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Significance of Cerebellar Atrophy in Intractable Temporal Lobe Epilepsy: A Quantitative MRI Study

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Summary: *Purpose:* To detennine the incidence of cerebellar atrophy (CA) in patients with intractable temporal lobe epilepsy, whether any clinical factors are significantly associated with CA, whether CA is unilateral or asymmetric and whether this feature has any relationship to the side of epileptogenicity, and whether the presence of CA is related to epilepsy surgery outcome.

Methods: We developed a magnetic resonance imaging method of measuring the presurgical volumes of the cerebellar hemispheres of 185 patients who underwent temporal lobectomy for intractable epilepsy and of 80 control subjects. In addition, cerebellar volumes were normalized to the total brain volumes. CA was detennined as being present when the measured volume was smaller than two standard deviations from the mean value found in control subjects.

Results: Both absolute and normalized cerebellar volumes were found to be significantly reduced in the epilepsy patients compared with the control subjects. Without normalization of the cerebellar volumes, CA was present in 25.9% of the epilepsy patients; with normalization, it was present in only 16.2%. The atrophy was symmetric between the cerebellar hemispheres, and there was no significant difference in volume between the hemisphere ipsilateral and the hemisphere contralateral to the side of the temporal lobectomy. The duration of epilepsy was significantly longer and the age at onset of epilepsy was younger in patients with CA than in those without CA. The presence of CA was not associated with the outcome of temporal lobectomy.

Conclusions: CA is symmetric and common in patients with intractable temporal lobe epilepsy. However, the results suggest that the atrophy in one third of patients with CA also proportionately affects the cerebral hemispheres. The duration of epilepsy and the age at onset of epilepsy are associated with the occurrence of CA. Seizure control after temporal lobectomy is not influenced by the presence of CA. Key Words: Cerebellar atrophy-Diaschisis-Epilepsy-MRI-Seizures.

Cerebellar atrophy (CA) is a common finding among patients with longstanding partial epilepsy (1-5). The cause, frequency, and degree of atrophy are largely unknown. Several hypotheses have been proposed to explain this phenomenon: excitotoxicity in patients with a long duration of intractable epilepsy (1,6,7), hypoxia during secondarily generalized tonic-clonic seizures (8), toxicity from antiepileptic drugs (AEDs), particularly phenytoin (4,9,10),.and preexisting brain injury resulting from the initial epileptogenic insult (4). Also, although there has been experimental and clinical evidence to support the role of the cerebellum in the inhibition of partial seizures (11-17), the exact role of the cerebellum in seizures is unclear.

Cerebrocerebellar diaschisis has been thought to be responsible for the CA seen in patients with partial seizures (18). Diaschisis is a disturbance of function in one region of the brain resulting from a focal disturbance in a physically remote but anatomically connected region. Diaschisis was first described by von Monakow in 1914 (19,20). Baron et al. (21) were the first to note, with positron emission tomography, the phenomenon of cerebellar hypoperfusion contralateral to a stroke lesion in the cerebral hemisphere. The contralateral cerebellar diaschisis is thought to occur most commonly in patients with a cerebral stroke when a major motor deficit is present, which suggests that disruption of the corticopontocerebellar pathways underlies the diaschisis (20). Contralateral cerebellar diaschisis has also been demonstrated in patients with partial epilepsy. Tien and Ashdown (18) found diaschisis with positron emission tomography studies and atrophy in the cerebellar hemisphere with magnetic resonance imaging (MRI) in 8 of 26 patients with a focal epileptogenic lesion in the opposite cerebral hemisphere. Several studies using periictal single photon emission computed tomography have demonstrated that cerebellar hyperperfusion may transiently occur during partial seizures (22-24). Thalamic damage has also been found to result from seizures origi-

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nating from a distant cortical focus (25). This damage has been postulated to be a result of neurotransmitter excitotoxicity from overstimulation by connecting pathways (26,27). It has also been suggested that the cerebellar hyperperfusion noted on single photon emission computed tomography may contribute to cellular injury and death in some patients with partial epilepsy (28,29).

