Thalamis and Hippocampal DTI Abnormalities in Children with Temporal Lobe Epilepsy.

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Introduction: Diffusion Tensor Magnetic Resonance Imaging (DT-MRI) allows in-vivo, non-invasive assessment of water diffusion in the cerebral tissues, which depends on the molecular and biochemical environment, on the structure of the analyzed tissue (viscosity, temperature, myelination, fiber packing, etc). Previous DT-MRI studies on temporal lobe epilepsy (TLE) reported abnormal mean diffusivity (ADC) and fractional anisotropy (FA) measurements in the epileptogenic hippocampus (HP), as compared to the contralateral side [1-4]. Most commonly, DT-MRI studies in interictal state of adults with relatively long history of medial TLE showed an increased ADC and decreased FA in the HP presumed seizure focus. Since the thalamus (TH) is considered important for the regulation of the cortical excitability and seizure propagation, we analyzed DT-MRI indices in the thalami and hippocampi of children with partial epilepsy of temporal lobe origin with and without secondary generalization. We hypothesized that changes in the values of FA and ADC, might be associated to secondary generalization of the seizures (sGTC).

Methods: We evaluated fourteen children (mean age 8.6 years) with unilateral TLE and a control group of 6 normal subjects (mean age 11.9 years) who had negative MRI scan. Three patients had MRI evidence of unilateral hippocampal sclerosis, 1 presented associated temporal cortical dysplasia (dual pathology), 3 had temporal tumor (1 DNET, 2 low grade gliomas), 2 had right temporal choroidal cyst, and 5 had negative MRI. None of the patients showed thalamic signal abnormalities detectable at visual inspection. DT-MRI was acquired in all patients, after they had been seizure free for at least 12 hours, on a 1.5T scanner (GEMS) equipped with 8-channel head coils. Twice refocusing pulse Single-shot EPI (TR/TE=13s/87ms, FOV=24cm, Matrix=128x28, 3mm thickness no gap) was performed on 40 axial planes with diffusion sensitization gradients in six non-collinear directions [b=1000 s/mm^2]. The same imaging parameters were applied to acquire one T2W imaging volume [b = 0 s/mm^2]. FA and ADC values were obtained in the thalami and hippocampi bilaterally, by including almost the whole thalamic structure and the hippocampal head.

Results: All analyzed patients had significantly increased ADC and decreased FA values in the HP ipsilateral to the seizure focus. The ADC and FA in the TH ipsilateral to the epileptic focus showed significantly higher values than on the contralateral side in children with sGTC. Patients with partial seizures without generalization showed increased ADC but did not show FA difference between the two thalami (table 1).

Conclusion: Increased ADC and decreased FA in the epileptogenic hippocampi of patients with unilateral TLE are confirmed. These findings in the epileptogenic HP have been interpreted as a result of a structural organization loss and expansion of the extracellular space [1-4]. The increased ADC values in the TH ipsilateral to the seizure focus, observed in all patients, are consistent with the DTI changes in the HP extending these changes to the TH, which is known to be an important component of the limbic seizure circuitry [5, 6]. In the thalami ipsilateral to the seizure focus, different changes in FA are demonstrated, according to the presence or absence of sGTC. In patients with sGTC, the increase of FA, in the TH ipsilateral to the focus, suggests secondary involvement of this structure, perhaps due to its recruitment into the epileptic network. A potential explanation for increased FA in the TH might be selective disruption of specific fibers entering or exiting this structure. When certain fibers are selectively affected, the preserved connections may show an increase in their coherence, producing increased FA. Moreover, because several patients included in this study were children with cortical lesions, it is possible that developmental alterations of the cortico-thalamic connectivity are partially responsible for the measured DTI abnormalities. Nevertheless, DTI is a sensitive method to detect remote subcortical abnormalities, even when no structural changes are detectable on conventional MRI. The potential significance of the observed changes in relation to the seizure semiology and the role of DTI in outcome prediction of the clinical evolution require further investigations in a larger patient population.

		ADC x 10^{-9} [mm^2/s]			**FA**		
		Ipsi	**Cont**	**p-value**	**Ipsi**	**Cont**	**p-value**
TH	WG (n=14)	682 ± 17	676 ± 18	**0.01**	0.307 ± 0.043	0.295±0.039	**0.001**
	PE + sGTC (n=7)	684 ±16	676 ± 18	**0.015**	0.314±0.055	0.297±0.049	**0.006**
	PE - sGTC (n=7)	680 ± 19	676 ± 20	0.26	0.302 ± 0.031	0.292±0.031	0.062
HP	WG (n=14)	831 ± 79	779 ± 35	**0.031**	0.162±0.028	0.180±0.020	**0.019**
	PE + sGTC (n=7)	869 ± 96	781 ± 32	**0.048**	0.165±0.030	0.180±0.020	0.106
	PE – sGTC (n=7)	800 ± 47	778 ± 40	0.39	0.160±0.028	0.108±0.023	0.111

Table : [WG]=whole group, [PE + sGTC] = partial epilepsy with sGTC, [PE – sGTC] = partial epilepsy without sGTC, [ipsi]=ipsilateral, [cont]=contralateral, [TH]=thalamus, [HP]=hippocampus.

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