Value Of Proton Magnetic Resonance Spectroscopy In Temporal Lobe Epilepsy

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Purpose

This study was conducted to investigate:

- The value of different parameters from different parts of the hippocampus derived from multi-voxel proton MR spectroscopy (MRS) in the lateralization of the epileptogenic zone in TLE patients which are clearly lateralized with electroencephalography (EEG).
- The distribution of metabolites along the longitudinal axis of the hippocampus in both healthy subjects and patients with TLE.
- Whether temporal lobe epilepsy is a fixed or a progressive disease.

Methods and Materials

We have studied 30 patients with temporal lobe epilepsy, which was clearly lateralized with EEG (13 male and 17 female, ages 7 to 55 years with the mean =29.8 years and SD=14.58) with a diagnosis of unilateral temporal lobe epilepsy and 10 healthy adult volunteers (4 males and 6 females, ages 22-50 years with the mean = 26.5 years and SD = 3.69). Informed consent was taken according to the commette of ethic in Alexandria University.

1- The mesial temporal lobes were investigated with MRI and multi-voxel MRS using a point-resolved spectroscopic sequence (PRESS) with an echo time of 135 ms. Magnetic resonance imaging was performed at 1.5 T using a standard head coil on closed Siemens Magnetom, Avanto (23 cases and 6 control subjects) and on Philips Medical System Nederland (7 cases and 4 control subjects).

There were three voxels in each hippocampus arranged in the anterior, middle and posterior parts of the hippocampal tissue, and each voxels had one spectrum (figure 1 and 2). From each spectrum the integral value of N-acetyl aspartate (NAA), Choline (Cho) and Creatine (Cr) were obtained and the NAA/Cho + Cr ratio was calculated. Additionally, the asymmetric index (AI) is calculated when bilateral normal or abnormal values are obtained. We used the EEG seizure localization finding as the standard against which data obtained by MRS were compared since none of our patients underwent surgery. We tested the ability of the investigated parameters in lateralization of TLE.

2- For the second aim; for each parameter (NAA, Cr, Cho and NAA/Cho+Cr) values from the anterior, middle and posterior parts of the hippocampus were grouped for each
location separately in the control subjects as well as in the TLE patients (both ipsilateral and contralateral sides).

3- for the third aim, a correlation analysis between the mean ipsilateral NAA/Cr and the duration of the seizure disorder in years was made.

**Statistical analyses**

Statistical analysis was done using the Statistical Package for the Social Science (SPSS) software package version 17.0 Statistical analyses. The probability "p" value was obtained from special table for probability. A "p" value of less than 0.05 was considered statistically significant. The Receiver operating characteristic curve (ROC curve) was used to evaluate the performance of classification schemes in which there is one variable with two categories by which subjects are classified.
**Fig. 1:** A series of the three orthogonal planes (a, b and c) needed for localization is obtained. The trans-axial CSI plane is approximately parallel to the long axis of the hippocampus. The VOI positioned over both hippocampi. The position is carefully checked and meticulously adjusted in all three orthogonal sections.

![Fig. 1: A series of the three orthogonal planes needed for localization.](image)

**Fig. 2:** There are three voxels in each hippocampus, the anterior (blue box), middle (red box) and posterior (green box) parts of the hippocampal tissue, and each voxel had one spectrum.

![Fig. 2: Three voxels in each hippocampus.](image)
Results

I-Magnetic resonance imaging (MRI).

According to MR imaging studies, only four of our patients had suspected unilateral abnormalities; this was depicted as subtle FLAIR hyperintense signal and mild temporal horn dilatation. Two patients showed temporal lobe atrophy, while the other two showed negative changes. None of examined patients had bilateral abnormalities and 26 patients had normal MRI results. (Figure 3)

II- Magnetic resonance spectroscopy (MRS).

• Proton MRS detected hippocampal abnormalities in all patients including those with normal MRI findings, where best concordant EEG lateralization findings was achieved by the NAA/Cho + Cr ratio from the posterior part of the hippocampus followed by the NAA/Cho + Cr ratio from the anterior position. However, by combining the lateralization results of the NAA/Cho + Cr ratio and the integral value of NAA from both anterior and posterior positions and with the additional use of asymmetry index, MRS was able to lateralize the epileptic focus in all patients. (figure 4,5&6)

• Regarding the integral value of NAA, the value is considered to be abnormal if less than or equal to 14.3 in the anterior hippocampal region and 34.4 posteriorly, while the cutoff value for the NAA/Cho+Cr ratio is 0.32 anteriorly and 0.65 posteriorly.

• From the ROC curves of the NAA integral values and NAA/Cho+Cr ratio, we found that the data from the middle location of the hippocampal in both curves has a large area under the curve, denoting high false positive results. Therefore middle position data were excluded from our statistical analysis and was not counted upon in the lateralization purpose. (figure 7,8)

• The asymmetric index (AI) is defined as the maximum asymmetry value found between right and left values in 10 healthy control subjects for a specific parameter (on individual basis). Here in our study, since the middle data are excluded from the lateralization purpose, the asymmetric index was calculated only for the anterior and posterior locations of the hippocampus.

