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Research Article

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DIAGNOSTIC VALUE OF MAGNETIC RESONANCE SPECTROSCOPY IN MORPHOMETRICAL ANALYSIS OF BASAL GANGLIA IN PATIENTS WITH IDIOPATHIC GENERALIZED EPILEPSY

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ABSTRACT

Idiopathic generalized epilepsy (IGE) is a kind of epilepsy that has tonic-clonic characteristic and myoclonic tensions and its clinical symptom starts from the first 20 years of the life. Proton magnetic resonance spectroscopy (H1-MRS) technique applies as a noninvasive procedure to find metabolic disorders by evaluating brain metabolites. Purpose of this study was to determine efficacy of the MRS in thalamus imaging of patients with IGE. Applying H1-MRS (technique: PRESS-CSI), we evaluated thalamus images of 63 people (35 controls: 23 males, 12 females, ranging in age 19-46 years, average: 34.8±0.62 years) and 28 IGE patients (10 males, 18 females, ranging in age 20-49 years, average: 37.4±1.04 years). The data analyzed by SPSS (v.20). Comparing the average NAA/Cr for the right thalamus, a significant reduction was seen between the control group and the IGE patients ($p<0.0001$). Likewise, for the left thalamus, the NAA/Cr was significantly decreased when we compared it for the control group and the IGE patients ($p<0.001$). H1-MRS could be a suitable diagnostic technique to evaluate epilepsy in IGE patients. The possible alteration of neuronal pathways in the thalamo-cortical circuit seems to play a critical role in epileptogenesis of IGE.

Keywords: Idiopathic epilepsy, thalamus, magnetic resonance spectroscopy.

INTRODUCTION

Epilepsy is brain disorders that mainly determine with frequently and depend on where in the brain the abnormal electrical signals occur. Epilepsy is not a disease with unique nature; however, diversity of the

neurologic symptoms shows signs of brain adventures which have different causes [1]. Idiopathic generalized epilepsy (IGE) is a sort of the epilepsy that from clinical point of view has tonic-clonic characteristic as well as myoclonic tensions, and its clinical symptom starts from the first two decades of the life [2]. In spite of the massive researches performed about IGE, the basic neuro-anatomical and neuro-chemical changes of IGE are not completely determined still; however, these two areas are under animal and clinical investigations. Over the years testimonials show that thalamus has a key role in synchronization of brain membrane [3]. Genetics researches, in animal models, reveal that in IGE the origin of pulses that cause discharging is thalamus and brain membrane [4]. Studies also demonstrate that due to different syndromes, there are various patterns in electroencephalogram (EEG); however, these findings are variable and thus sometimes EEG does not succeed in clinic [5]. On the other hand, usually evaluation of the images prepared by conventional MRI procedure from IGE patients is normal [6]. Furthermore, quantitative and functional evaluation increases sensitivity of the MRI in brain imaging. Studies have been illustrated that microscopic disorders and changes in IGE patients do not demonstrate by conventional MRI [7]. Proton-MR-spectroscopy (H1-MRS), as a noninvasive imaging procedure, prepares valuable information about metabolism rate of different tissues including brain [8, 9]. Moreover, it plays an important role in the evaluation of patients with traumatic spinal cord injury and multiple sclerosis patients [10, 11]. Nowadays, applying H1-MRS is increased; since it can differentiate various patterns of IEG [12]. Mory *et al.* [2003] used single voxel MRS to evaluate neuro malfunction of thalamus in adolescences with IEG; known as Juvenile myoclonic epilepsy [JME] [13]. They showed that the ratio of NAA/Cr of thalamus was decreased in 10% of the patients; which revealed a functional disorder in the thalamus of the IGE patients. This study of Mory *et al.* is an evidence for neuro malfunction of thalamus in JME patients, which could be in relation with productive mechanisms of epilepsy in the IGE [13]. Additionally, Savik *et al.* reported a considerable reduction in NAA in the thalamus of the tonic epilepsy patients [14]. Furthermore, Bernasconi *et al.* [2003] reported in NAA/Cr in the thalamus of the IGE patients; however, there was no difference in the NAA/Cr of other regions [9]. Moreover, there was no difference between NAA/Cr of the thalamus in well-control IGE patients and those with no uncontrolled epilepsy [15]. Some researchers demonstrated that thalamus NAA/Cr in IEG patients is significantly lower than that of the control cases; however, they showed no significant relation between the NAA/Cr and duration of the epilepsy or convulsion [16]. Purpose of the present study was to determine practical sensitivity and diagnostic value of H1-MRS in imaging of thalamus of IGE patients.

