Multinuclear localized spectroscopy in the human brain at 4.7T – dynamic observation of ethanol uptake and changes in cerebral metabolites from ^{1}H and ^{31}P windows

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Introduction

Multinuclear spectroscopy in the same localized area gives multiple windows for local metabolic events. We are developing a method for multinuclear localized spectroscopy for ^{1}H, ^{31}P, and ^{13}C (TRINITY) at 4.7T wholebody spectrometer [1]. In the present work the multinuclear spectroscopy for ^{1}H and ^{31}P was applied to the human brain after alcohol drinking. Ethanol reaches into the brain very rapidly after drinking, modulates BOLD responses in the visual and auditory cortex, and causes acute intoxication [2,3]. The goal of this work was to chase the dynamical uptake of ethanol in the occipital lobe and to detect associated changes in the cerebral metabolites from the windows of ^{1}H and ^{31}P MRS simultaneously. We also propose an absolute quantification method for ethanol and ^{1}H metabolites based on the tissue segmentation.

Methods

^{1}H and ^{31}P MRS measurements from the same localized area in the human brain was performed with a combined sequence of STEAM for ^{1}H [4] and ISIS for ^{31}P using a ^{1}H/^{31}P probe constructed with a quadrature ^{31}P surface coil and ^{1}H TEM coil for head as described before [1] at a 4.7T wholebody MRI system. Four healthy male subjects drank 38 (at one time) – 152 g (in two times) of ethanol in rice wine (ethanol 19%). ROI of 3x3x3cm^{3} was located at the occipital lobe before the administration of ethanol and localized shimming was performed to attain the half height width of unsuppressed water resonance of 9-11Hz. ^{1}H and ^{31}P spectra were obtained in 8 blocks of 32 transients with TR=5s, TE=4ms (for ^{1}H), and TM=33ms (for ^{1}H) before and after ethanol drinking. Ethanol and metabolites in the ^{1}H spectra in each block (32 transients) were quantified using an LCModel program with ethanol and water added into the basis set of major five cerebral metabolites. Comparison of the unsuppressed water signal in the ROI with that in the basis set gives the water concentration in the ROI multiplied with a factor x which is derived from the signal attenuation due to the difference between *in vivo* and basis set measurements, such as Q factor and B_1 inhomogeniety. If the water concentration *in vivo* were known, the factor x is calculated from this comparison, and can be used to calibrate results of LCModel to obtain absolute concentrations of ethanol and metabolites in the ROI. For this purpose the water concentration was calculated from the tissue segmentation in the ROI performed in the separate 3D MDEFT measurement by assuming concentrations of water in grey matter (GM), white matter (WM), and CSF are 43.30, 35.88, and 55.50 mol/l tissue, respectively [5]. In one subject the ROI located in the present work was segmented as GM=74.67, WM=9.97, and CSF=15.34%, thus the water concentration in the ROI was calculated as 44.42 mol/l tissue, being used for the quantification of ethanol and metabolites. Since TRs for the measurements were long enough (5s for water-suppressed *in vivo* metabolites, 15s for basis set, no accumulation for *in vivo* water), and TE was as short as 4ms, no further correction was performed for T_1 and T_2 differences. For visual inspection and subtraction analysis, 4 blocks of transients were further averaged at ^{1}H and ^{31}P spectra.

Results and Discussion

Figure 1 shows ^{1}H and ^{31}P spectra in the occipital lobe of one subject who drank ethanol twice (38g at t=0, and 23.8g at t=43 min). Methyl (1.18ppm) and methylene (3.65 ppm) resonances of ethanol are clearly identified in addition to the intrinsic metabolites after t=15.3min. Ethanol concentration in each spectrum was quantified as 0, 0, 7.25, 8.94, 18.98, and 19.55mmol/l tissue from the bottom to the top with corresponding NAA as 8.64, 9.53, 8.74, 9.11, 10.07, and 9.32mmol/l tissue. This result suggested no change in NAA while cerebral ethanol was stepwise increased corresponding to an amount of drinking. With cerebral ethanol up to 26.66mmol/l, no change was observed in the intrinsic metabolites in the ^{1}H spectrum in every 4 subject. On the other hand, broadening of the Pi resonance was observed in ^{31}P spectra in Fig.1 after the 2nd drinking of ethanol while no change in PCr, suggesting the inhomogeneous pH environments in the region. Even a slight acidification from 7.02 to 6.98 was observed along with the broadening of the Pi resonance in another subject whose cerebral ethanol was 26.66mmol/l.

Conclusions

Multinuclear localized spectroscopy was demonstrated to give a dynamical uptake of ethanol along with a change in the ^{31}P spectra in the human brain after ethanol drinking. A new approach of the quantification of ethanol and ^{1}H metabolites using water signal as the internal reference was also proposed.

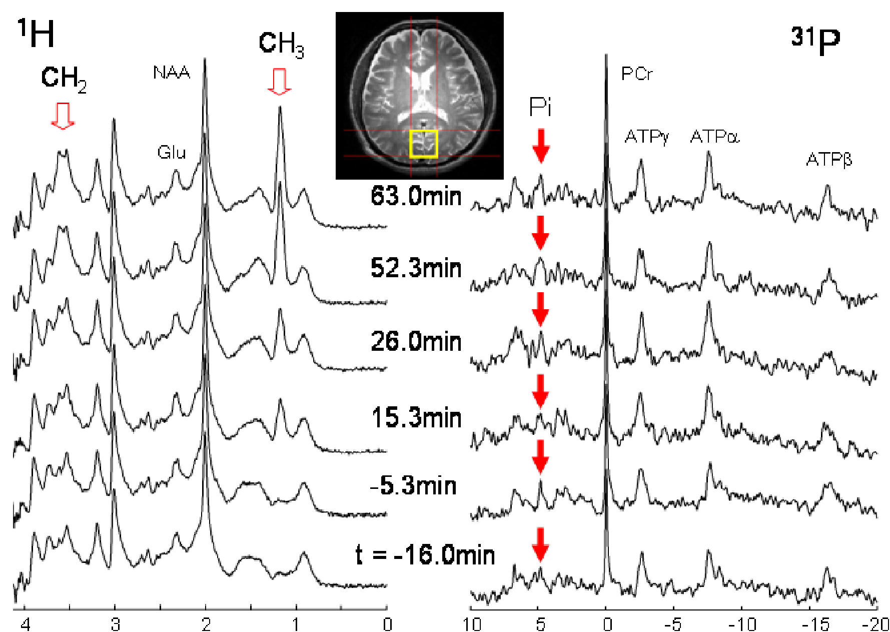

Fig.1. ^{1}H and ^{31}P localized spectra obtained from the area of 3x3x3 cm^{3} at the occipital lobe (see middle upper insertion) before and after drinking ethanol twice (38g at t=0, and 23.8g at t=43 min). Each spectrum is the sum of 4 blocks of 32 transients (10.7min). TR/TE/TM = 5000/4/33 ms. Open arrows show the methyl and methylene resonances of ethanol in ^{1}H spectra, and closed arrows show the Pi resonance in the ^{31}P spectra.

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