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MR in Temporal Lobe Epilepsy: Early Childhood Onset versus Later Onset

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PURPOSE: To study the relationship between the MR findings and the clinical features in temporal lobe epilepsy in childhood (less than 10 years of age). **METHODS:** MR studies were performed with a 1.5-T imager on 38 temporal lobe epilepsy patients receiving drug therapy at the psychiatric department. These patients were divided into two groups according to their age at onset (10 years or less, 11 years or more). The two groups were compared in terms of the MR findings and clinical features. **RESULTS:** The 11 younger-onset patients included 5 with a high-signal area attributed to mesial temporal sclerosis. Clinically, all of these 5 patients had a history of "complex" febrile convulsions, which sharply distinguished them from the older-onset group. **CONCLUSION:** The analysis suggests that complex febrile convulsions in infancy can be associated with high-signal areas on MR attributed to mesial temporal sclerosis.

Index terms: Brain, temporal lobe; Brain, magnetic resonance; Sclerosis, mesial temporal; Seizures, in infants and children

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One of the most characteristic magnetic resonance (MR) findings in temporal lobe epilepsy patients is a high-signal area observable on T2-weighted images, mainly in the mesial temporal region. Pathologic examinations conducted on the lobar tissue after temporal lobectomy have demonstrated that sclerosis of the mesial temporal lobe is primarily responsible for the high-signal area (1–3). However, not all cases of mesial temporal sclerosis manifest themselves on MR in the form of a high-intensity area (4–6), nor is it clear what clinical features are associated with this high-signal focus in the medial temporal lobe.

According to Falconer's investigations, however, temporal lobe epilepsy with surgically verified mesial temporal sclerosis often occurs in patients whose onset goes back to childhood (up to 10 years of age) and is frequently found in patients with a history of severe febrile convulsion in infancy (7–9). More recently, Kilpatrick et al have conducted MR studies on epilepsy patients whose age at onset was 25 years or older (10). The results of this study indicated, however, that only 1 of a total of 50 epileptic patients was found to have mesial temporal sclerosis.

Thus, the literature suggests that a high-signal area in MR may occur in the medial temporal lobe in epileptic patients with onset in childhood and in patients with severe febrile convulsions (in infancy). But the clinical features associated with this MR finding are still open to further investigations.

The purpose of this study was to elucidate the relation between the MR findings and clinical features of temporal lobe epileptic patients, especially their age-dependent features. The presence or absence of medial temporal hyperintense lesion in the MR images was checked particularly. As to clinical features, particular attention was paid to the age of onset, history of febrile convulsion, and severity of seizures and febrile convulsions.

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Materials and Methods

The present study was performed on 38 (21 female and 17 male) patients with temporal lobe epilepsy treated at the Psychiatric Department of Chiba University School of Medicine. These 38 patients, who agreed to MR examinations, were treated by the authors. Temporal lobe epilepsy was diagnosed in these patients on the basis of the classification of the International League Against Epilepsy (11). That is, they had partial seizures and temporal foci. MR was performed in the period from October 1988 through November 1991. The patients' mean age at onset was 18.0 ± 10.9 years (range, 3 to 50 years). Their mean age at the time of examination was 33.6 ± 13.6 years (range, 11 to 61 years), and their average duration of illness was 15.6 ± 10.6 years (range, 1 to 50 years).

The patients were divided into two groups according to their age at onset. Group 1 consisted of patients with an age at onset of 10 years or younger, and group 2 of patients with an age at onset of 11 years or older. Group 1 comprised 11 patients (7 female and 4 male), and group 2 comprised 27 patients (14 female and 13 male).

Patient history revealed that nine patients had febrile convulsions. These were classed as "complex" febrile convulsions if they lasted for 15 minutes or longer, if convulsive states occurred on several occasions within 24 hours, or if they had focal features (12). On the basis of these criteria, there were six patients with complex febrile convulsions. Two patients had a family history of febrile convulsions.

Excluded from this study were patients with serious head trauma (requiring therapy for this reason), patients with severe mental retardation, and patients with neurologic abnormalities other than epileptic seizures.

