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Cortical Atrophy in Parkinson Disease: Correlation between Clinical and CT Findings with Special Emphasis on Prefrontal Atrophy

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Thirty-seven patients with Parkinson disease were evaluated clinically and with computed tomography in order to determine the incidence of prefrontal atrophy. An age-matched healthy control group was also scanned. The computed tomographic criteria used were the width of cortical sulci and ventriculocerebral indices. Parkinsonian patients with frontal cortical atrophy represent only one patient out of three. They are much older than parkinsonian patients with normal computed tomographic scans, and the onset of their illness occurs later. No significant difference was found according to gender, parkinsonian clinical triad, psychomotor study, or mean duration of illness and/or dopatherapy to the time of computed tomography. This work seems to separate two Parkinson diseases: one beginning before 65 years and damaging the nigrostriate system, and another beginning after 65 years and damaging both the nigrostriate system and the cortex, particularly the frontal cortex.

Many investigators have reported cerebral atrophy in Parkinson disease. Pathologic-anatomic studies [1, 2] have demonstrated that parkinsonian patients have more degeneration of the cerebral cortex than an age-matched healthy control group. Selby [3], by means of pneumoencephalography, then Becker et al. [4], Fischer et al. [5], and Schneider et al. [6], with computed tomography (CT), have studied cerebral atrophic changes in Parkinson disease.

The effects of levodopa on frontal signs in parkinsonism [7] have suggested that depletion of dopamine could affect not only the nigrostriatal synapses but also other tracts of the accessory motor pathway. The histoenzymologic studies of Javoy-Agid and Agid [8] on parkinsonian brains have also confirmed an involvement of ascending mesocortical dopaminergic pathways.

With these physiopathogenic considerations in mind, the purpose of our work was to correlate clinical and CT findings in Parkinson disease with special emphasis on prefrontal atrophy.

Subjects and Methods

We studied cerebral atrophy in Parkinson disease in 37 patients, 19 women and 18 men, aged 47–79 years (mean age 65.6 years). We also scanned an age-matched control group of 20 neurologically normal subjects, 10 women and 10 men, aged 56–81 years (mean age 70.4 years). Reasons for exclusion were a history of any of the following: cranial surgery, cranial traumatism, epilepsy, dementia, migraine, stroke, normal pressure hydrocephalus, cerebral tumor, severe arterial hypertension, and causes of reversible cortical atrophy as anorexia nervosa, Cushing syndrome [9], and chronic alcoholism [10].

CT Scans

All scans were obtained with a CGR ND 8000 head scanner (256 × 256 matrix). The contiguous slices, 9 mm in thickness, were parallel to the orbitomeatal plane and without contrast injection.

The CT criteria used are essentially those of Hahn and Rim [11] and of Gyldensted [12]; they are shown in figure 1. For the study of the ventricular system we measured the following dimensions: maximum distance between the tips of the anterior horns (bifrontal diameter: A); distance between caudate nuclei (bicaudate diameter: B); maximum width of third ventricle (3V); and combined maximum width of both cellae mediae separated only by the septum pellucidum (C). The skull vault was appreciated by its inner width along the line of maximum distance between the tips of the anterior horns (A′), its inner width along the line of the bicaudate diameter (B′), and by its maximum outer (C′) and maximum inner widths (D). The following were obtained: bifrontal index (A/A′), bicaudate index (B/B′), Evans index [13] (A/D), and cella media index (C′/C). Bifrontal, bicaudate, and Evans indices are the criteria of frontal subcortical atrophy. For estimation of external cerebrospinal fluid spaces we measured the maximum width of hemispheric cortical sulci (frontal lobe excepted) (CS), maximum width of frontal hemispheric cortical sulci (FCS), and the width of the anterior interhemispheric fissure between frontal lobes (AIF). FCS and AIF are the criteria of frontal cortical atrophy.

The upper limit for third ventricle was considered as 7 mm under 60 years and 8 mm above 60 years. FCS, CS, and AIF were graded from 0 to 3: grading 0 (normal) = under or equal to 5 mm; 1 (slight atrophy) = 6–7 mm; 2 (mild atrophy) = 8–9 mm; and 3 (severe atrophy) = above 9 mm. We considered as pathological the bifrontal index above 0.40, the bicaudate index above 0.22, the Evans index above 0.32, and the cella media index under 4.2.

