1H MR spectroscopy in histopathological subgroups of mesial temporal lobe epilepsy

Abstract The aim of the study was to analyze the lateralizing value of proton magnetic resonance spectroscopy (1H MRS) in histopathologically different subgroups of mesial temporal lobe epilepsies (MTLE) and to correlate results with clinical, MRI and seizure outcome data. A group of 35 patients who underwent resective epilepsy surgery was retrospectively studied. Hippocampal 1H MR spectra were evaluated. Metabolite concentrations were obtained using LCModel and NAA/Cr, NAA/Cho, NAA/(Cr+Cho), Cho/Cr ratios and coefficients of asymmetry were calculated. MRI correctly lateralized 89% of subjects and 1H MRS 83%. MRI together with 1H MRS correctly lateralized 100% of patients. Nineteen subjects had “classical” hippocampal sclerosis (HS), whereas the remaining 16 patients had “mild” HS. Nineteen patients had histopathologically proven malformation of cortical development (MCD) in the temporal pole; 16 subjects had only HS. No difference in 1H MRS findings was found between patients in different histopathological subgroups of MTLE. Our results support the hypothesis that 1H MRS abnormalities do not directly reflect histopathological changes in MTLE patients. Subjects with non-lateralized 1H MRS abnormalities did not have a worse postoperative seizure outcome. We found no significant impact of contralateral 1H MRS abnormality on post-surgical seizure outcome.

Keywords MR spectroscopy · Temporal lobe epilepsy · Hippocampus · Malformations of cortical development · Treatment outcome

Introduction

Proton magnetic resonance spectroscopy (1H MRS) is a well-established non-invasive diagnostic method. In epilepsy, 1H MRS has been used for the lateralization or localization of the epileptogenic zone [1–6]. The majority of studies focused on temporal and especially mesial temporal lobe epilepsy (MTLE). It has been repeatedly demonstrated that the decrease in the N-acetylaspartate (NAA) signal intensity, ratios of NAA to total creatine (NAA/Cr), to choline (NAA/Cho) and to the sum of creatine and choline (NAA/[Cr+Cho]) well reflect the presence of the epileptogenic zone in the temporal area [7–11]. A good relation between 1H MRS findings and the
results of other diagnostic techniques such as MRI, EEG and PET was reported [12–14]. The nature of metabolite abnormalities in MTLE is not fully understood. They were originally attributed to neuronal loss in the presence of hippocampal sclerosis (HS) [15]. Numerous studies, however, demonstrated that $^1$H MR spectra describe a more complex brain pathology [16–20].

MTLE is not a uniform entity. Various degrees of neuronal loss and reactive astrogliosis in the hippocampus and adjacent temporal structures have been described [21]. Further HS could be only a part of temporal lobe pathology [16–20]. It has been suggested that different histopathological subgroups of MTLE may have different etiopathogeneses [23, 26], but a relationship to $^1$H MRS findings has been only rarely approached [27].

The aim of the present study was to analyze $^1$H MRS findings in histopathological subgroups of MTLE associated with HS as well as to assess their relation to clinical data and post-surgical seizure outcome.

**Methods**

**Subjects**

A cohort of patients who underwent resective surgery for intractable epilepsy between 1999 and 2005 was retrospectively reviewed (see Table 1). We selected patients who (1) underwent anteromedial temporal lobe resection because of MTLE, (2) had good-quality preoperative MRI and hippocampal $^1$H MRS, (3) had available neuropathological analysis of the hippocampus and the temporal pole, and (4) were followed for at least 2 years after the surgery. A total of 35 patients (20 women and 15 men) met the inclusion criteria. Their seizure semiology was always consistent with MTLE. Seizure frequency ranged from 1 to 100 per month. For the purpose of a relationship with $^1$H MRS findings, we divided patients into two groups according to their seizure frequency: (1) frequency ≤10 seizures per month (n = 27, mean seizure frequency 4.7 seizures per month) and (2) frequency ≥12 seizures per month (n = 8, mean seizure frequency 38.9 seizures per month). Secondary generalized tonic-clonic seizures occurred in 27 subjects. Ten patients had a lateralization sign in their neurological findings (mild central facial nerve paresis and/or hemiparesis). Three other patients expressed different non-lateralizing neurological findings (e.g. ataxia).