As to epileptic seizures, division was first made into partial and generalized seizures. Then the frequencies of epileptic seizures were rated on the following score scale at the worst period in the patients' clinical course: P-1 indicated no partial seizures; P-2, partial seizures occur a few times a year; P-3, partial seizures occur a few times a month; P-4, partial seizures occur a few times a week; P-5, partial seizures occur every day; G-1, no generalized seizures; G-2, generalized seizures occur a few times a year; G-3, generalized seizures occur a few times a month; and G-4, generalized seizures occur a few times a week.

In terms of this division, the 38 patients were categorized as follows: P-1, 0 patients; P-2, 10 patients; P-3, 9 patients; P-4, 14 patients; P-5, 5 patients; G-1, 14 patients; G-2, 18 patients; G-3, 2 patients; and G-4, 4 patients.

The MR unit used had a static magnetic field strength of 1.5 T. For all patients, proton density–weighted axial and coronal images were obtained at pulse sequence of 2000 or 2300/30/1.0 (repetition time/echo time/excitations) or 2500/30/0.75, and T2-weighted axial and coronal images at 2000 or 2300/80/1.0 or 2500/80/0.75. A section thickness of 5 mm, intersection gap of 2 mm, and field of view of 24 cm for axial scan and 20 cm for coronal scan were used to obtain 15 to 19 images per scan (number of images depended on each patient's head size). The sampling matrix was 256 × 192, and the image matrix was 256 × 192. In the evaluation of the MR findings, attention was particularly concentrated on the presence of focal abnormal signal intensity in the mesial temporal area. The evaluation was made independently by two neuroradiologists who were blinded to the patients' clinical and electroencephalographic data.

As mentioned before, clinical features such as age at onset, age at examination, duration of illness, frequency of seizures, and history and severity of febrile convulsions were assessed. Correlations between MR findings and these clinical features were evaluated.

Results

MR Findings

Unilateral high-signal areas in the mesial temporal region (in the axial and coronal sections, in either T2-weighted images or proton density–weighted images; hereinafter referred to as *HTS* [hyperintense T2 signal]) (Fig 1) were detected in six patients. No other abnormal areas with focal high intensity were found. T2-weighted images were more effective in four cases (patients 3, 7, 9, and 11) and proton density–weighted images were more efficient in two cases (patients 4 and 25) in confirming HTS.

Comparison between Group 1 and 2 Patients for Clinical Features and MR Findings (Table 1)

As expected, the subjects in group 1 were significantly younger at the time of examination than those in group 2 ($P = .02$, Student's t test). In terms of the patients' duration of illness, however, there was no statistically significant difference. There was no statistically significant difference between the two groups for the score of the frequency of partial and generalized seizures. In terms of the patients' history of febrile convulsions, however, there was a significant difference between group 1 (7 of 11 patients) and group 2 (only 2 of 27): $P < .001$, Fisher's direct probability method. The 6 patients with a history of complex febrile convulsions included 5 from group 1 and 1 from group 2. A family history of febrile convulsions was confirmed in 2 of the group 1 patients.

HTS was detected in 5 of the 11 patients in group 1 and only 1 of the 27 patients in group 2, and the incidence of HTS on MR was significantly greater in group 1 ($P = .005$, Fisher's direct probability method).

Fig 1. MR image of patient 11. A 25-year-old woman had experienced complex febrile convulsions at age 14 months and complex partial seizures since age 10 years.

A, Axial T2-weighted image (2500/80/0.75).

B, Coronal T2-weighted image (2500/80/0.75). Hyperintense signal of left hippocampus.

Clinical Features for Patients with HTS (Table 2)

In all six patients with HTS, the high-signal area was found on the same side as temporal spiking in the electroencephalogram. These patients had a significantly higher score for the frequency of partial seizure than the patients without HTS (average 4.3 as compared with 3.2; $P = .02$, Wilcoxon's test). A history of febrile convulsions was definitely more prevalent in this group ($P = .002$, Fisher's direct probability method). The severity of febrile convulsions or complex nature of the febrile episodes will be considered in the next section. As shown in this table, five of the six patients had onset before age 10. The average age of onset was 9.5 ± 5.1 years for this group, and 19.6 ± 11.0 years for those without HTS ($P = .04$, Student's *t* test).