Clinical Study of Parkinsonian Patients

Clinical criteria used were present age of patients, age of patients at beginning of illness, duration of illness and of dopatherapy until

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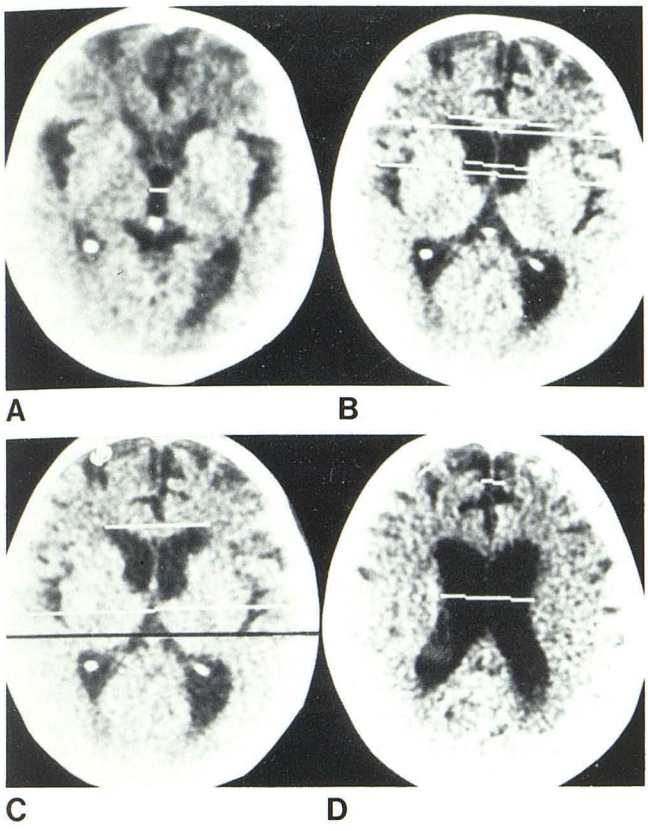

Fig. 1.—CT criteria used for the study of cerebral atrophy. **A,** Maximum width of third ventricle. **B,** Measurements used for determination of bifrontal and bicaudate indices. **C,** Measurements used for determination of Evans and cella media indices (maximum inner and outer skull widths). **D,** Measurement of maximum width of hemispheric cortical sulci (frontal lobe excepted), frontal hemispheric cortical sulci, anterior interhemispheric fissure, and combined both cellae mediae.

the time of CT, and degree of parkinsonian clinical triad. Tremor, rigidity, and akinesia were graded from 1 to 5 (1 = normal).

The patients were also examined by means of psychometric tests exploring frontal lobe and other areas of the brain to distinguish between merely frontal and global deteriorations. The battery of tests used for the study of frontal functions included tests of Luria [14], psycholinguistic tests (criticism, judgment, reasoning), and study of apprenticeship ability [15]. The battery of tests estimating instrumental functions [16] included study of language, praxia, gnosia, and immediate memory. Each test was graded from 1 to 4 and the sums of results for frontal and instrumental tests were both reduced to a percentage (100% was success for the whole test battery). These percentages were graded from I to IV: I over or equal to 90%; II between 75% and 90%; III between 50% and 75%; and IV under or equal to 50%.

Results

CT findings in parkinsonian patients and normal subjects are distributed in five groups (fig. 2): group 1 with normal CT scan, group 2 with frontal cortical atrophy only, group 3 with diffuse cortical atrophy only, group 4 with subcortical atrophy only, and group 5 with mixed atrophy.

Table 1 presents the values of cortical atrophy (FCS, AIF, and CS gradings) and of subcortical atrophy (bifrontal, bicaudate, Evans, and cella media indices; and maximum width of the third ventricle) in parkinsonian patients and normal subjects (CT group 1 is excluded). There was no normal subject in the CT group with diffuse cortical atrophy only.

