High resolution ^{31}P Magnetic Resonance Spectroscopic Imaging with polarization transfer of phosphomono and -diesters in the human brain at 3T.

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Introduction:

Besides the signals of high energy phosphates and phosphocreatine, signals for phosphocholine (PC), glycerol phosphocholine (GPC), phophoryl elthanolamine (PE) and glycerol phosphoethanolamine (GPE) can be detected in the human brain by ^{31}P MRS. These phosphoesters are involved in major metabolic processes and their signals are explored in the clinic to evaluate diseases such as tumors and mental disorders [1-5]. However, the sensitivity of ^{31}P MRS is low, resulting in relatively long measurements, large voxels and low SNR. To increase sensitivity we developed a ^{1}H - ^{31}P polarization method that cancels the homonuclear J-coupling between ^{1}H spins by chemical shift selective refocusing [6]. This selective refocused insensitive nuclei enhanced by polarization transfer (sRINEPT) technique provides efficient polarization transfer and a distinct selection of the resonances of PE, GPE, PC and GPC.

Aim: to implement sRINEPT in a 3D spectroscopic imaging sequence and test this in the normal human brain to evaluate possible spatial and age variations of the phosphoester compounds .

Methods:

Thirteen healthy volunteers - 5 female, 8 male - participated in this study (n=8 for age 23-34y, n=4 for age 50-59y and n=1 for age 45y). Informed consent was obtained and the volunteers were measured at a 3T MR system (Siemens, Erlangen) using an optimized coil concept for multi-nuclear MRS of the human brain [7] (volume TxRx ^{1}H coil and a quadrature TxRx surface coil for ^{31}P). The sRINEPT sequence [6] was combined with spatial localization by applying phase encode gradients before acquisition of the signal (Figure 1). A DC correct phase cycling scheme was implemented to eliminate residual signals from ^{31}P spins not coupled to ^{1}H spins. The field of view, matrix size and number of acquisition-weighted averages were adapted to obtain voxels of approximately 18 cm^3 within a total acquisition time of 16 minutes (TR 1.5 s). A hamming filter in 3 directions was applied before spatial Fourier transformation. Data was analyzed with JRMUI 3.0 software. Gaussian singlets with equal line widths (applied from the line width of PE) were fitted to the 4 peaks in the spectrum. To avoid influence of B1-Rx-inhomogeneities of the ^{31}P surface coil, ratios of the different metabolites were calculated. From each volunteer non-overlapping voxels were selected in the cerebellum and in the gray (GM) and white matter (WM) of the occipital-parietal lobe of the brain (Figure 2).

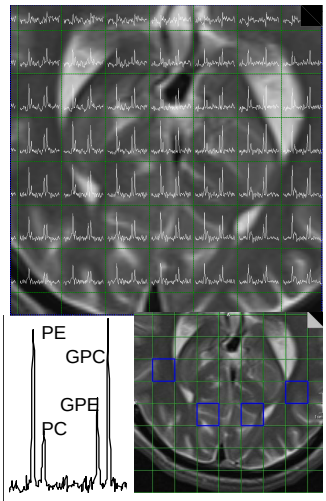

Figure 2: spectral map of sRINEPT in the normal brain. One spectrum is enlarged (bottom left). Selected voxels in mainly gray and white matter are indicated in blue.

Results and discussion:

Taking all measurements together, no significant differences were found between metabolite ratios of voxels in the GM, WM and cerebellum (Figure 3). However, an analysis per person showed small differences between the gray and white matter. For PE/GPE the mean difference was 0.16±0.17, for PC/GPC this was 0.05±0.07 (Figure 3, data not shown for PC/GPC). The PE/GPE and PE/GPC ratio were related to the age of the volunteer: the older the person, the lower the PE/GPE or PE/GPC value (significant non-zero slope after linear regression analysis, p=0.0001, Figure 4). There was no relation between the PC/GPC or GPE/GPC ratio and age. The mean ± standard deviation of the PE/GPE and PC/GPC ratios were 1.9±0.35 and 1.5±0.27 and 0.35±0.13 and 0.29±0.11 for the age groups 23-34 and 50-59 respectively. It is known that the levels of several brain metabolites are age dependent, particularly in children (< 16 yr) [8]. In a study using single voxel ^{1}H decoupled ^{31}PMRS the age dependencies for phosphocholine and -ethanolamine compounds were evaluated and this showed a striking inverse correlation for the PE/GPE ratio with age at younger age [9]. This phenomenon is possibly related to myelination. Our study, using a more sensitive ^{31}P MRS approach, demonstrates a continuation at older age of this inverse correlation. As we are looking at metabolite ratios it likely represents an intrinsic property of brain metabolism rather than a morphological change.