TABLE 1: Comparison between group 1 (onset up to age 10) and group 2 (onset after age 10)

	Group 1 (11 cases)	Group 2 (27 cases)	Significance
Average age at onset of temporal lobe epilepsy, y ± SD	6.8 ± 2.4	22.6 ± 9.7	
Average age at examination, y ± SD	25.4 ± 11.8	36.9 ± 12.8	.02*
Average duration of temporal lobe epilepsy, y ± SD	18.5 ± 13.0	14.3 ± 9.2	ns*
No. of patients with history of febrile convulsions	7	2	<.001†
No. of patients with HTS	5	1	.005†

Note.—HTS indicates unilateral high-signal area in the mesial temporal region on MR; and ns, not significant.

* Student's two-tailed *t* test.

† Fisher's direct probability method.

Clinical Features and MR Findings for Patients with History of Febrile Convulsions (Table 3)

A history of febrile convulsions was confirmed in 9 cases among the 38; 6 of the 9 had complex febrile convulsions. Five of the 6 patients had HTS and belonged to group 1, that is, the group of patients with onset before 10 years of age. The complex nature of their febrile convulsions was evident. Thus, febrile convulsions of patients 3, 4, 7, and 9 lasted 15 minutes or longer; patients 11 and 16 had convulsions more than several times a day (24 hours). Focal characteristics were also noted in two patients (patients 3 and 11). Family history of febrile convulsions was ascertained in 2 of the group 1 patients (patients 4 and 11).

Discussion

MR Evidence of Mesial Temporal Sclerosis

Mesial temporal sclerosis is a disease primarily of the gray matter in the medial area of the temporal lobe, but sometimes sclerosis can extend over the entire temporal lobe, presenting extensive atrophy and gliosis of the cortex and white matter (7). It is very interesting that some researchers produced experimental lesions closely resembling those of mesial temporal sclerosis in many respects, and proposed etio-

TABLE 2: Summary of patients with HTS

Patient	Sex	Age at Onset, y	Age at Examination, y	Duration of TLE, y	History of Febrile Convulsions?	Score of Frequency of Seizures		Side of EEG Focus	Location of High-Intensity Area on MR
						P*	G†		
3	F	4	13	9	Yes	5	1	R	R hippocampus, uncus
4	F	6	35	29	Yes	5	2	L	L hippocampus, uncus
7	F	8	18	10	Yes	4	2	R	R hippocampus
9	M	9	19	10	Yes	3	2	L	L hippocampus
11	F	10	25	15	Yes	4	1	L	L hippocampus
25	F	20	39	19	No	5	4	R	R uncus, amygdaloid nucleus

Note.—TLE indicates temporal lobe epilepsy; EEG, electroencephalogram; L, left temporal lobe; and R, right temporal lobe.
* Partial seizures: P-1 indicates none; P-2, a few times a year; P-3, a few times a month; P-4, a few times a week; and P-5, every day.
† Generalized seizures: G-1 indicates none; G-2, a few times a year; G-3, a few times a month; and G-4, a few times a week.

logic hypotheses concerning mesial temporal sclerosis. Franck and Robert reported that combined intraventricular kainate and forebrain ischemia on animal models produced a hippocampal lesion much like that observed clinically in temporal lobe epileptic patients (13). Schlitt et al proposed that a common infectious agent, herpes simplex virus type 1, may cause mesial temporal sclerosis by means of nonfulminant infection of mesial temporal structures, which is resolved by the immune system and becomes gliotic in the course of healing by the central nervous system (14).

Until recently, this lesion has escaped in vivo depiction with laboratory procedures. Whereas computed tomography generally could show evidence of mesial temporal sclerosis only in cases with coincidental calcification (15), MR (mainly T2-weighted images) could reportedly depict sclerosis in the form of a high-signal area (1–3). These findings, however, depended largely on the equipment used and the pulse sequence applied. So there have been many discrepancies as to the incidence of MR abnormality and the clinical significance of these findings (1, 2, 4–6).