A risk factor for epilepsy (initial precipitating injury) was present in the history of 19 patients. This consisted of complicated febrile seizures in ten patients, meningitis in six patients, encephalitis in one patient, meningoencephalitis in three patients, and perinatal asphyxia in four patients. Further, eight subjects had a history of simple febrile seizures. The remaining eight patients had no risk factors for epilepsy.

Besides MRI and $^1$H MRS, all the patients had video-EEG monitoring. Intracranial EEG investigations were conducted in two subjects. Selected patients also underwent $^{18}$FDG-PET, ictal or interictal $^{99m}$Tc-ECD, and the intracarotid amobarbital procedure. The side of the surgery was based on the relation of the patient’s history with results of all preoperative investigations. Only MRI, $^1$H MRS and histopathology were evaluated in this study.

**$^1$H MR imaging**

Routine MRI examinations were performed on a 1.5-T whole-body MR imager (Gyroscan Intera, Philips) with a standard head coil. The MRI protocol included 1.5-mm thick T2-weighted turbo spin echo (TSE) and T1-weighted inversion recovery slices as well as 5-mm thick fluid attenuated inversion recovery (FLAIR) in the coronal and axial planes. Hippocampal atrophy and signal changes were visually assessed by four neuroradiologists.

**$^1$H MR spectroscopy**

$^1$H MRS examinations were performed on a Siemens Vision 1.5 T. Symmetrical areas of the left and right hippocampus were selected for single voxel $^1$H MRS [PRESS sequence: TR/TE = 5,000/135ms, 64 acquisitions, a volume of interest (VOI) of 3–5 ml]. VOI was represented by rectangle with the longest side in transversal slice.

Spectra were evaluated using the LCModel method [28, 29] and signal intensities corresponding to concentrations of choline compounds (Cho), total creatine (Cr) and N-acetylaspartate (NAA) in laboratory units were obtained.

The signal ratios R of NAA/Cr, NAA/Cho and NAA/(Cr+Cho) were calculated in each hippocampus, and the coefficient of asymmetry $C_a$

$$C_a = 2 * (R_{\text{sin}} - R_{\text{dx}}) / (R_{\text{sin}} + R_{\text{dx}})$$

representing a difference between left (sin) and right (dx) hippocampus in these ratios was also used for comparison with controls (see Table 2). Hippocampal spectra were considered abnormal if any of the calculated metabolite ratios were outside the interval of confidence ($p = 0.05$) of the control values.

