Alterations of Phosmomono- and Phosphodiesters in the Brain of Patients with Major Depression Detected with 3D ^{31}P RINEPT

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Introduction

We report preliminary results from our ongoing 3D ^{31}P RINEPT MRSI study in 20 patients with major depression (MDD) compared to 10 healthy controls. In contrast to the results reported last year at the ISMRM meeting we used a 3D ^{31}P RINEPT sequence with an optimized TR of 1350 ms (previously 500 ms) which gives superior S/N within the same measurement time. The most frequent finding of the few published ^{31}P MRS studies in MDD is an increased phosphomonoester signal. We previously found reduced hippocampal choline-containing compounds (Cho) and increased Cho in the putamen in MDD with ^{1}H MRSI (1, 2). These findings let us to the hypothesis that phosphomono- and/or phosphodiester (PME and PDE) resonances measured via ^{31}P RINEPT would be altered. This study is supported by the German Research Foundation (SFB 636, project D1).

Methods

Twenty patients (4 males, age 45.5 +/- 16.1 years) with MDD (HAMD 25 +/- 6) and 10 matched healthy controls (4 males, age 47.3 +/- 10.6 years) participated in this study. All measurements were performed on a 1.5 T Siemens Vision system with a double resonant ^{31}P-^{1}H 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, $TE_{1/2}$ = 40 / 32 ms and FOV = 400 mm (4). 3D spatial localization ($8 \times 8 \times 8$ 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. Voxel selection was done using home developed software and SID from SITools (3). The PC signal was often too small to be reliably quantified. Thus we concentrated on GPC, GPE and PE. We also included an external reference (MDPA phantom) and confirmed the linear reciprocal function of the phantom signal with the transmitter reference voltage. 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. Since the segmentation is not yet fully accomplished the results are expressed as ratios of GPC and GPE to PE, respectively.

Results

Patients and controls from a wide age range (28 - 77) were included and a 3D MRSI sequence covering the whole brain was used (spectra were evaluated from 11 distinct brain regions). We tested the results for region specific differences and age effects. Regional differences were analysed with use of a general linear model for repeated measures in SPSS with group as between subject factor and age as covariate. We found significant regional differences for GPC/PE ($F = 4.3$, $p = .006$) and GPE/PE ($F = 3.9$, $p = .009$) with a sign. influence of age for GPE/PE ($F = 2.8$, $p = .035$) but not for GPC/PE and a trend for a group effect for GPE/PE ($F = 2.4$, $p = .06$). In univariate analyses of the ratios, again with group as between subject factor and age as covariate, we found a sign. influence of age in 6 (for GPC/PE) and 8 (for GPE/PE) regions and sign. group differences for 5 regions (see Figure 1).

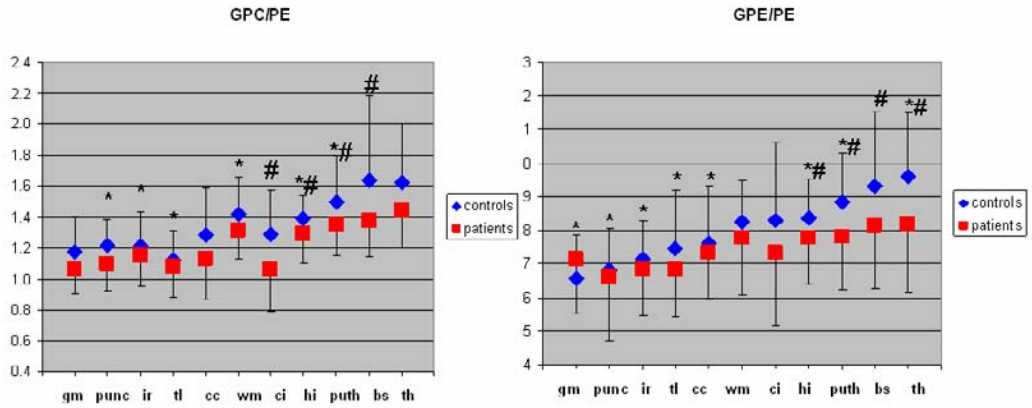
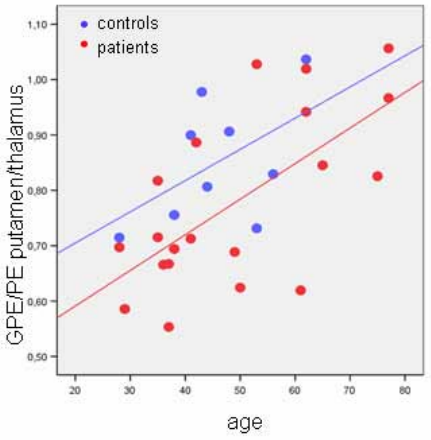


*Figure 1: Regional distribution of GPC/PE and GPE/PE. gm: frontal GM, punc: putamen/caudate, ir: insular, tl: temporal lobe, cc: cerebellum, wm: frontal WM, ci: ant. cingulate, hi: hippocampus, puth: putamen/thalamus, bs: brainstem, th:thalamus. Repeated measure analyses for brain region, between subject factor: group (patient/control), covariate: age; reveals sign. region effects for GPC/PE and GPE/PE ($p < 0.001$) with sign. interaction of region and age for GPE/PE ($p = 0.04$). Univariate GLM analyses for group (patient/control) with covariate: age; *indicates sign. age effects, # sign. group effects ($p \leq 0.05$).*

Figure 2: GPE/PE in the putamen/thalamus region plotted against age.



Discussion

These preliminary results give further evidence for a disturbed phospholipid metabolism in depressed patients. They could be interpreted as trait- and possibly state-dependent abnormalities of membrane phospholipid metabolism, which may reflect a dysregulation in brain-signal transduction systems of relevance in MDD. They are furthermore inline with a reported mitochondrial dysfunction in MDD and the assumption that there is a relationship between mitochondrial dysfunction and altered phospholipid metabolism in the brains of patients with MDD (5).

References

1. Ende G, Braus DF, Walter S, Weber-Fahr W, Henn FA. Arch Gen Psychiatry 2000; 57(10):937-43
2. Ende G, Demirakca T, Walter S, et al. Eur Arch Psychiatry Clin Neurosci. 2006 Aug 16; [epub]
3. Wokrina T , Ende G. Proc. Intl. Soc. Mag. Reson. Med. Miami 2005; 347
4. Wokrina T , Ende G. Proc. Intl. Soc. Mag. Reson. Med. Seattle 2006; 2071
5. Modica-Napolitano JS, Renshaw PF. Biol Psychiatry. 2004; 55: 273-7