The present study demonstrated that 6 of the total of 38 patients had a high-signal area in the medial region of the temporal lobe. This high-signal area was in the same side of temporal lobe with epileptogenic focus as shown by electroencephalography. The location of this high-signal area was quite relevant clinically (Table 2), indicating a certain pathologic process related to temporal lobe epilepsy. Although HTS was based on either proton density–weighted or

TABLE 3: Summary of patients with history of febrile convulsion

Patient	Age at Time of Febrile Convulsion (no. of times)	Age at Onset of TLE, y	Score of Frequency of Seizures		Prolonged Febrile Convulsion?	Focal Features of Febrile Convulsion?	Family History of Febrile Convulsion?	High-Signal Area in the Mesial Temporal Region on MR?
			P*	G†				
2	2 y (1)	3	4	4	No	No	No	No
3	1 y, 4 m (1) 1 y, 6 m (1)	4	5	1	Yes	Yes	No	Yes
4	2 y (1)	6	5	2	Yes	No	Yes	Yes
7	10 m (1)	8	4	2	Yes	No	No	Yes
9	4 y (1)	9	3	2	Yes	No	No	Yes
10	0 m (1)	9	4	2	No	No	No	No
11	1 y, 2 m (3)	10	4	1	No	Yes	Yes	Yes
13	3 y (1) 5 y (1)	11	3	2	No	No	No	No
16	4 y (4)	13	4	2	Yes	No	No	No

Note.—TLE indicates temporal lobe epilepsy.
* Partial seizures: P-1 indicates none; P-2, a few times a year; P-3, a few times a month; P-4, a few times a week; and P-5, every day.
† Generalized seizures: G-1 indicates none; G-2, a few times a year; G-3, a few times a month; and G-4, a few times a week.

T2-weighted images, it was not depicted clearly by both images. None of the 6 patients had shown any aberrant progress in their clinical constellation during the follow-up periods ranging from 4 to 5 years. Also, these HTSs were unchanged in size and appearance in repeated MR scans performed on 4 of the 6 patients. This indicates that HTS represents gliosis (mesial temporal sclerosis) rather than tumor or edema. Triulzi et al and Franceschi et al found hyperintense MR lesions in the mesial temporal region of some nonrefractory temporal lobe epileptics (1.5-T imager, T2-weighted image) (16, 17). They inferred that this MR abnormality was compatible with mesial temporal sclerosis, although pathologic examination was not performed.

Most literature suggests that T2-weighted images lead to favorable results in imaging this mesial temporal sclerosis. However, Dowd et al have recently reported that proton density–weighted images are more effective in the diagnostic imaging of mesial temporal sclerosis. They also used a 1.5-T MR unit to obtain proton density–weighted images at 2800/30 (18). In our study, proton density–weighted images proved more effective in two cases in the imaging of mesial temporal sclerosis. Therefore, at least two pulse sequences including these should be used in the MR of temporal lobe epilepsy.

Comparison of Clinical Features and MR Findings for Group 1 and Group 2 Patients

Falconer reported that his patients with mesial temporal sclerosis had a high incidence of severe febrile convulsions in early infancy, with onset of epileptic seizures occurring up to the age of 10 (8, 9). Similarly, Ounsted et al found that febrile convulsions occurring in infancy from 6 months to 3 years of age lead to sclerosis of the cornu ammonis (Ammon's horn in the hippocampus), thereby increasing the risk of early onset of temporal lobe epilepsy (19). In the more recent work, Ounsted et al stressed this causal connection between mesial temporal sclerosis and febrile convulsions (20). Both Falconer and Ounsted et al proposed the view that the ischemic changes in the cerebrovascular system associated with febrile convulsions (particularly when prolonged or repetitive) played an important causal role in temporal lobe epilepsy. The works by Chevrie and Aicardi (21) and Wallace (22) supported the view of Falconer and Ounsted. But subsequent research by Nelson et al (23), Annerger et al (24), Lee et al (25), and Wolf (26) were not consistent with the hypothesis because only a few of their patients with temporal lobe epilepsy had a history of febrile convulsions.