The finding was considered “lateralized” if at least two coefficients of asymmetry were not within the intervals of confidence derived from the $C_a$ values of controls in the same orientation. The side of $^1$H MRS abnormality was then compared with the side of surgery and classified as
<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex/age at surgery (years)</th>
<th>Initial insult</th>
<th>Age at start of SZ (years)</th>
<th>Duration of epilepsy (years)</th>
<th>SGTC S</th>
<th>SGTCS Frequency (per month)</th>
<th>MRI lateralization</th>
<th>MRS lateralization</th>
<th>MRS group</th>
<th>HS type</th>
<th>Temporal pole histology</th>
<th>Outcome at 2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/18</td>
<td>CFS</td>
<td>2</td>
<td>16</td>
<td>Yes</td>
<td>≥12</td>
<td>Bilat Ipsi</td>
<td>B</td>
<td>Classical</td>
<td>Normal</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>F/21</td>
<td>ME-itis</td>
<td>1</td>
<td>20</td>
<td>Yes</td>
<td>≤10</td>
<td>Ipsi Ipsi B</td>
<td>A</td>
<td>Classical</td>
<td>Normal</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>M/38</td>
<td>FS</td>
<td>12</td>
<td>26</td>
<td>Yes</td>
<td>≥12</td>
<td>Ipsi Ipsi A</td>
<td>Classical</td>
<td>Normal</td>
<td>Ia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F/20</td>
<td>CFS</td>
<td>12</td>
<td>8</td>
<td>No</td>
<td>≤10</td>
<td>Ipsi Ipsi A</td>
<td>A</td>
<td>Classical</td>
<td>Normal</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F/17</td>
<td>CFS</td>
<td>8</td>
<td>9</td>
<td>Yes</td>
<td>≤10</td>
<td>Ipsi Non-lateralized</td>
<td>A</td>
<td>Classical</td>
<td>Normal</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M/30</td>
<td>FS</td>
<td>5</td>
<td>25</td>
<td>Yes</td>
<td>≤10</td>
<td>Ipsi Non-lateralized</td>
<td>B</td>
<td>Classical</td>
<td>Normal</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>M/31</td>
<td>Perinat, FS</td>
<td>7</td>
<td>24</td>
<td>Yes</td>
<td>≤10</td>
<td>Ipsi Non-lateralized</td>
<td>B</td>
<td>Classical</td>
<td>Normal</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M/37</td>
<td>CFS</td>
<td>12</td>
<td>25</td>
<td>Yes</td>
<td>≤10</td>
<td>Ipsi Ipsi B</td>
<td>B</td>
<td>Classical</td>
<td>Gliosis</td>
<td>II</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M/26</td>
<td>Perinat, E-itis, CFS</td>
<td>3</td>
<td>23</td>
<td>No</td>
<td>≤10</td>
<td>Ipsi Ipsi B</td>
<td>B</td>
<td>Classical</td>
<td>Gliosis</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>F/24</td>
<td>M-itis</td>
<td>3</td>
<td>21</td>
<td>No</td>
<td>≤10</td>
<td>Ipsi Ipsi A</td>
<td>A</td>
<td>Classical</td>
<td>Gliosis</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>M/10</td>
<td>CFS</td>
<td>4</td>
<td>6</td>
<td>Yes</td>
<td>≥12</td>
<td>Bilat Ipsi</td>
<td>A</td>
<td>Classical</td>
<td>mMCD I</td>
<td>Ib</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>M/39</td>
<td>CFS</td>
<td>22</td>
<td>17</td>
<td>Yes</td>
<td>≤10</td>
<td>Ipsi Ipsi B</td>
<td>Classical</td>
<td>mMCD II</td>
<td>Ia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>M/16</td>
<td>CFS</td>
<td>2</td>
<td>14</td>
<td>No</td>
<td>≥12</td>
<td>Ipsi Ipsi B</td>
<td>Classical</td>
<td>FCD IA</td>
<td>Ia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>F/21</td>
<td>FS</td>
<td>8</td>
<td>13</td>
<td>Yes</td>
<td>≤10</td>
<td>Bilat Ipsi</td>
<td>A</td>
<td>Classical</td>
<td>FCD IA</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>F/17</td>
<td>Perinat, CFS</td>
<td>6</td>
<td>11</td>
<td>Yes</td>
<td>≤10</td>
<td>Ipsi Ipsi A</td>
<td>Classical</td>
<td>FCD IA</td>
<td>Ib</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>M/13</td>
<td>CFS</td>
<td>3</td>
<td>10</td>
<td>No</td>
<td>≤10</td>
<td>Ipsi Non-lateralized</td>
<td>A</td>
<td>Classical</td>
<td>FCD IA</td>
<td>II</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>F/21</td>
<td>M-itis, FS</td>
<td>16</td>
<td>5</td>
<td>Yes</td>
<td>≥12</td>
<td>Ipsi Ipsi A</td>
<td>A</td>
<td>Classical</td>
<td>FCD IA</td>
<td>Ia</td>
<td></td>
</tr>
</tbody>
</table>

*Note: For patients 18-32, the table continues with the same format.*
ipsilateral if abnormal MR spectra corresponded to the side of surgery.

The control group consisted of 30 MR spectra from 15 healthy volunteers. Written consent was obtained from all subjects according to the local Ethical Committee rules.

Neuropathology

All specimens were fixed in 10% neutral buffered formalin. Hematoxylin and eosin staining was available for all specimens. To assess the degree of gliosis and the altered antigenic properties of cells in MCD, standard immunoperoxidase staining was performed using antibodies against glial fibrillary acidic protein (clone 6F2, DakoCytomation) and neurofilaments (clone 2F11, DakoCytomation). The finding in the hippocampus was interpreted as a HS of classical type when there was a complete absence of pyramidal neurons (only solitary residual neurons were accepted) in both the CA1 and CA4 hippocampal sectors accompanied by gliotic scarring. As a mild type of HS, we considered those cases in which there was a milder degree of neuronal loss (but still at least a 50% decline in neuronal numbers) in CA1 and/or CA4 and the accompanying gliosis was only minimal. The current classification [30] was used for evaluating malformations of cortical development.