We have previously found evidence that CA may be associated with a poor prognosis in epilepsy surgery for intractable epilepsy (24). Specht et al. (5) also found that patients with CA were more often not free from seizures after surgery compared with patients without CA. These findings suggest that the presence of CA in patients undergoing epilepsy surgery may have some value in predicting surgical outcome. Some experimental and clinical evidence suggests that the cerebellum may exert an inhibitory effect on seizures (11-17). Our previous study was limited by its inclusion of a mixture of patients with temporal and extratemporal epilepsy, and of those with and without lesions. It was believed that a more homogeneous subject group might help to clarify this issue. The study by Specht et al. used only a subjective grading system for the presence of CA. No previous study has used quantitative measures to study CA systematically in a homogeneous group of patients undergoing epilepsy surgery.

The primary objectives of the current study were to determine the incidence of CA in patients with intractable temporal lobe epilepsy and to determine whether any clinical factors are significantly associated with CA. Secondary objectives were to establish whether CA is unilateral or asymmetric, and whether this feature bears any relationship to the side of epileptogenicity to suggest diaschisis. We further aimed to establish whether the presence of CA is related to surgical outcome after temporal lobectomy for intractable epilepsy.

METHODS

Patients

From 1992 through 1997, 329 patients underwent temporai lobectomy for intractable nonlesional partial epilepsy (epilepsy not due to lesions such as vascular malformations, neoplasms, neuronal migration disorders, and so forth) at the Mayo Clinic. Of these, 144 patients were excluded because of insufficient volumetric MRI data for the measurements required in this study. The remaining 185 patients bad adequate volumetric MRI studies.

A control group comprising 80 age-matched patients without epilepsy underwent similar volumetric brain MRI studies during this same period. The most common reason for the MRI studies in this group was headaches. None of the control subjects had strokes, demyelinating lesions, neoplasms, or cerebellar disorders.

Collection of clinical and seizure information

Medical records were abstracted for demographic and clinical information. Postsurgical seizure outcome was measured by using a four-point scale: class I = seizure-free, auras only, or single seizure with AED doses decreased but none with stable dose of AED; class II = fewer than three seizures per year or >95% reduction in seizures; class III = 80-94% reduction in seizures; class IV = <80% reduction in seizures.

MRI technique

MRI scans were performed with a 1.5 Tesla Signa scanner (GE Medical Systems, Milwaukee, WI, U.S.A.) according to a standardized seizure protocol described by Jack (30,31). This protocol includes a spin-echo T1-weighted "whole brain" volumetric series consisting of 124 contiguous slices at 1.5- or 1.6-mm thickness, acquired either coronally or orthogonal to the long axis of the hippocampal formation. The voxel dimensions were 0.875 x 0.875 x 15 mm and 0.875 x 0.875 x 1.6 mm, respectively, depending on the thickness of the acquired slices.

Cerebellar measurement technique

The volumetric MRI images were transferred to an off-line workstation and quantitatively analyzed by a single operator (E.K.S.) who did not know the clinical history and patient group assignment. The volumetric image analyses were performed with the aid of an image-analysis software package (ANALYZE 7.5 and Analyze/AVW, Biomedical Imaging Resource, Mayo Foundation). The brain images were translated into an axial plane, and manual corrections were made to ensure that the plane of the slices was perpendicular to the base of the brain. The brain slices were visually inspected, and the contiguous slices that included the cerebellum were extracted from the rest of the brain slices.