Conclusion:

We demonstrated a MRSI method for optimal polarization transfer of ^{1}H to ^{31}P spins in the molecules PE, PC, GPE and GPC. Mean values and standard deviations were established for ratios of these compounds in the normal human brain. The ratio PE/GPE in the brain decreases with increasing age. PC/GPC did not show this dependency. With the current resolution we detected differences in metabolite ratios between GM and WM. Given the available SNR it is possible to increase resolution and decrease partial volume effects for a better evaluation of metabolite levels of specific tissues in the brain. The sRINEPT MRSI technique enables further exploration of the phosholipid metabolism of brain diseases in vivo with a better sensitivity than earlier ^{31}P MRS methods.

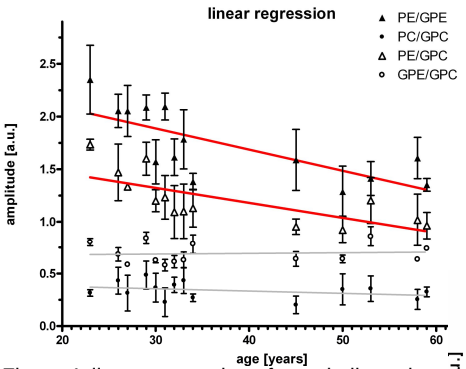

Figure 4: linear regression of metabolite ratios and volunteer age. Data points are mean ± sd of 5 independent voxels in the brain.

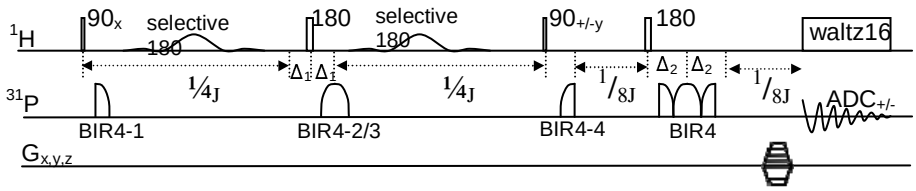

Figure 1: Pulse sequence of sRINEPT with chemical shift selective refocusing pulses applied on a single transmit channel (pulses are applied sequentially with Δ_1=1.3ms and Δ_2=2.3ms). The second hard 90^0 pulse was phase-cycled together with the phase of the receiver.

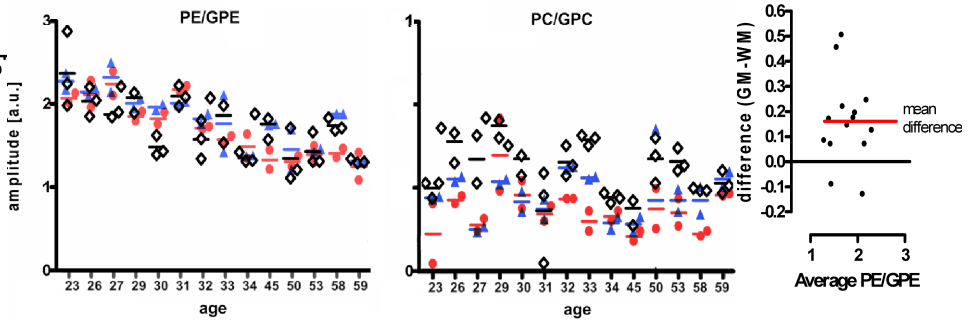

Figure 3: PE/GPE and PC/GPC ratios of WM (red circles), GM (blue triangles) and cerebellum (black squares) of the selected voxels in each volunteer. Plot of difference of ratio GE/GPE between GM and WM of all volunteers.

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