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T1 and T2 Alterations in the Brains of Patients with Hepatic Cirrhosis

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PURPOSE: To determine whether previously reported T1-weighted MR hyperintensities in the brains of patients with hepatic cirrhosis are accompanied by changes in T2. **METHODS:** We measured T1 and T2 in the brains of 10 patients with chronic liver disease and 7 age-matched healthy volunteers, using classic spin-echo sequences with multiple saturation recovery times and multiple echoes. **RESULTS:** Both T1 and T2 were shortened in the basal ganglia, cortex, and white matter of the patients, with the greatest shortening in the globus pallidus, where 1/T1 was increased by 0.76 s^{-1} or 74%, and 1/T2 by 1.45 s^{-1} or 11%. **CONCLUSIONS:** The T1 changes were accompanied by T2 changes of greater magnitude that were not as visible because T2 is normally much shorter than T1, especially in the globus pallidus.

Index terms: Liver; Brain, magnetic resonance

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There have been reports of radiologic (computed tomography [CT] and magnetic resonance [MR] imaging) changes in the brains of patients with chronic liver disease, beginning with reports of morphologic change, such as atrophy (1, 2). MR studies have revealed alterations in signal intensity, such as T2-weighted hyperintensity in the dentate nucleus (3), but mostly T1-weighted hyperintensity in the basal ganglia, particularly in the globus pallidus (4–10). These signal changes do not necessarily correlate with atrophy (10) or with the presence of acquired hepatocerebral degeneration (8). It has been suggested that the MR changes may precede the emergence of neurologic symptoms or reflect the presence of a subclinical hepatic encephalopathy (8). The sometimes transient character of the lesion appears to exclude gross morphologic changes, although an increase in protoplasmic astrocytes has been reported (11). The MR changes are generally thought to arise from T1 shortening caused by some (possibly paramagnetic) substance, perhaps shunted away from the liver. Similar changes have been seen in patients receiving hyperalimentation therapy (12). Despite the widespread interest, we know of no direct measurements of T1 or reports of T2 shortening (which necessarily accompanies T1 shortening), except for small localized T2 changes that were attributed to calcification (4). Therefore, we measured both T1 and T2 in the basal ganglia of patients with chronic liver disease to see if T2 shortening is present and to compare its magnitude with the T1 shortening.

Materials and Methods

Ten patients (54 ± 13 years old) with hepatic cirrhosis of alcoholic or hepatitic origin were studied. All were candidates for liver transplantation, which was subsequently performed in some cases. Seven age-matched healthy volunteers (49 ± 10 years old) were also studied. The MR images were obtained on a 1.5-T scanner equipped with a head coil. A single 5-mm section at the level of the basal ganglia was scanned with classic spin-echo sequences as follows: For T1 determination, six T1-weighted sequences (100/22, 200/22, 400/22, 600/22, 1000/22, and 1500/22 [repetition time/echo time]) were used with one excitation and a field of view of 208 × 208 mm and a matrix of 256 × 256. For T2 determination, a multiecho T2-weighted sequence was used (16 echoes: 2000/22,

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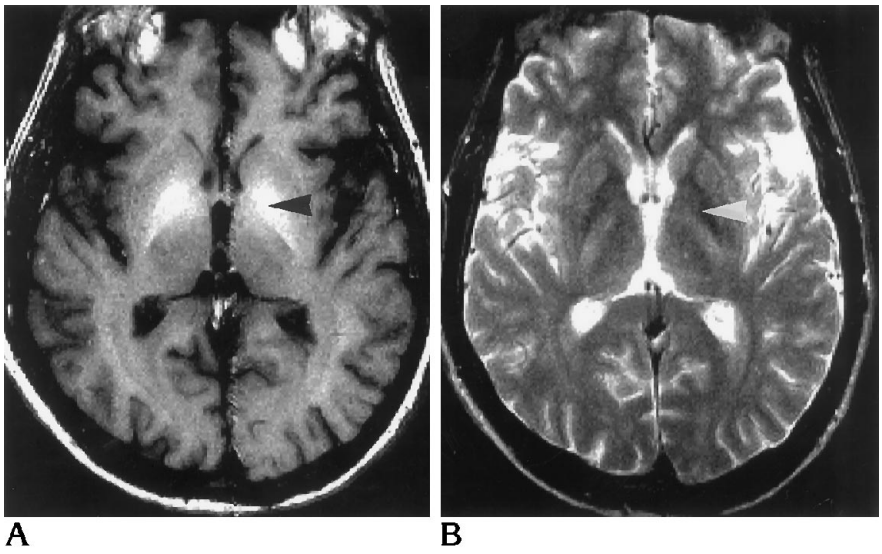

Fig 1. MR images in a patient with hepatic cirrhosis.

A and *B*, On T1-weighted (400/22) (*A*) and T2-weighted (2000/80) (*B*) images, T1 effect is evident in globus pallidus but T2 effect is masked by normal hypointensity (*arrowheads*).