The slices were then subjected to a program that corrected for inhomogeneity within an MRI slice and between contiguous slices. The program also established a threshold of pixel intensity that would include the complete brain tissue. This program established the pixel intensity of the cerebrospinal fluid as the minimum extreme and the pixel intensity of the cerebral white matter as the maximum extreme. These values were used to establish the range of pixel intensities within which cerebral tissue could be measured and the threshold of cerebrospinal fluid to cerebral tissue. (This program, Inh3, was written by Armando Manduca, PhD, of the Biomedical Imaging Resource Department at the Mayo Clinic. Unpublished work compared the results of the program with manual threshold identification in 100 patients, and a variance of <2% was found.) The volume measurements of brain tissue were then compared by using both the manual and the computer-generated thresholds on identical slices in IO different patients, and

TABLE 1. ***Comparison of cerebellar volumes***

Volume measurement	Patients (n = 185)	Controls (n = 80)	p value*
Right cerebellar (mean mm^3 ± SD)	90,667.9 ± 21,164.9	103,822.2 ± 12,602.7	<0.0001
Left cerebellar (mean mm^3 ± SD)	89,393.0 ± 20,355.9	101,323.6 ± 12,928.1	<0.0001
Cerebellar, right/left ratio	1.0	1.0	NS
Total cerebellar (mean mm^3 ± SD)	180,060.8 ± 40,998.8	205,145.7 ± 25,297.6	0.002

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

these were also found to have a variance of <2% (unpublished data).

Every other individual brain slice was measured. Each slice was then manually segmented to separate the cerebellar tissue from the brain stem and the surrounding meningeal tissue. Each segmented slice was then changed to a binary file. This procedure involved changing the coding of each pixel from gray scale to one-bit (black and white) by using the threshold of brain to cerebrospinal fluid derived by the program described above. This change left the cerebellar tissue as white and the surrounding region as black for each slice.

The binary cerebellar slices were then individually examined, and the left and right hemispheres were separated from each other. The total number of pixels (area) were added together in each cerebellar hemisphere and then multiplied by 2 to correct for the removal of half the slices. This total was then multiplied by 0.875 x 0.875 x 1.5 (or by 0.875 x 0.875 x 1.6, depending on the slice size at which the image was acquired) x 100 to find the volume in cubic centimeters.

Both absolute and normalized cerebellar sizes were measured. Cerebellar volume was normalized to the total brain volume (cerebellar volume/total brain volume x 100) to detect cerebellar atrophy that was independent of generalized brain volume reduction. Total brain volume was obtained by using an automated morphologic segmentation technique (Object Extractor, Analyze/AVW) to segment the brain from the extracerebral structures. This technique facilitated rapid and accurate segmentation of the patient's volumetric MRI scans by using visually defined pixel-intensity threshold levels to determine the boundaries. CA was determined as being present when the cerebellar volume measurement was smaller than two standard deviations from the mean value found in control subjects.

Statistical methods

Fisher's exact test (two variables) and the chi-square test (three or more variables) were used for comparisons between proportions. Student's *t* tests (two-tailed) were applied for comparison on continuous variables between two groups. Variables that were significantly different between groups compared were subjected to multivariate logistic regression analysis by means of a maximum likelihood loss function.

RESULTS

Demographic and clinical details

In the study group, 78 patients were male and 107 were female. The control group comprised 24 men and 56 women. The mean age was 33 years for the epilepsy patients and 40 years for the control subjects ($p > 0.05$). The mean age at onset of epilepsy was 13 years, and the mean duration of epilepsy was 20 years.

MRI findings

Total brain volumes were not significantly different between epilepsy patients and control subjects (mean 1,132,679.7 ± 167,094.45 mm^3 vs. 1,140,178.5" ± 152,777.3 mm^3, respectively; $p = 0.73$). However, the absolute cerebellar hemisphere volumes and the total cerebellar volumes in epilepsy patients were significantly smaller than those in control subjects (Table 1). The ratio of right-to-left hemisphere volume was not different between epilepsy patients and control subjects.

When the patients were analyzed according to the side of subsequent temporal lobectomy, there was no difference in the right or the left cerebellar hemisphere volume, the ratio between the right and the left hemisphere volumes, or the total cerebellar volumes (Table 2).

