1H MR Spectroscopic Imaging in Patients with MRI-Negative Extratemporal Focal Epilepsy

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Introduction

It seems probable that ^{1}H MRS may help in the lateralization of extratemporal epilepsy. In the study we aimed to verify the hypothesis that ^{1}H MRS could also help in the localization of the epileptogenic zone. We report on seven patients who underwent epilepsy surgery for refractory extratemporal epilepsy with normal MRI findings. In all cases, ^{1}H MRS abnormalities were precisely correlated with the findings from other non-invasive diagnostic tests, subdural electrode mapping and histopathology.

Subjects & Methods

Seven patients (8 - 23 years old) with the diagnosis of intractable extratemporal epilepsy based on the seizure semiology and EEG findings and at least two negative MRI examinations were examined. The presurgical protocol included ^{1}H MRS, video-EEG monitoring, SPECT and PET; the resected tissue was histopathologically examined. Six healthy controls (25 - 32 years old) were examined by ^{1}H MRS for comparison with patients. All subjects were informed about the examination protocol, which was approved by the local ethical committee.

^{1}H MRS examination was performed on a 1.5T MR system using CSI technique focused to supposed epileptogenic zone localized by the previous results of scalp EEG, FDG-PET, and/or ictal SPECT. CSI was performed by standard Siemens sequence in transversal plane with the following parameters: TR/TE=1500/135 ms, 16x16 steps, 1 acquisition, slice thickness 20 mm, nominal voxel volume 2 ml. The evaluation of CSI data was done using the program CULICH which is based on the LCModel technique [1]. Signal intensities of NAA, Cr and Cho and their ratios were used for the calculation of metabolic maps. Error maps characterizing the statistical significance of the calculated results were used to exclude parts of the spectra with an error greater than 15% for metabolite images and 30% for their ratios. The description of metabolic abnormalities was done in two steps. First, metabolic images were evaluated visually and the position of the lesion was proposed on the basis of minima in the metabolic maps. In the second step, the coefficient of asymmetry C_a was calculated [2]. The lateralization of a metabolic abnormality in patients was based on the calculation of the C_a and its comparison with C_a of controls. The localization of the preoperative ^{1}H MRS metabolite maps was co-registered with the resection cavity on postoperative MRI.

Results

In the first step of CSI analysis, metabolic ratio maps were visually inspected; all patients had a visible asymmetry in images of metabolite concentrations (or their ratios). In the second step, the signal intensities obtained from the analysis of individual spectra from voxels in gray or white mater were used to calculate the coefficient of asymmetry C_a.

In patients 1, 2, 5 and 6, the lateralization and localization of the metabolic abnormalities corresponded well with the position of the resection (for a case, see Figure); the coefficient of asymmetry also confirmed the lateralization (see Table). In patient 4, visual inspection showed two visible metabolite minima (in both lobes), however without any significant difference in C_a to controls. In patients 3 and 7, only lateralization based on overall changes in C_a in gray matter was described because no local minima in the examined CSI areas were visible. In these subjects, the resection was outside the regions examined by CSI.

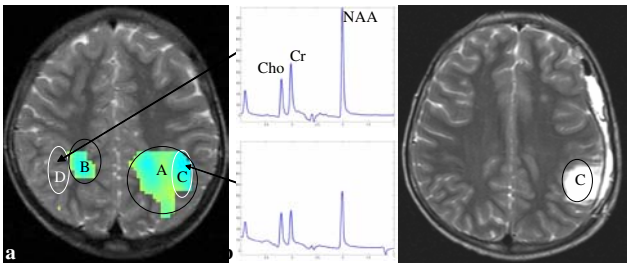
Table. Comparison of CSI results and final results of surgery and histopathology.

	C_a(NAA/Cr)	C_a(NAA/Cho)	C_a(Cho/Cr)	Surgery
Gray matter in controls	**0.08** *(0.16)*	**-0.05** *(0.19)*	**0.13**$^+$ *(0.21)*	
Patient 1	**-0.20*** *(0.11)*	**-0.19** *(0.24)*	**-0.01** *(0.31)*	P sin
Patient 2	**0.12** *(0.04)*	**0.26*** *(0.05)*	**0.14*** *(0.08)*	F dx
Patient 3	**-0.11*** *(0.21)*	**-0.33*** *(0.25)*	**0.22** *(0.33)*	O sin
Patient 4	**0.04** *(0.10)*	**-0.10** *(0.14)*	**0.15** *(0.11)*	F sin
Patient 5	**0.22*** *(0.22)*	**-0.27*** *(0.17)*	**0.48*** *(0.21)*	F sin
Patient 6	**-0.12*** *(0.12)*	**-0.24*** *(0.10)*	**0.09** *(0.16)*	F sin
Patient 7	**-0.17*** *(0.15)*	**-0.24** *(0.32)*	**0.07** *(0.22)*	P sin

Coefficient of asymmetry (C_a; standard deviations are in brackets) was calculated by the equation $C_a=2*({}^xR_{sin} - {}^xR_{dx})/({}^xR_{sin} + {}^xR_{dx})$, where ^{x} is the metabolite under investigation (NAA, Cr or Cho) and R is the metabolite concentration ratio in the left (sin) and right (dx) hemispheres (symmetrically with respect to the central line).

Significance was defined as $p<0.05$;
Abbreviations: P- parietal; F- frontal; O- occipital; sin - left; dx - right;
$^+p<0.05$ between C_a in gray matter and white matter;
$^*p<0.05$ between C_a in gray matter

Figure. Results from patient 1.



a) The projection CSI map of NAA/Cho minima onto the T2w image of patient 1 before surgery; a much large hypointensive area was observed in the left lobe (A) compared to the right one (B). In area (A), a hypointensive minimum was found in the gray matter (C) and the coefficient of asymmetry (see Table) was calculated for voxels in the gray matter (C) and contralaterally (D);
b) ^{1}H MR spectra from symmetrical voxels in areas C and D represent the differences in the relative concentrations of NAA/Cho: C/D ~ 4.8/8.3. Also, the decrease in the total intensity of the signals in the spectrum from the area C is clearly visible;
c) T2w image obtained one month after resection. The location of surgery corresponds to the minima in the CSI image (C).

Discussion

Retrospective correlation of ^{1}H MRS and ictal SPECT changes with the localization of the resection cavity on postoperative MRI showed an overlap of these regions in all the patients with a localized ^{1}H MRS and/or ictal SPECT abnormality. In the patients with a clearly localized metabolic abnormality (1, 2, 4, 5, 6), the ictal onset zone (based on the subdural electrode mapping) overlapped with ^{1}H MRS changes. In all cases, histological examination of the resected brain tissue revealed an MRI-undetected focal cortical dysplasia.

In conclusion, the present study found promising results concerning the sensitivity of ^{1}H MRS in patients with MRI-undetectable malformations of cortical development. In our group of patients, ^{1}H MRS helped not only to lateralize, but also to localize the epileptogenic zone and therefore showed practical value for designing the surgical approach. The most important message of the study is the good correlation among ^{1}H MRS, ictal SPECT and subdural mapping, which was subsequently confirmed by histopathological analysis of the resected tissue. We suggest that ^{1}H MRS may provide important additional data in the presurgical evaluation of patients without apparent MRI lesions.

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References

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