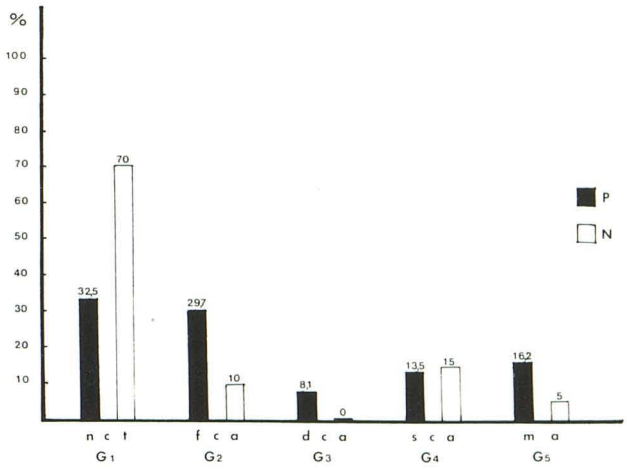

Fig. 2.—Distribution of 37 parkinsonian patients (P) and 20 normal subjects (N) in CT groups: G1 = normal CT scan (nct); G2 = frontal cortical atrophy only (fca); G3 = diffuse cortical atrophy only (dca); G4 = subcortical atrophy only (sca); and G5 = mixed atrophy (ma).

The most important groups are group 1 with normal CT scan (70% of normal subjects and 32.5% of parkinsonian patients), and group 2 with frontal cortical atrophy only (10% of normal subjects and almost 30% of parkinsonian patients). By adding CT groups with frontal cortical atrophy only, diffuse cortical atrophy only, and mixed atrophy, 54% of parkinsonian patients are found to show frontal cortical atrophy. Among parkinsonian patients with cortical atrophy, the frontal lobe is always affected. By adding CT groups with subcortical atrophy only and mixed atrophy, 24.3% of parkinsonian patients are shown to have frontal subcortical atrophy.

With parkinsonian patients, mean age is 60.2 years in the group with normal CT scan, 68.5 years in the group with frontal cortical atrophy only, 73.3 years in the group with diffuse cortical atrophy only, 61.2 years in the group with subcortical atrophy only, and 70.8 years in the group with mixed atrophy.

With normal subjects, mean age is 69.6 years in the group with normal CT scan, 70 years in the group with frontal cortical atrophy only, and 70.7 years in the group with subcortical atrophy only. There is only 1 patient aged 81 years with mixed atrophy.

Table 2 gives the distribution of CT groups in parkinsonian patients according to clinical and psychological data. The total clinical scores attributed to the parkinsonian triad correspond to the sum of mean gradings given to tremor, rigidity, and akinesia in each CT group. The numbers of parkinsonian patients treated with levodopa are the following: seven of 12 in the group with normal CT scan, eight of 11 in the group with frontal cortical atrophy only, one of three in the group with diffuse cortical atrophy only, three of five in the group with subcortical atrophy only, and six of six in the group with mixed atrophy. The numbers of patients with complete psychometric study are the following: 10 of 12 in the group with normal CT scan, 11 of 11 in the group with frontal cortical atrophy only, and three of six in the group with mixed atrophy.

Discussion

From experience with pneumoencephalography [3] and CT [4–6] we have learned the high incidence of cerebral atrophy in Parkinson

TABLE 1: **Abnormal CT Findings in Parkinsonian Patients and Normal Subjects (Groups 2–5)**