Outcome analysis

The follow-up period ranged from 24 to 91 months (mean, 47.7 months). For the purpose of the study, seizure outcome at 2 years of follow-up was analyzed. A modified Engel outcome scale [31] was used for the classification of the seizure outcome: seizure-free patients (Engel Ia category); subjects with persisting auras (Engel Ib); Engel II, ≥90% seizure reduction or nocturnal seizures only; Engel III, ≥50% seizure reduction; Engel IV, <50% seizure reduction.

Statistical analysis

For the statistics, 1H MR spectra were divided into lateralized and non-lateralized. The results of 1H MRS lateralization were also compared with the side of surgery and divided into groups A and B (see below). 1H MRS results were then compared with clinical and histopathological data. ANOVA and t-tests (Statistica6 software) were used for comparison of patients from group A and group B of 1H MRS findings. Fisher’s exact test (two-tailed) was used to test for differences between the groups for dichotomous variables. The Mann-Whitney U test (two-tailed) was used for continuous or ordinal variables. The level of statistical significance was set at 5%.
Results

MRI and \(^1\)H MRS

Clinical, MRI, \(^1\)H MRS and histopathological features of selected patients are reported in Table 1. No patient exhibited MRI or \(^1\)H MRS abnormalities solely contralateral to the side of surgery. No MRI abnormalities outside the temporal lobes were found. Twenty-five patients had unilateral and concordant MRI and \(^1\)H MRS abnormality in agreement with the side of surgery. In six patients with unilateral MRI abnormality (nos. 5, 6, 7, 16, 18 and 22, see Table 1), \(^1\)H MRS did not reveal asymmetry between the left and right hippocampus, and these findings were considered as MRS non-lateralized. Three of them had normal values at least in two metabolite ratios in the contralateral side to surgery (nos. 5, 16, 18). In four cases (nos. 1, 11, 14 and 28) MRI found bilateral hippocampal atrophy and signal change; these MRI abnormalities were classified as bilateral. In all of them \(^1\)H MRS showed asymmetry that correctly lateralized the epileptogenic zone and the side of the surgery.

Concerning spectroscopic data, we compared ratios of signal intensities calculated from spectra (for example, see Fig. 1) of the ipsilateral and contralateral hippocampal areas with respect to the side of surgery (see Table 2). Groups of subjects are presented in the Fig. 2. A tt h e contralateral side, metabolite ratios were inside the control range in 23 patients (including 3 patients with non-lateralized finding on the base of Ca), and statistically significant metabolic abnormalities were found in all ipsilateral areas (unilateral MRS findings — group A). The remaining 12 patients (including 3 patients with non-lateralized finding on the base of Ca) had values of ipsi- and contralateral

![Fig. 1 An example of the \(^1\)H MR spectra obtained in the left and right hippocampal areas in patient 25 with right hippocampal sclerosis. The asymmetry in signal ratios between the ipsilateral (right) and contralateral (left) hippocampus is clearly visible. NAA, N-acetylaspartate; Cr, total creatine; Cho, choline compounds](image)
metabolite ratios significantly different from control values in both sides (bilateral MRS findings — group B), and also from values of the contralateral side of the group A.

Neuropathology

Neuropathological results are depicted in Tables 1 and 3. HS was proven in all the subjects. More pronounced (“classical”) HS was encountered in 19 (54%) patients, and a “mild” type of HS was present in 16 (46%) patients. Regarding temporal pole pathology, HS was associated with MCD (“dual pathology”) in 19 (54%) cases, whereas 16 (46%) subjects had isolated HS. Nine (26%) patients had another temporal pole pathology such as gliosis or meningeal fibrosis.