PATIENTS AND METHODS

Patients: This cross-sectional study was performed in Hazrat Rasool Hospital, Tehran, Iran, from June 2013 to December 2015. This study was performed on the dataset of 63 people of whom 28 people were IEG patients. All patients had symptoms and signs of IEG. Using EEG, history of the patients had been confirmed by an experienced neurologist. A signed written consent was obtained from each person.

Imaging parameters: In this study we used a 1.5 Tesla MRI system (Siemens Co., Avanto model, Germany). The H1-MRS preparation was similar to those for conventional MRI. The H1-MRS technique was PRESS-CSI. Head of the person was placed and adjusted in the brain coil. In order to achieve a higher SNR (signal to noise ratio), we used a multichannel phased array coil. The following protocols were performed to access the reference images of coronal, sagittal, and axial planes: T1-weighted, T2-weighted, and T2-tirm dark fluid. Applying H1-MRS protocol, the place of the desired volume was determined and then the order of the MRS was performed. In the next step, the scanogram images were recorded. Then, high resolution T₁-weighted images were prepared in sagittal and coronal planes. Likewise, T2-weighted images were provided in axial as well as coronal planes. Additionally, T2-tirm dark fluid images were compiled in axial, sagittal, and coronal planes applying image parameters of TE=88 ms, TR=6000 ms, TI=2027 ms, and FA=150. These routine images were used as a matrix for MRS and as an assistant to determine the volume of interest (VOI). Position of the VOI was adjusted on the right and left side of the thalamus respecting the person anatomy ((Figure 1). Then, MRS protocol was performed applying the following parameters: TE=135 ms, TR= 1200 ms, FA= 90, FOV=80mm×80mm×80mm (FOV: field of view), VOI= 65mm×65mm×55mm, and voxel size = 10mm×10mm×10mm.

Statistical analysis: The data analyzed applying SPSS (v.20). Group differences for age were tested by T-test. To evaluate the differences of the NAA/Cr ratio in the determined voxels and in order to compare the patients and the healthy controls as well as to contrast the right and left thalamus in the patients and healthy controls; a two-way ANOVA test was performed. The Pearson correlation was computed between spectroscopic data and the duration of epilepsy in the patient group. The p-values are two-sided at a significance level of ≤ 0.05 . SPSS software (Version 20; SPSS Inc., Chicago, USA) was used for the statistical analysis.

RESULTS

In the present study we evaluated the thalamus images of 63 people including 35 healthy people (23 males and 12 females; ranging in age from 19 to 46 years with average of 34.8 ± 0.62 years) and 28 IEG patients (10 males, 18 females; ranging in age from 20 to 49 years with average of 37.4 ± 1.04 years). Comparing the average NAA/Cr for the right thalamus, a significant reduction was seen between the control group and the IGE patients ($p < 0.0001$). Similarly, for the left thalamus, the NAA/Cr was significantly decreased when we compared it for the control group and the IGE patients ($p < 0.001$) (Figure 2). In this study we also evaluated the recorded NAA/Cho of the right and left thalamus. No significant difference was seen between the control group and the IGE patients neither for the right thalamus nor for the left thalamus. Moreover, there was a significant decrease in the level of NAA in the central part of the membrane, cingulum, as well as thalamus. Glutamine [Glx] has been extensively increased in both hemispheres, especially in the central part, insular membrane, cingulum, and left putamen as well as left thalamus (Figure 2). Otherwise, the choline level in the white and gray matters of the central region was decreased.

