

Brain Matter corrected Quantification of Phosphomono- and Phosphodiesters in the Brain of Patients with Schizophrenia

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Introduction

Since the finding of an altered phosphomono and -diester metabolism in cell membranes of postmortem brains of schizophrenic patients [1] several studies have used ^{31}P -MRS for in vivo investigation of schizophrenic groups [2-4] in different brain regions, partly with contradictory results. Because of the scalar coupling between ^1H and ^{31}P in the molecules the resonances of phospho-mono- and/or phosphodiester (Phosphorylethanolamine PE, Phosphocholine PC and Glycero-phosphorylethanolamine GPE, Glycerophosphocholine GPC) show a multiplet structure overlying the broad phospholipid-component, their concentrations are difficult to quantify reliably. 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 ^{31}P RINEPT sequence with an optimized TR of 1350 ms. Included in the current analysis are 13 patients (12 males, age 30.54 +/- 7.7 years) with schizophrenia and 15 matched healthy controls (13 males, age 28.3 +/- 6.0 years).

All measurements were performed on a 1.5 T Siemens Vision system with a double resonant ^{31}P - ^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 ^{31}P RINEPT MRSI included TR = 1.35 s, TE1/2 = 40 / 32 ms and FOV = 400 mm [5]. 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 [6]. Due to the large voxel size of the acquired MRSI voxel tissue segmentation 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 SPM2 using high resolution anatomical data and MRSI sequence simulation for 3D-PSF correction [7], assuming negligible metabolite concentration in CSF. An external reference phantom containing hexamethylphosphorous triamide (HMPT) was measured with each subject.

Results

The metabolite concentrations were grouped for several ROIs which are shown in Fig. 1. The effect of the tissue segmentation and CSF correction is shown in Fig. 2 over all analyzed voxels. Two sampled t-tests of the corrected metabolite concentrations show a significant reduction of PC and GPC in the basal ganglia and thalamus of schizophrenic patients compared to controls. GPC was also significantly lower in the cerebellum while PE showed a trend for lower concentration in patients in the frontal region (Fig. 3). Previous findings of elevated GPC in the frontal cortex [4] could not be corroborated.

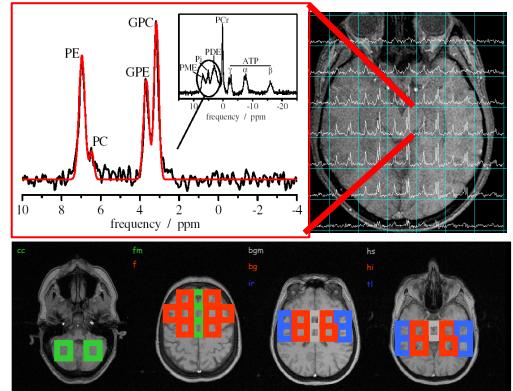
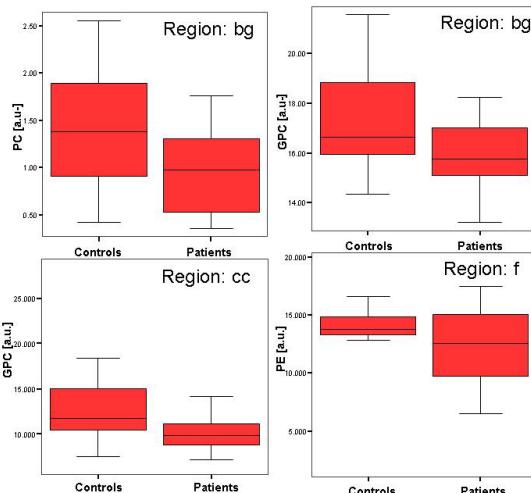


Figure 1: top: typical RINEPT spectrum and the corresponding 3D-MRSI spectral map. Bottom: locations of the Regions of Interest: cerebellum: cc, frontal: f, cingulate: fm, basal ganglia: bg, thalamus/BG: bgm, insular: ir, Hippocampus: hi, Temporal Lobe: tl, Brainstem: hs

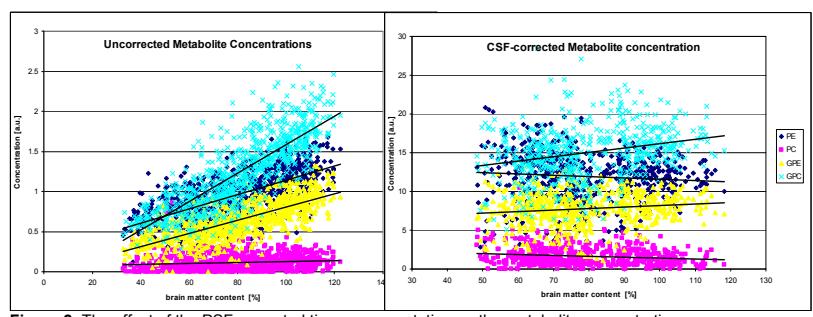


Figure 2: The effect of the PSF-corrected tissue segmentation on the metabolite concentrations.

Discussion

The low spatial resolution of a 8x8x8 chemical shift imaging sequence leads to pronounced artifacts and voxel-bleeding in the signal contribution of the different metabolites over the whole dataset. The adapted CSF-correction shows that for a reliable estimation of the tissue contents for these large voxel, the effects of the PSF need to be taken into account.

The decreased GPC signal in schizophrenic patients in the basal ganglia and thalamus region are in line with findings of lower PDE in other studies [8] but we could not replicate findings of elevated PDE in the frontal cortex. Since most studies do not use any spectral editing for selective PME and PDE signal detection, the role of the broad phospholipid resonance underlying these signals needs to be further investigated.

References

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