Average Relaxation Times (ms) and Rates (s^{-1}), with Standard Deviations (in Parentheses)

Relaxation Time/ Rate	Caudate	Putamen	Pallidum	Thalamus	White Matter
T1					
Patients	1075 (185)	950 (145)	560 (120)	900 (155)	570 (82)
Control subjects	1615 (310)	1370 (244)	970 (150)	1135 (168)	770 (47)
Difference	540	420	410	235	200
1/T1					
Patients	0.93 (0.16)	1.05 (0.16)	1.79 (0.38)	1.11 (0.19)	1.75 (0.25)
Control subjects	0.62 (0.12)	0.73 (0.13)	1.03 (0.16)	0.88 (0.13)	1.30 (0.08)
Difference	0.31	0.32	0.76	0.23	0.46
T2					
Patients	84 (2)	75 (2)	66 (5)	77 (3)	75 (6)
Control subjects	90 (6)	83 (4)	73 (3)	85 (6)	80 (3)
Difference	6	8	7	8	5
1/T2					
Patients	11.90 (0.28)	13.33 (0.36)	15.15 (1.15)	12.99 (0.51)	13.33 (1.07)
Control subjects	11.11 (0.74)	12.05 (0.58)	13.70 (0.56)	11.63 (0.81)	12.50 (0.47)
Difference	0.79	1.28	1.45	1.36	0.83

40, 60, . . . 320) with two excitations and a field of view of 224 × 224 mm and a matrix of 256 × 256. No saturation pulses were applied to eliminate flow effects. Values of T1 and T2 were calculated for regions of interest 5 mm in diameter (about 30 pixels) in the white matter, caudate, putamen, pallidum, and thalamus. T1 was calculated by curve-fitting the six saturation recovery points with an exponential function, whereas T2 was determined directly from a T2 map calculated by the scanner software from the 16-echo sequence. Differences between populations were evaluated statistically with a two-tailed Student's *t* test. A "T1/T2 alteration ratio" was also calculated, which was defined as the difference in the relaxation rate 1/T1 between the patients and the volunteers divided by the corresponding difference in 1/T2.

Results

Figure 1 shows T1-weighted and T2-weighted images of a patient with hepatic cirrhosis. The calculated relaxation times and rates are shown in the Table. Note that 1/T1 for the patients is increased significantly (ie, T1 is reduced) compared with that for the control subjects. The increase in the globus pallidus, 0.76 s^{-1} is twice as great as in the other regions. Also, 1/T2 is increased in all regions, with the globus pallidus again showing the greatest effect, 1.45 s^{-1}. This is not visually evident on the T2-weighted images because it is masked by the normal T2 shortening caused by iron accumulation. All differences were significant at the $P = .05$ level except for T2 of white matter.

The T1/T2 alteration ratio (the change in 1/T1 divided by the change in 1/T2) was 0.52 in the globus pallidus, 0.39 in the caudate, 0.25 in the putamen, and 0.17 in the thalamus. In the white matter it was 0.55.

Discussion

T1 and T2 are often affected by the same relaxation mechanisms. In particular, any substance or process that shortens T1 must also shorten T2, although the converse is not true. The effect is described quantitatively as an additive contribution to 1/T1 or 1/T2, the latter of which must theoretically be at least as great as the former. Therefore, it is not surprising that we found a contribution to 1/T2 that is greater than the corresponding T1 effect by a factor of two or more. The reason the T2 shortening is not visually noticeable is because T2 throughout the brain is normally very short, especially in the globus pallidus.

The relative magnitude of the T1 and T2 shortening may be useful in evaluating possible mechanisms, although one must be wary of comparing in vitro and in vivo data, since diffusion rates and chemical forms may be different. A number of suggested agents may be found in the literature, although usually without any supporting pathologic data. One such possibility is ammonia, for which a correlation between plasma ammonia level and hyperintensity in the globus pallidus was found (7); however, ammonia is not paramagnetic and would produce negligible relaxation unless present in huge concentrations. Copper (13), which is paramagnetic, can also probably be ruled out because its magnetic moment is so small as to barely affect T1 and T2 (14), even in concentrations as large as 0.4 mg/g, found in Wilson disease. Iron in the form of ferritin has a strong effect in the normal brain, but the in vivo T1/T2 alteration ratio is 0.07 (15), much lower than the present results. A more compatible possibility is phospholipids (5), which may be responsible for T1 shortening in the normal neurohypophysis (16); measurements in suspensions of phospholipid vesicles (simulating tissue) yielded a T1/T2 alteration ratio of about 0.6 at 1.5 T (17), not much different from our results. Another possibility is manganese, which is elevated in the blood of patients with liver disease (18), accumulates preferentially in the globus pallidus and pituitary gland (19), and may cause T1 shortening in the globus pallidus of patients receiving hyperalimentation therapy (13). Although ionic manganese has a very low T1/T2 alteration ratio (0.08) in solution, chelated manganese would be compatible with our findings (14).

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