MR Relaxometry in PKAN Patients at 1.5T, 3T and 7T

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Introduction

Panthotenate-kinase associated neurodegeneration (PKAN) disease (formerly called Hallervorden-Spatz syndrome) is characterized by an irreversible accumulation of iron ions in the brain. High concentrations of iron deposits are visible on MR images of PKAN patients mainly in the basal ganglia region and their concentration and form can quantitatively be assessed by MR relaxometry.
The goal of the study was to measure the iron load of brain tissue in PKAN patients and controls using MR relaxometry and to perform an analysis of the magnetic field dependency of T2 relaxation times to prove the ferritin-based hypothesis for the chemical form of iron deposits in the brain of patients.

Subjects and Methods

Three patients (females 18 and 30 y/o, male 32 y/o) from different families with genetically proved PKAN and five healthy volunteers C1-C5 (three males, 41, 43 and 62 y/o, and two females 23 and 39 y/o) were studied using T2 MR relaxometry on 1.5T, 3T and 7T whole-body systems. Data were compared to other control groups of healthy volunteers routinely used for clinical purposes at 1.5T (16 subjects) and 3T (19 subjects). All controls and PKAN patients were informed about the examination protocol and their written consent was obtained according to the local Ethical Committee rules.
MR examinations were performed using three Siemens MR Systems working with various magnetic fields (1.5T Avanto and 3T Trio in Prague, 7T system in Vienna); 12-channel (1.5T), transmit/receive (3T) and 24-channel (7T) head coils were used. T2 relaxometry was done using a CPMG sequence with 32 echoes (echo-spacing TE=6.9 ms, TR=3000 ms at 1.5T and 3T, TR≥5000 ms at 7T). The field of view and matrix were held the same for each subject in all magnetic fields. A 5 mm thick tilted axial slice through the basal ganglia was chosen for T2 relaxation map calculation using three-parameter fit. T2 values were then obtained from the regions of the globus pallidus (GP), putamen, caudate nucleus, thalamus and frontal white matter in both hemispheres. T2 values obtained from the globus pallidus at 1.5T were used for the calculation of iron concentration assuming that iron is accumulated in the form of ferritin [1].

Results/Discussion

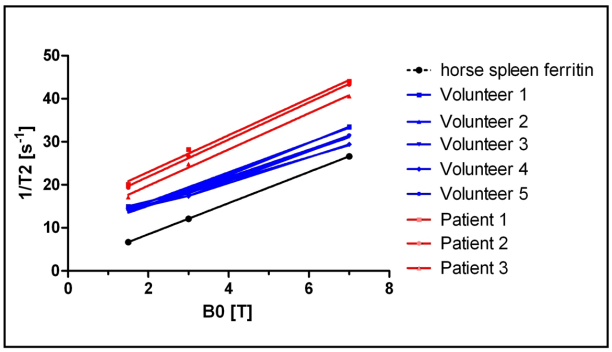
Characteristic MRI hypointensive lesions in the globus pallidus and substantia nigra were observed in all patients, "eye-of-the-tiger sign" hyperintensities in the globus pallidus were seen only in two patients. There was no asymmetry between T2 values obtained in the left and right hemispheres in any subject in any area of interest.
Compared to controls, we found that the T2 relaxation times of all patients decrease significantly in the GP as expected from MRI. Interestingly, a significant increase in T2 relaxation times was found in the putamen and caudate nucleus in all patients compared to controls. The reason is as yet unclear. No differences were found between patients and controls in the areas of the thalamus and frontal white matter. The patient comparison was independent if the group of five volunteers or relevant control clinical group was used. Statistical significance was found in all three magnetic fields (see Table). The concentrations of iron in the dark rim of the GP calculated for B_0=1.5T were approximately two times higher in patients as compared to controls and thus significantly different.
Measurements of relaxation times at three different magnetic field strengths enabled us to analyze the dependence of T2 on static magnetic field B_0. Calculated dependences of 1/T2 vs B_0 for patients and five controls show linear behavior in the magnetic fields used, however with different slopes (see Figure). The calculated slopes are similar to previously published results on horse spleen ferritin [2] and in vitro studies [3].

Table. Means and standard deviations of T2 relaxation times [ms] in the basal ganglia of PKAN patients and control groups.

	B_0	Controls C1-C5 N=5	Control clinical groups N=16 (1.5T) N=19 (3T)	Patients N=3
Globus pallidus	1.5T	69.0±1.7[a]	69.0±1.8[a]	53.3±3.8
	3T	55.4±2.0[a]	55.8±1.9[a]	37.7±2.2
	7T	31.5±1.6[a]	-	23.5±0.9
Putamen	1.5T	82.5±1.3[a]	81.3±2.8[a]	86.1±3.6
	3T	72.2±2.5[a]	69.6±4.2[a]	75.9±2.4
	7T	45.4±2.4[a]	-	48.7±3.0
Caudate Nucleus	1.5T	91.0±2.5[a]	91.0±2.8[a]	95.3±4.5
	3T	80.1±2.8[a]	81.0±3.0[a]	86.3±1.4
	7T	52.4±2.3[a]	-	57.1±1.8

[a] $p<0.05$ from patients

Figure. 1/T2 dependence on B_0 in the globus pallidus.



Conclusion

Our data suggest that the significant difference between T2 relaxation times in patients and controls could be explained by a different ferritin "loading factor" in various parts of the basal ganglia. However, the presence of other metallic proteins cannot be fully excluded.

Acknowledgement: *The study was supported by grant projects IGA MZ CR NS/10523-3, MZ0IKEM2005 and AKTION CZ-Austria: 56p22.*

References

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