• The AI in the control group for the integral value of NAA was 12.9 for the anterior group and for the posterior group it was 7.68. While the AI for the NAA/Cho+ Cr ratio was 0.14 for the anterior group and 0.09 for the posterior group.

• In epileptic patients, the asymmetry for a particular parameter was considered abnormal if it exceeded the control asymmetry index.

• Both Control subjects and patients showed significantly lower value for the integral value of NAA as well as for the ratio NAA/Cho+Cr in the anterior as
compared with the posterior part of the hippocampus. Moreover; ipsilateral integral values of NAA and NAA/ Cho + Cr ratios in TLE patients were lower than their corresponding hippocampal locations in the control group. These proportionate reductions were greatest in voxels from anterior hippocampal regions. *(figure 9-10)*

- **Coefficient of correlation** (*r*) was performed between the ipsilateral NAA/ Cr and the duration of seizures in years in 30 patients with unilateral TLE. *There was no significant correlation between duration of epilepsy in years and the ipsilateral temporal lobe NAA/Cr ratio in either parts of the hippocampus*

Images for this section:

Fig. 1: A series of the three orthogonal planes (a, b and c) needed for localization is obtained. The trans-axial CSI plane is approximately parallel to the long axis of the hippocampus. The VOI positioned over both hippocampi. The position is carefully checked and meticulously adjusted in all three orthogonal sections.
Fig. 2: There are three voxels in each hippocampus, the anterior (blue box), middle (red box) and posterior (green box) parts of the hippocampal tissue, and each voxel had one spectrum.
**Fig. 3:** Coronal FLAIR MR imaging in two different patients with temporal lobe epilepsy. (a): Showing mild right temporal horn dilatation. (b): Suspected hyperintense signal at the left hippocampus.

**Fig. 4:** Normal spectra from the hippocampus (on the left) and normal integral values for NAA, Cho and Cr in a healthy control subject (on the right).
Fig. 5: (A and B) 2D MRS applied in both axial and Sagittal section in a 21 years old female patient suffering from EEG proven left temporal lobe epilepsy. (C and D): spectra from anterior (E and F) posterior voxels revealed clear lateralization to the left side by the ratio NAA/Cho+Cr. (Anteriorly it was 0.53 on the right and 0.05 on the left and posteriorly it was 0.78 and 0.61 respectively). And by using the integral value of NAA as a mean of lateralization, clear lateralization was also made to the left side (The NAA anteriorly was 29.6 on the right and 5.14 on the left and posteriorly was 41.32 and 33 respectively). So this case was lateralized to the left side.
**Fig. 6:** 46 years old female patient suffering from left temporal epilepsy. (A) Axial FLAIR sequence showing suspected left mesial temporal sclerosis, with an 2D spectroscopy applied (as shown in image B). The NAA/ Cho +Cr ratio was calculated from the anterior position both on the right and left side(C and D), and it was 0.37 and 0.12 respectively, showing clear lateralization to the left side anteriorly. However, posteriorly (as shown in image E and F), bilateral abnormalities were detected with clear lateralization to the left (0.61 on the right and 0.44 on the left with AI#0.09). So lateralization in this case was made to the left side.
Fig. 7: ROC curve for NAA/Cho+Cr in the three locations of the hippocampus and its statistical analyses
**Fig. 8:** ROC curve for NAA in the three locations of the hippocampus and its statistical analyses
Fig. 9: Comparison between different locations of the hippocampus regarding the integral value of NAA (a) and the NAA/Cho+Cr ratio (b) in the control group.

Fig. 10: Comparison between different locations of the hippocampus regarding the integral value of NAA (a) and the NAA/Cho+Cr ratio (b) in the ipsilateral side in the patient group.
Conclusion

- $^1$H-MRS is able to contribute reasonable information in terms of metabolic alterations for assessing the affected hemisphere in MRI positive and even MRI negative TLE patients.
- It is also a useful and promising diagnostic tool in the evaluation of temporal lobe epilepsy, particularly for the detection of bilateral abnormalities.
- With an adequate AI, NAA/Cho+Cr ratio followed by the integral value of NAA are sensitive parameters in lateralization of the epileptogenic focus in patients with unilateral TLE. Furthermore; contralateral abnormalities are more common than previously thought, and may also indicate the appearance of metabolic abnormalities before morphologic changes take place in the disease pattern for complex partial seizures.
- In all control subjects and patients, for both ipsilateral and contralateral hippocampal tissue, the integral values of NAA and the NAA/Cho + Cr ratios exhibited a positive slope from anterior to posterior emphasizing the need for exact voxel selection in the clinical application of MRS.
- Hippocampal NAA/Cr does not correlate with duration of epilepsy in temporal lobe epilepsy. Our findings suggest that hippocampal neuronal dysfunction do not suggest a progressive damage.

References

REFERENCES


Personal Information