

Absolute Quantification of Phosphomono- and Phosphodiester in the Brain of Patients with Major Depression

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Introduction

We previously found reduced hippocampal choline-containing compounds (Cho) and increased Cho in the putamen in MDD with 1H MRSI (1, 2). These findings led us to the hypothesis that phosphomono- and/or phosphodiester (PE, PC and GPE, GPC) resonances measured via ³¹P MRS would be altered. We used a 3D-whole head RINEPT Sequence together with point-spread function (PSF) corrected tissue segmentation for robust absolute quantification.

Methods

For the MRS data reported here, we used a 3D ³¹P RINEPT sequence with an optimized TR of 1350 ms. Included in the current analysis are 18 patients (8 males, age 50.8 +/- 16.1 years) with MDD (HAMD 25 +/- 7) and 22 matched healthy controls (6 males, age 45.8 +/- 12.8 years). All measurements were performed on a 1.5 T Siemens Vision system with a double resonant ³¹P-¹H volume head coil (RAPID Biomedical, Würzburg, Germany) and a second RF channel.

For localization, 2D FLASH images in sagittal and transverse orientation were acquired. The measurement parameters for the 3D ³¹P RINEPT MRSI included TR = 1.35 s, TE1/2 = 40 / 32 ms and FOV = 400 mm (4). 3D spatial localization (8 x 8 x 8 encoding) is obtained by phase encoding gradient pulses which are free from chemical shift displacement errors. In all MRSI measurements proton decoupling during acquisition was employed using a WALTZ-4 pulse train on a second independent transmit channel. The MRSI data were fitted in the time domain with jMRUI using the AMARES algorithm (5). Due to the large voxel size of the acquired MRSI voxel tissue segmentation it is mandatory to account for partial volume/CSF influences on the evaluated signals for quantitation avoiding ratios. Tissue segmentation for gray matter (GM) white matter (WM) and csf was done with SOM2 and MRSI Sequence Simulation for PSF correction (7). An external Reference Phantom containing hexamethylphosphorous triamide (HMPT) was measured with each subject.

Results

The effect of the tissue segmentation (8) and CSF correction is shown in Fig. 1 over all analyzed Voxel. The CSF-corrected concentrations were grouped for several ROIs shown in Fig. 2. Correlation analysis of these voxels over the GM/WM ratio revealed a strong effect of tissue type i.e. significantly higher GM PE in all regions but lower GPC in GM in FL and BG as well as higher GM GPC and PC in the FL and TL respectively (Fig. 3). A strong negative correlation of metabolite concentrations (averaged over regions) with age could be detected for PE and GPC in the cerebellum, while a positive correlation was found for GPE in the FL for the patient group only. Interestingly, group interaction was only found with a GLM analysis (Factors age, GM/WM, group) for PC in the TL and CC (Fig.5).

Diskussion

The most pronounced findings of this study are the strong correlations of the different phosphomono- and diester metabolites and age throughout all of the brain regions mostly but not always independent of MDD. The metabolite concentration differences in different tissue type underline the necessity of segmentation for absolute quantitation. Nevertheless, the differences in age-dependence in the FL as well as the group differences of PC concentration in the TL and the cerebellum show some altered phosphor-lipid metabolism in the brains of patients with MDD (8).

References

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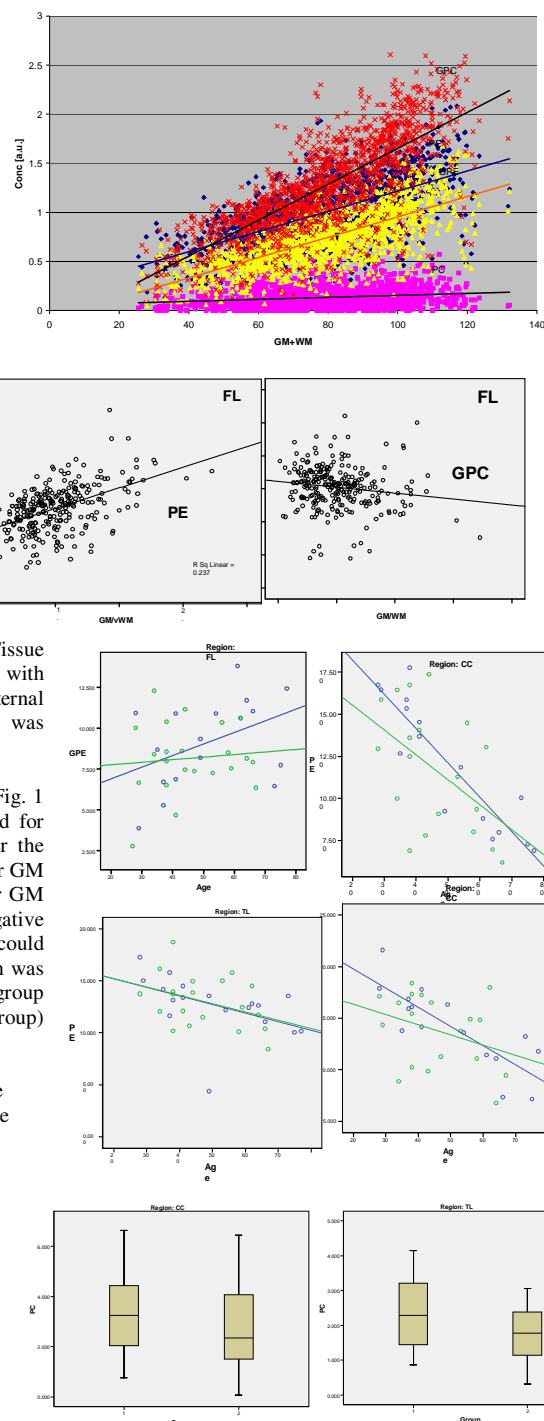


Fig 3