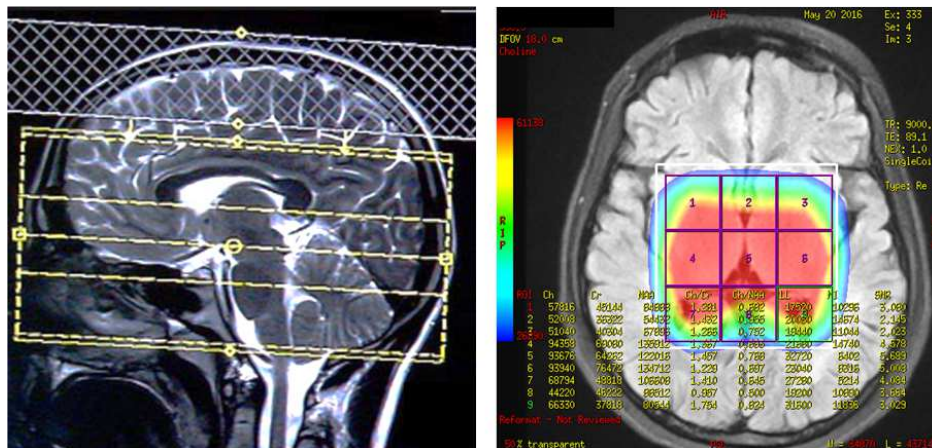


Figure1. Magnetic-resonance proton spectroscopy from thalamus both sides shows that the levels of metabolites.

DISCUSSION

Our results using spectroscopic images acquired with the multivoxel proton MRS technique in shows a significant reduction in the thalamic NAA/Cr ratio in the IGE patients. As the loss of NAA in some cases could be accompanied by an increase of Cr signal, the NAA/Cr ratios may show the higher relative value, rather than an absolute value in any individual signal. However, it is assumed that Cr is relatively homogenously distributed throughout the brain and is not significantly influenced by the epileptic state.

In the study of Mory *et al.* [2003] they evaluated neuromalfunction of thalamus in JME adolescences with myoclonic IEG [13]. They demonstrated a considerable reduction in NAA/Cr in 10% of the patients showing a functional disorder in the thalamus. They believed that this is an evidence for neuromalfunction of thalamus in JME patients that might be in respect to productive mechanisms of epilepsy in the IGE [15]. Furthermore, Savic *et al.* [2004] in a single voxel evaluation found a significant decreasing in the NAA of left thalamus in tonic-colonic epilepsy patients [12]. In another study Savic *et al.* [2000] reported a substantial reduction in NAA of the prefrontal region of the brain in JME patients; however, the NAA and other metabolites such as

choline, creatine, and myoinositol, were normal for the other regions, *i.e.* right cerebellum, right thalamus, and occipital cortex [14]. Recently, applying MRS, Bernasconi *et al.* [2003] reported a remarkable reduction in NAA/Cr of the thalamus in IGE patients [9].

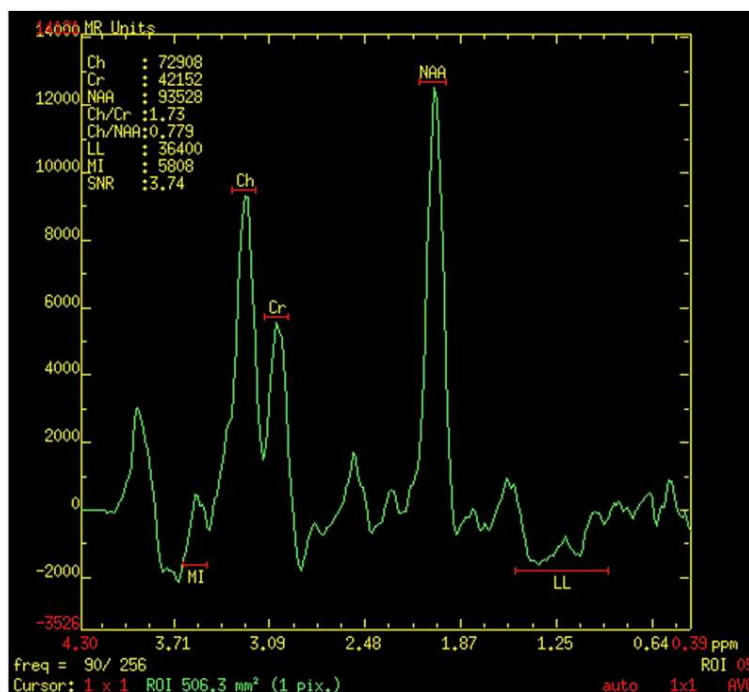


Figure1. MR spectrum of left thalamus of IGE patient that represent decreasing of NAA/Cr ratio and increasing of lipid metabolite.