Normalized cerebellar volume was also significantly reduced in epilepsy patients compared with control sub-

TABLE 2. ***Absolute cerebellar volumes according to side of temporal lobectomy***

Volume measurement	Right temporal lobectomy (n = 89)	Left temporal lobectomy (n = 96)	p value*
Right cerebellar (mean mm^3 ± SD)	91,417.4 ± 23,076.6	89,973.0 ± 19,321.2	NS
Left cerebellar (mean mm^3 ± SD)	89,231.6 ± 21,185.4	89,542.6 ± 19,666.2	NS
Cerebellar, right/left ratio	1.02	1.01	NS
Total cerebellar (mean mm^3 ± SD)	180,649 ± 43,513.3	179,515.5 ± 38,744.4	NS

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

TABLE 3. *Clinical factors in patients with and without cerebellar atrophy before normalization for total brain volume*

Factor	With cerebellar atrophy (n = 48)	Without cerebellar atrophy (n = 137)	p value*
Age at time of MRI, yr (mean ± SD)	37 ± 11	31 ± 13	0.008
Age at onset of epilepsy, yr (mean± SD)	11 ± 11	14± 12	NS
Duration of epilepsy, yr (mean± SD)	25 ± 11	18 ± 12	0.0001

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

jects (mean± SD = 16.1 ± 3.9 vs. 18.3 ± 2.9, Student's *t* test, two-tailed, $p < 0.0001$). After normalization of the volumes, there was no difference between the two groups in the ratio between the right and the left cerebellar hemisphere volumes (1.0 vs. 1.0).

Forty-eight (25.9%) of the 185 epilepsy patients had significant CA by absolute total volume measurements–that is, smaller than two standard deviations from the mean found in control subjects. However, after normalization of the cerebellar volume for total brain volume, the number of patients with significant CA decreased to 30 (16.2%).

In patients with CA before normalization of cerebellar volumes, the mean age at the time of the MRI and the mean duration of epilepsy were significantly greater than those of patients without CA (Table 3). There was no difference in the age at onset of epilepsy between the two groups. Table 4 shows the results of the logistic regression analysis to determine whether age at the time of the MRI or duration of epilepsy was independently associated with CA as defined by total cerebellar volumes. Only duration of epilepsy was found to be associated with CA.

When the analysis was repeated in patients who had significant CA after normalization for total brain volume, duration of epilepsy was significantly longer and the age at onset of epilepsy was younger in patients with CA (Table 5). However, the age at the time of MRI was not significantly different. Multivariate logistic regression showed a trend for longer duration of epilepsy and younger age at epilepsy onset to be independently associated with cerebellar atrophy, but the analysis did not reach statistical significance for both factors (Table 6).

Surgical outcome

Eighty-nine patients had a right temporal lobectomy, and 96 had a left temporal lobectomy. The mean duration of follow-up was 23.0 months (range 15.8-49.0). The number and percentage of patients in each outcome class are given in Table 7. Of the 185 patients, 178 had sufficient outcome information. There was no significant difference in the postsurgical outcomes between patients with and those without CA, whether CA was defined by absolute or by normalized volumes (Tables 7 and 8).

DISCUSSION

Previous studies suggested that the incidence of CA in epilepsy patients was approximately 30% (4,5). However, until this study, no work had quantitatively measured the cerebellar volumes in patients with nonJesional intractable temporal lobe epilepsy. Prior studies used visual inspection to determine whether CA was present, and CA was categorized in some studies as mild, moderate, or severe (5). The methods we used allowed a more accurate determination of the presence of CA and its relation to clinical factors pertaining to the epilepsy.

When absolute cerebellar volumes were used, the prevalence of CA in our patients (25.9%) was lower than that previously reported in epilepsy patients. The reason for this difference may be the rigorous methods by which we measured cerebellar volumes and defined CA. After normalization for total brain volume, the prevalence of CA in our patients decreased to 16.2%. This finding suggests that in as many as a third of patients with apparent CA, a proportionate degree of generalized cerebral atrophy is also present.