Outcome

Twenty-one patients were seizure-free 2 years after surgery (outcome Engel Ia). Four patients had auras only (outcome Engel Ib). Five subjects had ≥90% seizure reduction or nocturnal seizures only (outcome Engel II). Four patients had significant (≥50%) reduction of seizure frequency (outcome Engel III). There was only one patient without any improvement (outcome Engel IV). For comparison of outcomes with results of imaging techniques and histopathology, we divided patients into groups of completely seizure-free (Engel Ia, n = 21) and not-seizure-free (n = 14).

Relation of 1H MRS findings to clinical data, seizure outcome and histopathology

Comparisons between 1H MRS findings and clinical, seizure outcome and histopathological data are shown in Table 4. There were no differences between patients with lateralized and non-lateralized 1H MRS abnormalities in incidence of initial precipitating injuries and mean duration of epilepsy. Subjects with non-lateralized 1H MRS changes tended to have earlier age at seizure onset, less frequent seizures and a higher proportion of secondarily generalized tonic-clonic seizures. Five of six cases with non-lateralized 1H MRS findings were seizure-free after the surgery (Engel

<table>
<thead>
<tr>
<th>Table 3 Histopathological results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>HS without MCD</td>
</tr>
<tr>
<td>HS+MCD</td>
</tr>
</tbody>
</table>

HS, hippocampal sclerosis; MCD, malformation of cortical development. See text for comments
Ia category). There was no statistically significant difference between MRS parameters of lateralized and non-lateralized groups of subjects. No significant differences in clinical parameters and in seizure outcome (2 years from surgery) were found between subjects from group A and group B.

Regarding comparisons of 1H MRS data with histopathology, we found no differences between patients with lateralized and non-lateralized 1H MRS findings as well as subjects from group A and group B relative to HS types (classical vs. mild) and incidence of temporal pole MCD.

Discussion

We found in our cohort that 1H MRS changes in hippocampi: (1) were not in relationship with the histopathological severity of HS as well as with the presence of other histopathological abnormalities in the temporal pole, (2) were not unequivocally related to clinical data such as history of initial precipitating injuries, seizure frequency and types of seizures and (3) were not associated with unfavorable post-surgical seizure outcome. Our results moreover proved a high lateralization value of 1H MRS in the MTLE population and suggested its contribution in cases with bilateral MRI abnormalities.

We defined two groups of patients with different 1H MRS findings contralaterally to the side of surgery. First, subjects of group A had ipsi-laterally abnormal spectra only. Second, group B consisted of all subjects with bilateral metabolic changes. In both groups we found patients with lateralized or non-lateralized 1H MRS findings based on C_{a}. In all lateralized patients with 1H MRS findings corresponded to the side of surgery. When comparing clinical and histopathological variables, no significant differences were found between groups A and B.

Our results agree with recent studies showing no relation between 1H MRS findings and the extent of hippocampal cell loss. It was concluded that the NAA/Cr ratio may not reflect the full extent of hippocampal neuronal cell loss and may provide a more accurate measurement of recent neuronal injury caused by epileptic activity [19, 20, 32].

We tried to explain the 1H MRS findings by comparing the results with clinical data, such as risk factors of epilepsy, duration of epilepsy, types and frequency of seizures. If the theory about a functional background of 1H MRS abnormalities is valid, higher seizure frequency, longer duration of epilepsy or more frequent secondary generalization of seizures might be expected in subjects with bilateral 1H MRS changes. However, our analysis failed to show these associations, contrary to studies [33] that have recently reported lower NAA and higher Cr values in patients with a higher frequency of interictal epileptiform discharges. Further studies on a larger series of patients are needed.

Significantly more frequent bilateral 1H MRS abnormalities in MTLE patients with histopathologically proven temporal pole MCD were reported [27], and the authors speculated about more widespread developmental changes in patients with cortical malformations that could be responsible for bilateral 1H MRS changes as well as for worse surgical outcomes in this group of patients. In contrast, four of our six cases with bilateral 1H MRS abnormalities had no MCD in their temporal poles.

Regarding the lateralization ability of 1H MRS, the method correctly lateralized 29 of 35 (83%) patients. The lateralization value of 1H MRS was thus comparable to that of MRI (89% correctly lateralized patients). Our results are in agreement with previous studies analyzing the lateralization ability of 1H MRS in MTLE. Most of these found correct lateralization results between 86% to 97% of subjects in a series [5, 7, 11, 15, 34–38].

