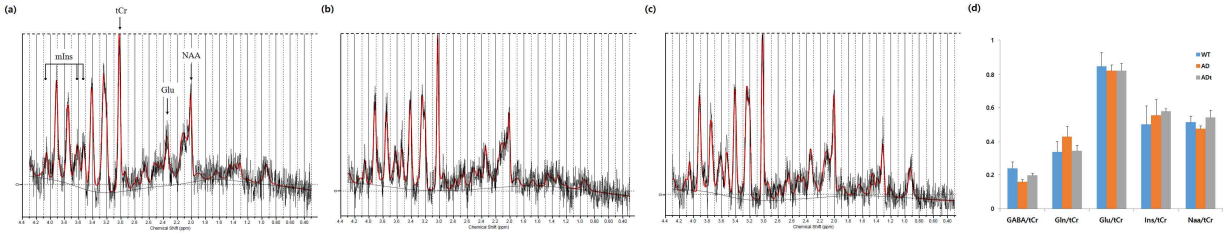

Fig. 2. Localized *in vivo* ^{1}H MR spectra obtain from 36-ml voxel (Fig.1) from (a) WT, (b) AD, and (c) AD_t . The spectra are shown with similar linewidths and with amplitude adjusted by using the total creatine (tCr) peak at 3.03 ppm. (d) The ratios of concentration of metabolites to tCr for WT, AD and ADt.

II. CONCLUSIONS

We evaluate the taurine treatment effect in transgenic mouse model of AD using ^{1}H-MRS. Quantitative analysis of metabolite change may provide important clues for theranostics of AD.

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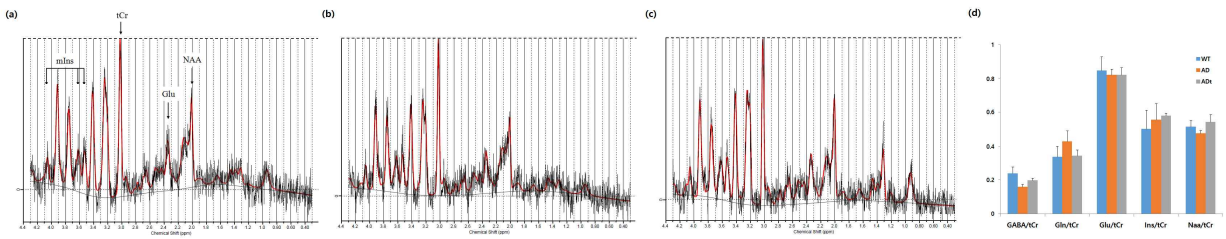

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