Magnetic Resonance Spectroscopy and Imaging of the Thalamus in Idiopathic Generalized Epilepsy

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Synopsis

We assessed thalamic chemical and structural integrity in 20 patients with idiopathic generalized epilepsy (IGE) using proton MRS and volumetric MRI. Compared to a group of healthy subjects, IGE patients showed a significant reduction of thalamic NAA/Cr. We found a negative correlation between thalamic NAA/Cr and duration of epilepsy. On the other hand, mean thalamic volume in IGE patients was not different from that of healthy controls. These findings indicate progressive thalamic neuronal dysfunction in patients with IGE, supporting the notion of abnormal thalamo-cortical circuitry as a substrate of seizure generation in this form of epilepsy.

Introduction

The neuroanatomical and neurochemical abnormalities underlying idiopathic generalized epilepsy (IGE) are not fully defined. Neuropathological studies of IGE patients failed to demonstrate structural abnormalities in the thalamus. Experimental work on animal models of generalized epilepsy indicates that the thalamic-cortical circuitry is involved in spike and wave discharge generation. N-acetylaspartate (NAA) can be used as a neuronal marker. Reduction in NAA levels as assessed by proton magnetic resonance spectroscopy (1H-MRSI) has been useful for quantifying brain neuronal and axonal integrity in vivo. Given the evidence for thalamic neuronal involvement in IGE, we conducted a study using 1H-MRSI to test the hypothesis that concentrations of thalamic NAA would be lower in patients with IGE than in healthy control subjects. To assess structural integrity of the thalamus, we used high-resolution volumetric MRI.

Methods

Subjects. We studied 20 consecutive patients with IGE (14 males, mean age = 37 yrs) and 11 healthy subjects (7 males, mean age = 34 yrs). IGE diagnosis was based on seizure history and semiology, routine EEG in all patients and video-EEG telemetry in 11 of them. Ten patients had well-controlled seizures and 9 had poorly controlled seizures (1-4 seizures/month).

Proton MRSI/MRI. 1H-MRSI examinations of the brain were obtained using a 1.5 T Philips Gyroscan ACS II (Philips Medical Systems, Best, The Netherlands). A set of transverse spin-echo images (TR 2000, TE 30) parallel to the AC-PC line10 were used to select a VOI for 1H-MRSI of approximately 90x90x18 mm3 centered on the thalamus. MRSI data were acquired using a double spin-echo excitation method (TR 2000, TE 272 ms, 32x32 phase-encodes, 250x250 mm field-of-view, 18 mm slab thickness) and post-processed as previously described. Metabolite resonance intensities were determined automatically relative to a spline-corrected baseline and expressed relative to intra-voxel creatine (Cr). The number of spectra averaged for each thalamus was 3.8 ± 0.3 in healthy controls and 3.6 ± 0.5 in the patients. MRI volumetric images were acquired using a T1-fast field echo sequence (TR=18, TE=10, 1 acquisition average pulse sequence, flip angle=30°, matrix size=256x256, FOV=256, thickness=1 mm giving approximately 170 isotropic images with a voxel size of 1x1x1 mm3). Manual segmentation of the thalamus was done after automatic registration in a standard stereotaxic space and correction for intensity non-uniformity.

Statistics. In healthy controls, statistical significance of differences in mean NAA/Cr and volumes between right and left sides was assessed using the paired t-test. Group differences were evaluated using the Student’s t-test. We assessed relationships between spectroscopic/volumetric measurements and duration of epilepsy using Pearson correlation.

Results

MRI volumetry. In healthy controls, the mean volume of the left thalamus was 9670±744 mm3 and that of the right thalamus was 9417±635 mm3 (p=0.08). We used a single thalamic volume in controls and patients by obtaining the average value between right and left volumes (thalamic volume). There was no difference between the mean thalamic volume of IGE patients and healthy controls. We found no correlation between thalamic volume and age in healthy controls (r = -0.141, p = 0.5). There was no correlation between thalamic volumes and duration of epilepsy (r = -0.16, p = 0.6).

Proton MRSI. In healthy controls the mean NAA/Cr of the left thalamus was 2.49±0.13 and that of the right thalamus was 2.47±0.13 (p = 0.3). There was no difference between left and right mean thalamic NAA/Cr in our healthy controls, and no lateralized abnormalities were expected to be found in IGE, we used a single thalamic NAA/Cr ratio in all subjects by obtaining a weighted average value between right and left NAA/Cr (thalamic NAA/Cr). There was no correlation between thalamic NAA/Cr and age in healthy controls (r = -0.120, p = 0.7). We found a significant reduction in thalamic NAA/Cr of IGE patients compared to the healthy controls (p = 0.006). There was no difference in NAA/Cr between IGE patients with well-controlled seizures and those with poorly controlled seizures. We found a negative correlation between thalamic NAA/Cr and duration of epilepsy (r = -0.55, p = 0.01).

Conclusions

Abnormally low concentration of thalamic NAA/Cr in IGE patients in the presence of normal thalamic volume suggest that NAA reduction can be due to neuronal metabolic dysfunction rather than neuronal loss. The lack of difference in NAA/Cr between patients with adequate seizure control and those with persistent seizures indicates that neuronal dysfunction in IGE is related primarily to the underlying epileptogenic process rather than to the effect of seizures themselves. As indicated by the negative correlation between NAA and duration of epilepsy, neuronal dysfunction in IGE seems to be progressive.

References