In our series, 1H MRS was able to lateralize all patients with bilateral MRI changes. This interesting finding and possible contribution of 1H MRS to the diagnostics of patients with bilateral HS needs to be confirmed in further studies.

### Table 4: Comparison of 1H MRS findings with clinical, histopathological and seizure outcome data

<table>
<thead>
<tr>
<th></th>
<th>Lateralized</th>
<th>Non-lateralized</th>
<th>*Group A</th>
<th>*Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial insult</td>
<td>15/29 (52%)</td>
<td>4/6 (66%)</td>
<td>10/23 (43%)</td>
<td>9/12 (75%)</td>
</tr>
<tr>
<td>Mean age at SZ onset (years)</td>
<td>10.6</td>
<td>5.2</td>
<td>10.0</td>
<td>9.2</td>
</tr>
<tr>
<td>Mean duration of epilepsy (years)</td>
<td>19.6</td>
<td>20.2</td>
<td>17.4</td>
<td>24.2</td>
</tr>
<tr>
<td>SZ frequency ≥12 per month</td>
<td>8/29 (28%)</td>
<td>0/6</td>
<td>6/23 (26%)</td>
<td>2/12 (17%)</td>
</tr>
<tr>
<td>SGTCS</td>
<td>21/29 (72%)</td>
<td>6/6 (100%)</td>
<td>17/23 (74%)</td>
<td>10/12 (83%)</td>
</tr>
<tr>
<td>Seizure outcome Engel Ia</td>
<td>16/29 (55%)</td>
<td>5/6 (83%)</td>
<td>13/23 (57%)</td>
<td>8/12 (67%)</td>
</tr>
<tr>
<td>Classical HS</td>
<td>14/29 (48%)</td>
<td>5/6 (83%)</td>
<td>13/23 (57%)</td>
<td>6/12 (50%)</td>
</tr>
<tr>
<td>Mild HS</td>
<td>15/29 (52%)</td>
<td>1/6 (17%)</td>
<td>10/23 (43%)</td>
<td>6/12 (50%)</td>
</tr>
<tr>
<td>Temporal pole MCD</td>
<td>16/29 (55%)</td>
<td>3/6 (50%)</td>
<td>14/23 (61%)</td>
<td>5/12 (42%)</td>
</tr>
</tbody>
</table>

SZ, seizures; SGTCS, secondarily generalized tonic-clonic seizures; HS, hippocampal sclerosis, MCD, malformation of cortical development. (*See text and the Fig. 2 for explanation of 1H MRS groups)
When comparing the $^1$H MRS results with seizure outcome, the most striking observation was that 67% of patients in group B, and five of the six patients with non-lateralized $^1$H MRS abnormalities were seizure-free following surgery. Bilateral metabolite changes were therefore not a predictor of surgical failures in our series. This result did not support some previous studies [10, 38–40]. Recent meta-analysis supported the association of ipsilateral $^1$H MRS abnormality with favorable surgical outcome [41]. These series are, however, not directly comparable to ours since unilateral MRI changes prevailed in our subjects.

We suggest the explanation of the controversy may lie in the fact that $^1$H MRS findings are complex and dynamic. Besides neuronal loss, they are also influenced by concentration of astrocytes and membrane turnover. Moreover, functional changes such as epileptiform activity could also have an impact on the results. This may be supported by our findings in $^1$H MRS non-lateralized cases when majority of them had the classical (more pronounced) form of HS. The relationship of $^1$H MRS, histopathology and surgical outcome should therefore be resolved using a larger series of MTLE patients.

In conclusion, our $^1$H MRS findings were not influenced by the type of hippocampal pathology or the presence of MCD in the temporal pole. In agreement with previous studies [18, 19], no relation between MRS results and histopathology was found. We thus supported the view that $^1$H MRS metabolite changes are more probably caused by reversible neuronal dysfunction rather than by neuronal cell loss. As opposed to several previous studies [38–41], we found no significant impact of contralateral $^1$H MRS abnormality on post-surgical seizure outcome. This clinically important finding may assist in the management of MTLE patients.

Acknowledgement Supported by grants GACR no. 309/02/D076 and IGA no. NR/8843–4 and Research Projects nos. 00000064203 and MZ0002EM2005.

References