Of the many reports in the literature of MR findings for patients with temporal lobe epilepsy or complex partial seizures, a few make reference to febrile convulsion. Berkovic et al investigated 10 patients with temporal lobe epilepsy, and all had a history of prolonged infantile convulsions (27). In their study, proton density–weighted and T2-weighted oblique coronal images by 0.5-T MR unit were used; the result confirmed that all patients had unilateral hippocampal atrophy with increased signal intensity. Histologic studies made in 6 of their patients revealed hippocampal and/or amygdaloid gliosis or neuronal loss in 5 cases. More importantly, 9 of the 10 patients investigated by Berkovic et al had onset of epilepsy by the age of 10. The studies by Bronen et al, referring to 9 patients with pathologic evidence of hippocampal sclerosis, revealed that 7 of these patients had a history of febrile convulsions, and 6 of the 7 had high-signal areas in the mesial temporal lobe on T2-weighted images (28). Miura et al, studying intractable temporal lobe epilepsy cases with onset in infancy, found that 12 patients with abnormal MR findings seemingly caused by mesial temporal sclerosis included 9 with a history of repeated convulsions in infancy (29).

Kuks et al investigated 107 patients with drug-resistant epilepsy including 20 patients with history of childhood febrile seizures, and they confirmed hippocampal volume loss in 45 patients with volumetric MR. The frequency of childhood febrile seizures was significantly higher in the patients with hippocampal volume loss; therefore, they inferred that hippocampal sclerosis was strongly associated with a history of childhood febrile seizures (30).

There are also several reports about children and young adults with epilepsy with similar MR findings suggesting mesial temporal sclerosis. Laster et al (31) mentioned an 18-year-old patient (with febrile convulsion at 3 months of age and onset of tonic-clonic convulsions at the age of 3 years), Theodore et al (32) referred to an 18-year-old patient with onset at 10 months; Jabbari et al (33) to a 9-year-old patient with

onset at 8 years; Stefan et al (34) to a 19-year-old patient with onset at the age of 14 years; Maertens et al (35) to a 13-year-old patient with febrile convulsions at 9 months and onset of complex partial seizures at the age of 3 years; and Heinz et al (36) to a 17-year-old patient with onset at three years and a 19-year-old patient (whose age of onset is not known). Although these authors did not pay particular attention to etiologic interrelation, their cases also suggest rather clear linkage among febrile convulsions, age of onset, and MR findings.

It should be reiterated here that Kilpatrick's patients showed only one MR hyperintense lesion; their 50 patients had onset of epilepsy after age 25 years (10). Thus, high-signal area in MR of the mesial temporal lobe can be said to be common in patients with the onset of temporal lobe epilepsy in childhood and in patients with history of febrile convulsions.

In our present study we divided the patients into two groups according to the age of onset, with 10 years of age as the marker. This division was based on the observation by Falconer et al (8, 9) that patients with a history of febrile convulsions and mesial temporal sclerosis experienced onset of temporal lobe epilepsy by the age of 10 years. The comparison of these two groups showed a significant difference in the history of febrile convulsions (more frequent among the subjects in group 1). The patients in group 1 had a significantly larger number of subjects with HTS on MR. As to febrile convulsions, the 38 patients in this study included 9 with a history of febrile convulsions, and 5 of these 9 cases belonged to group 1. The febrile convulsions of these 5 patients were of the complex type in all cases. Therefore, among the patients who experienced the onset of temporal lobe epilepsy at an early age, there was a significantly higher number of cases with a high-signal area in the mesial temporal region on MR than among the cases with later onset. The younger-onset group also contained a significantly higher number of patients with a history of complex febrile convulsions. The 6 patients with a high-signal area attributed to mesial temporal sclerosis included 5 with a history of febrile convulsions and an age of onset of temporal lobe epilepsy of up to 10 years. This may be interpreted as supporting the views forwarded by Falconer (8, 9) and Ounsted et al (19). Our study shows that there is a definite association between complex febrile convulsions and the presence of mesial temporal sclerosis. As to the causal nature of the two, further analysis with additional studies is required.