Compared with control subjects, the degree of absolute cerebellar volume reduction in our patients averaged 37%. When normalized volumes were used, a mean reduction of 44% was observed. Because previous studies did not quantitatively measure cerebellar volumes, our study provides for the first time the degree of reduction in cerebellar volume observed in patients with intractable temporal lobe epilepsy.

The phenomenon of diaschisis has been said to explain the development of CA in patients with epilepsy (18).

TABLE 4. *Logistic regression analysis of clinical factors that differentiate between patients with and without cerebellar atrophy defined by absolute cerebellar volume measurements*

Independent variable	*b*	SE(b)	p value
Constant	-2.45	0.55	<0.0001
Age at onset	0.012	0.018	0.51
Duration of epilepsy	0.05	0.02	<0.001

b = regression coefficient; SE(b) = standard error of regression coefficient; $x^2 = 14.6$, $p < 0.001$.

TABLE 5. *Clinical factors in patients with and without cerebellar atrophy after normalization for total brain volume*

Factor	With cerebellar atrophy (n = 30)	Without cerebellar atrophy (n = 137)	p value*
Age at time of MRI, yr (mean ± SD)	33.9± 7.5	32.7 ± 13.4	NS
Age at onset of epilepsy, yr (mean ± SD)	7.7 ±6.6	13.98 ± 11.8	0.0076
Duration of epilepsy, yr (mean± SD)	26.1 ± 10.7	18.6± 12.3	0.004

* Student's **I** test, two-tailed.

Diaschisis is defined as a disturbance of function in one region of the brain, occurring as a result of a focal disturbance in a remote but anatomically connected region (19,20). Ictal single photon emission computed tomography studies have demonstrated hyperperfusion in the cerebellar hemisphere contralateral to the cerebral hemisphere in which seizures occur (22-24). Recurrent hyperexcitation and subsequent neurotransmitter excitotoxicity at the contralateral cerebellar hemisphere have been thought to induce or aggravate CA (25,26). However, our results do not support the concept that CA is due to diaschisis in the cerebellar hemisphere that was induced by seizures in the contralateral cerebral hemisphere. Using quantitative measurements, we found that CA was symmetric between the two hemispheres, regardless of the side of surgical seizure focus in the temporal lobe. Generalized CA, rather than unilateral or asymmetric CA, was observed in our patients with intractable nonlesional temporal lobe epilepsy. This finding seems to suggest that the pathogenesis of the CA is related either to long-term exposure to AEDs (1,4) or to the effects of repeated bilateral excitotoxkity at the cerebellar hemispheres, such as may occur in generalized seizures.

The findings of this study also suggest that the presence of CA does not influence the surgical outcome of temporal lobectomy. This observation is contrary to the findings of Specht et al. (5), who reported that the presence of CA seemed to worsen the postoperative prognosis. Their study used visual inspection of MRI to determine the presence or absence of CA; this approach may have overestimated the prevalence of CA by failing to compare the cerebellar volume with the total brain volume. In our previous study, we found a trend suggesting that smaller cerebellar volumes are associated with a lower probability of excellent outcome after focal epilepsy surgery (p = 0.08) (24). However, that study was based on a heterogeneous group of patients with temporal or extratemporal epilepsy, and lesional or nonlesional epilepsy.

Longer duration of epilepsy was the only factor that was associated with the presence of CA defined on the basis of absolute or normalized cerebellar volume measurements. Age at onset of epilepsy was associated with the presence of CA, but only after cerebellar volumes were normalized to the total brain volumes. These findings are compatible with either a chronic AED effect or a recurrent seizure effect as a pathogenic mechanism underlying CA. Further, earlier age at onset of epilepsy in patients with CA may suggest other contributing pathogenic factors, such as genetic, perinatal, or developmental factors. Further studies are needed to determine which factors are important in the occurrence of CA. We are planning to study this issue in patients who have been taking AEDs for Jong periods but whose seizures have been well controlled.