The purpose of their study was evaluation of chemical and structural of thalamus in IGE patients. They used H₁-MRS technique to measure metabolites including NAA, compounds including choline and creatine [16]. For the other one patient who was diagnosed in early stage they started drug treatment after a MRI and MRS evaluations. The H₁-MRS evaluation illustrated decreasing in the NAA/Cr of thalamus in the IGE patients; however, there was no difference for the NAA/Cr of the other regions of brain. Moreover, there was no difference for the NAA/Cr of the well-controlled and non-controlled IGE patients [11]. They did not find a relationship between NAA/Cr of thalamus and frequency of spikes and waves of the obtained curves [8,9]. Additionally, there was a negative correlation between the NAA/Cr of the thalamus and duration of convulsion [9].

Applying MRS-CSI [CSI: chemical shifted imaging], Fojtiková *et al.* (2006) investigated neurodisorder of thalamus in 18 matched- age and gender people (9 controls and 9 cases with absent epilepsy) to measure the NAA level, creatine, and NAA/Cr. Additionally, they found that NAA/Cr in the thalamus of the cases was remarkably lower than that for the control group [18]. Moreover, no significant relation was found between NAA/Cr of the thalamus of their patients and duration of the convulsion or epilepsy [18]. At present study, MRS data clearly demonstrate that disorder in neurofunction of thalamus of the absent epilepsy patients is in agreement with other findings of MRS in different syndromes of the IGE. The results of this study confirm the role of thalamus, as an important conformation, in the pathogenesis of the absent epilepsy [19].

Simister *et al.* found a significant increase in the level of Glx of the patients; however, there was a significant decrease in the NAA of the patients ($p < 0.05$). Furthermore, they have seen a significant increase in the value of Glx/NAA as well as Glx/mI in the IGE group ($p = 0.01$) [20]. Moreover, they showed that metabolic changes in the frontal lobe of the IGE group were bilateral [20]. Additionally, they claimed that increasing observed in

the level of Glx may imply increasing in the irritability of the nervous system; while decreasing of NAA shows reduction in the total number of nervous cells or disorder in the function of the nervous system [19].

NAA decreasing is a sign showing reduction of nerve cells and or axons. It also reveals nerve damage and disorder in the metabolism [14]. Considering these findings, in the IGE patients of the present study there was no a remarkable reduction in the thalamus volume showing in the high sharpness MR images. The results of the current research propound disorder in the thalamus nervous function in the IEG patients. As we know up to now this is the first study in Iran using H1-MRS data to evaluate disorder in the thalamus nervous function in the IEG patients. The study of Savic *et al.* (2000) was the first in the world, and they used a single voxel evaluation; while in our study we used information of a multi voxel prepared dataset. We found evidences of metabolic and functional disorder of thalamus in the IGE patients which is an environment to produce convulsion in the IGE. Although it is not clear yet that disorder in the thalamus nervous function is only due to IGE [14, 20, 21]. The analysis of the multi voxel MRS images of the present study demonstrated that there was a considerable reduction in the NAA/Cr in thalamus of the IGE patients. The results of our study illustrate that thalamus has an important role in pathophysiology of the IGE. Based on our current knowledge role of thalamus is not still clear in the other types of epilepsy.

CONCLUSION

According to findings of the present study it seemed interference of thalamus as a part of the basic environment in pathogenesis of IGE. Also, the thalamus has a key role in production of convulsion in IGE; which thalamocortical disorders providing a patophysiological environment for IGE. It seems that nervous disorder of thalamus and brain membrane circuit play a key role in production of IGE; however, it is not confirmed still. The results of our study and those of the other similar clinical datasets state that H1-MRS is a suitable diagnostic technique to evaluate epilepsy in IGE patients.

Ethical Clearance

This project approved by in Hazrat Rasool Hospital deputy of research (Code no.HR/1395.38).

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Conflict of Interest

No conflict of interest has been done.

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