Comparison with Volumetric MR

Recently, the literature has contained some reports of measurement of the hippocampal volume by means of T1-weighted images. Cendes et al, in their study of 45 temporal lobe epilepsy patients without foreign tissue lesions, reported that the qualitative histopathology of 32 patients available confirmed some degree of mesial temporal sclerosis related to atrophic changes; the more severe were medial sclerosis, the more pronounced atrophic changes in amygdala and hippocampal formation (37). On the other hand, Jackson et al admitted that hippocampal volume measurement or atrophy alone would not always detect all MR-visible disease (38). Heinz et al have pointed out recently that the high-signal area in the medial part of the temporal lobe was a useful diagnostic indicator of mesial temporal sclerosis (39).

There are some limitations in our research methods. In this study, we used only T2-weighted and proton density–weighted images to investigate mesial temporal sclerosis. Based on our experience, we decided these images were best to examine the presence of organic lesions. We could not perform pathologic examination on our patients, so there is no direct pathologic proof of mesial temporal sclerosis. We are now measuring the hippocampal volume using oblique T1-weighted images on patients with epilepsy. We think both detection of high-signal lesion and volumetric measurement are needed to assess mesial temporal sclerosis and temporal lobe epilepsy more precisely.

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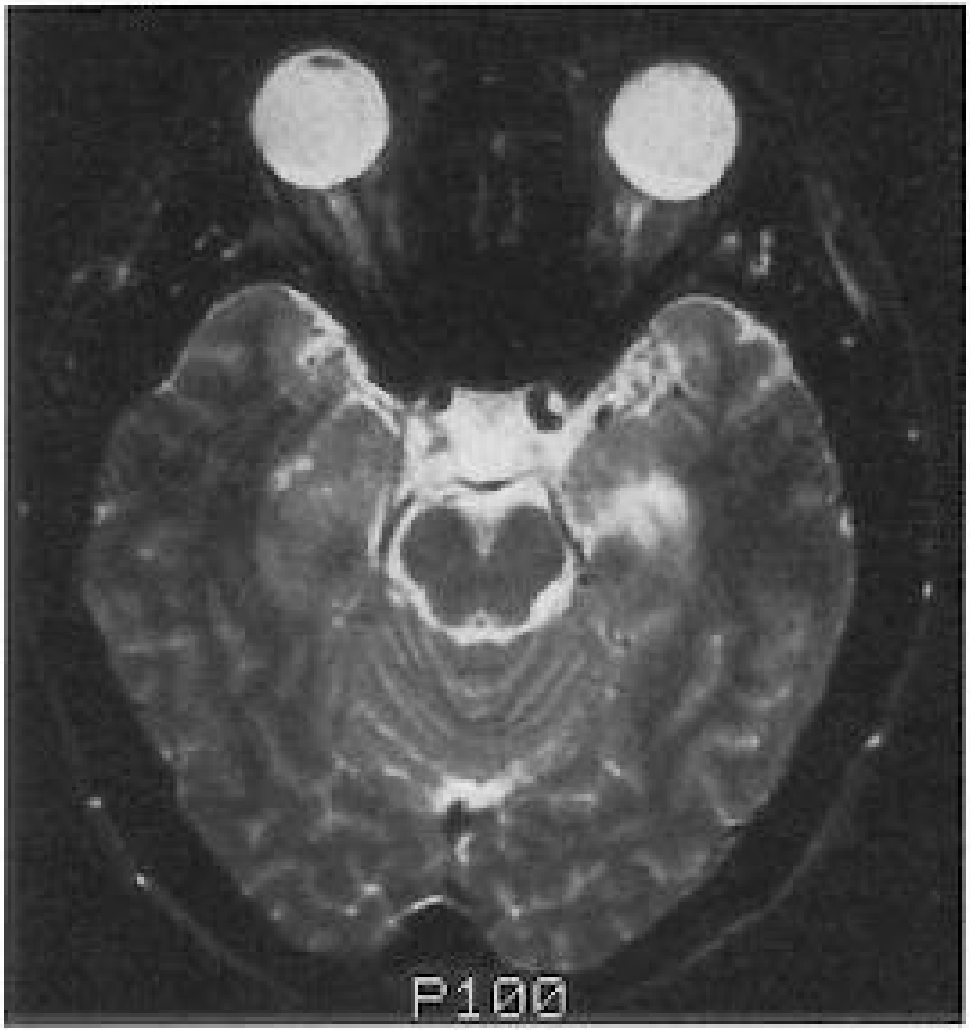