By design, we confined our study to a homogeneous group of patients with nonlesional temporal Jobe epilepsy. We did not include patients with focal structural lesions, because some lesions in the cerebral hemisphere are also associated with cerebellar diaschisis (19). The overall objective of our study was to evaluate CA as it relates to the condition of intractable temporal lobe epilepsy. Nonetheless, further studies are needed to determine whether our results are applicable to other types of epilepsy.

TABLE 6. *Logistic regression analysis for clinical factors that differentiate between patients with and without cerebellar atrophy defined by normalized cerebellar volume measurements*

Independent variable	*b*	SE(b)	p value
Constant	1.88	0.61	<0.005
Age at onset	-0.05	0.03	0.07
Duration of epilepsy	0.03	0.02	0.06

b = regression coefficient; SE(b) = standard error of regression coefficient.

TABLE 7. *Postsurgical outcomes before normalization for total brain volume*

Outcome class	With cerebellar atrophy (n = 98), n (%)	Without cerebellar atrophy (n = 137), n (%)	p value*
I	35 (72.9)	102 (74.4)	NS
II	2 (4.2)	6 (4.4)	NS
ill	3 (6.3)	9(6.6)	NS
IV	5 (10.3)	16(11.7)	NS
No outcome information	3 (6.3)	4 (2.9)	

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

TABLE 8. *Postsurgical outcomes after normalization for total brain volume*

Outcome class	With cerebellar atrophy (n = 30), n (%)	Without cerebellar atrophy (n = 155), n (%)	p value*
I	22 (73.3)	115 (74.2)	NS
Il	2 (6.7)	6 (3.9)	NS
Ill	2 (6.7)	10 (6.4)	NS
IV	3 (10.0)	18 (11.6)	NS
No outcome information	I (3.3)	6 (3.9)	