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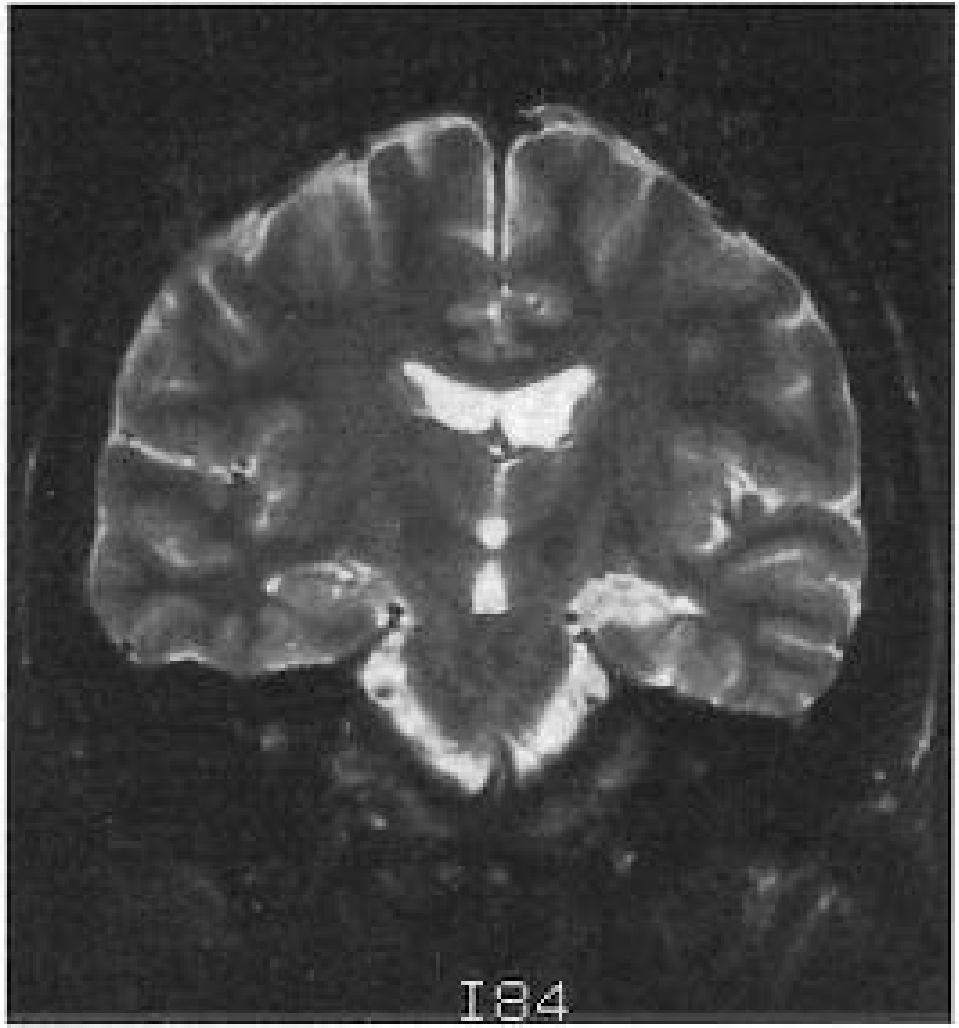

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