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

REFERENCES

1. Dam M. Number of Purkinje cells in patients with grand mal epilepsy treated with diphenylhydantoin. ***Epilepsia*** 1970;11:313-20.
2. Koller WC, Glatt SL, Perlik S, Huckman MS, Fox JH. Cerebellar atrophy demonstrated by computed tomography. ***Neurology*** 1981; 31:405-12.
3. Luef G, Chemelli A, Birbamer G, Aichner F, Bauer G. Phenytoin overdosage and cerebellar atrophy in epileptic patients: clinical and ***MRI*** findings. ***Eur Neurol*** 1994;34(supp11):79--81.
4. Ney GC, Lantos G, Barr WB, Schaul N. Cerebellar atrophy in patients with long-term phenytoin exposure and epilepsy. ***Arch Neurol*** 1994;51:767–71.
5. Specht U, May T, Schulz R, et al. Cerebellar atrophy and prognosis after temporal lobe resection. ***J Neural Neurosurg Psychiatry*** 1997;62:501-6.
6. Meldrum B. Physiological changes during prolonged seizures and epileptic brain damage. ***Neuropiidiatrie*** I978;9:203-12.
7. Salcman M, Defendini R, Correll J, Gilman S. Neuropathological changes in cerebellar biopsies of epileptic patients. ***Ann Neural*** 1978;3:J0-9.
8. Zimmerman HM. Histopathology of convulsive disorders in children. ***J Pediatr*** 1938;13:859–90.
9. Ghatak NR, Santoso RA, McKinney WM. Cerebellar degeneration following long-term phenytoin therapy. ***Neurology*** 1976;26:818-20.
10. Lindvall 0, Nilsson B. Cerebellar atrophy following phenytoin intoxication. ***Ann Neural*** 1984; 16:258-60.
11. Cooke PM, Snider RS. Some cerebellar influences on electrically-induced cerebral seizures. ***Epilepsia*** 1955;4: 19–28.
12. Snider RS, Maiti A. Septal afterdischarges and their modification by the cerebellum. ***Exp Neurol*** 1975;49:529-39.
13. Hutton JT, Frost JD Jr, Foster J. The influence of the cerebellum in cat penicillin epilepsy. ***Epilepsia*** 1972;13:401-8.
14. Cooper IS, Amin I, Upton A, Riklan M, Watkins S, McLellan L. Safety and efficacy of chronic stimulation. ***Neurosurgery*** 1977; I: 203-5.
15. Laxer KD, Robertson LT, Julien RM, Dow RS. Phenytoin: relationship between cerebellar function and epileptic discharges. In: Glaser GH, Penry JK, Woodbury DM, eds. ***Advances in neurology.*** Vol 27. New York: Raven Press, 1980:415-27.
16. Davis R, Emmonds SE. Cerebellar stimulation for seizure control: 17-year study. ***Stereotact Funct Neurosurg*** 1992;58:200-8.
17. Kraus GL, Fisher RS. Cerebellar and thalamic stimulation for epilepsy. In: Devinsky 0, Beric A, Dogali M, eds. ***Electrical and magnetic stimulation of the brain and spinal cord.*** New York: Raven Press, 1993:231--45.
18. Tien RD, Ashdown BC. Crossed cerebellar diaschisis and crossed cerebellar atrophy: correlation of MR findings, clinical symptoms, and supratentorial diseases in 26 patients. ***AJR*** 1992;158:1155-9.
19. Von Monakow C. ***Die Lokalisation im Grosshim und der Abbau der Funktion durch Kortikale Herde.*** Weisbaden: ***IF*** Bergman, 1914:26--34.
20. Meyer JS, Ohara K, Muramatsu K. Diaschisis. ***Neural Res*** 1993; 15:362--6.
21. Baron JC, Bousser MG, Comar D, Castaigne P. "Crossed cerebellar di.aschisis" in human supratentorial brain infarction. ***Trans Am Neural Assoc*** 1980;105:459--61.
22. Duncan R, Patterson J, Bone I, Wyper DJ. Reversible cerebellar diaschisis in focal epilepsy (letter). ***Lancet*** I987;2:625--6.
23. Won JH, Lee JD, Chung TS, Park CY, Lee Bl. Increased contralateral cerebellar uptake oftechnetium-99m-HMPAO on ictal brain SPECT. ***J Nucl Med*** 1996;37:426--9.
24. Bohnen NI, O'Brien TJ, Mullan BP, So EL. Cerebellar changes in partial seizures: clinical correlations of quantitative SPECT and MRI analysis. ***Epilepsia*** 1998;39:640-50.
25. Stubgen JP. Crossed cerebellar diaschlsis related to recurrent focal seizures. ***Epilepsia*** I995;36:316--8.
26. Collins RC, Olney JW. Focal cortical seizures cause distant thalamic lesions. ***Science*** 1982;218:177–9.
27. Clifford DB, Zorumski CF, Olney JW. Ketamine and MK-801 prevent degeneration of thalarnic neurons induced by focal cortical seizures. ***Exp Neurol*** 1989;105:272-9.
28. Strefling AM, Urich H. Crossed cerebellar atrophy: an old problem revisited. ***Acta Neuropathol (Berl)*** 1982;57: 197-202.
29. Pantano P, Baron JC, Samson Y, Bousser MG, Derouesne C, Comar D. Crossed cerebellar diaschlsis. Further studies. ***Brain*** 1986; 109:677–94.
30. Jack CR Jr. Magnetic resonance imaging in epilepsy. ***Mayo Clin Proc*** 1996;71:695–711.
31. Jack CR Jr. MRI-based bippocampal volume measurements in epilepsy. ***Epilepsia*** 1994;35(suppl 6):S21-9.