Group: Age, Gender	Grade			Group: Age, Gender	Index				3V (mm)
	FCS	AIF	CS		BF	BC	Evans	Cella Media	
P2:				P4:					
63, F	0	2	0	67, F	0.44	0.23	0.35	4.18	7
57, M	1	2	0	61, M	0.41	0.18	0.33	5.34	6
64, F	1	2	0	63, F	0.41	0.24	0.34	4.62	9
76, F	1	1	0	51, F	0.48	0.21	0.38	3.81	11
71, M	2	0	0	64, F	0.37	0.19	0.30	3.97	7
71, M	1	1	0	N4:					
65, F	2	1	0	67, M	0.40	0.27	0.34	3.5	16
72, F	2	1	0	75, M	0.44	0.34	0.37	4	10
63, F	2	0	0	70, M	0.26	0.20	0.23	4.81	11
75, F	2	1	0						
79, M	2	2	0						
N2:									
68, F	1	0	0						
72, M	1	2	0						
P3:									
77, M	2	2	2						
70, M	1	1	1						
73, M	2	0	2						
P5:									
68, M	3	3	2		0.42	0.24	0.35	3.65	8
69, F	2	1	0		0.42	0.22	0.37	4.17	9
71, M	2	2	1		0.41	0.22	0.35	4	6
64, M	3	3	1		0.41	0.17	0.35	4	7
74, M	3	1	1		0.24	0.20	0.20	5.64	9
79, F	0	2	0		0.41	0.30	0.31	4.31	8
N5:									
81, F	3	3	3		0.33	0.20	0.28	3.97	8

Note.—P = parkinsonian patients: P2 with frontal cortical atrophy only, P3 with diffuse cortical atrophy only, P4 with subcortical atrophy only, P5 with mixed atrophy. N = normal subjects: N2 with frontal cortical atrophy, N4 with subcortical atrophy only, N5 with mixed atrophy. FCS = frontal cortical sulci, AIF = anterior interhemispheric fissure, CS = cortical sulci (frontal excepted). BF = bifrontal, BC = bicaudate, 3V = maximum width of third ventricle.

TABLE 2: **Distribution of CT Groups in Parkinsonian Patients According to Clinical and Psychological Data**

	CT Group				
	NCT	FCA	DCA	SCA	MA
Clinical data:					
Mean age (years)	60.2 ± 6.2*	68.5 ± 6.5*	73.3	61.2	70.8
Mean age at onset of illness (years)	53.8 ± 6.1*	63.1 ± 7.4*	69	56	63.2
Mean duration of illness (years)	6.4	6	4.3	4.7	8.3
Mean duration of dopatherapy (years)	3.6	5	1.3	3.8	5.8
Total clinical score	6.9	7.1	7.9	8.4	7
Psychological data:					
Grade of frontal functions (nos. of patients):					
I	1	0	0	0	1
II	2	3	0	0	1
III	7	4	2	1	1
IV	0	4	1	1	0
Grade of instrumental functions (nos. of patients):					
I	6	6	1	0	3
II	4	1	0	0	0
III	0	4	1	2	0
IV	0	0	1	0	0

Note.—NCT = normal CT scan; FCA = frontal cortical atrophy only; DCA = diffuse cortical atrophy only; SCA = subcortical atrophy only; MA = mixed atrophy.

* $p < 0.05$

disease, but the topography of atrophy has not been specified. We have been specially interested in the study of the morphology of the frontal lobe by CT. We have observed CT abnormalities in 67.5% of parkinsonian patients against only 30% of normal subjects. The largest CT group in parkinsonian patients is the CT group with frontal cortical atrophy only: almost 30% of patients against 10% of normal subjects. Therefore, about one parkinsonian patient of three has frontal cortical atrophy only. These results are not really comparable with those of Becker et al. [4] or Schneider et al [6]; in fact these authors have not specified the topography of cortical atrophy. The common point is the high incidence of CT abnormalities in Parkinson disease. We found no difference with gender. For Becker et al. [4], isolated cortical atrophy was more common in women, but the life expectancy of women is longer than that of men.

In parkinsonian patients the group with normal CT scan is the youngest (mean age 60.2 years) and the group with diffuse cortical atrophy only the oldest (mean age 73.3 years). Between these extremes we found, with increasing age, the groups with subcortical atrophy only (mean age 61.2 years), frontal cortical atrophy only (mean age 68.5 years), and mixed atrophy (mean age 70.8 years). Like Becker et al. [4] we ascertained that in parkinsonian patients atrophy increases with the age of the patients, and particularly that parkinsonian patients with frontal cortical atrophy only are much older than parkinsonian patients with normal CT scans (68.5 years versus 60.2 years).

There is no significant difference between the group with normal CT scans and the group with frontal cortical atrophy only according to mean duration of illness until the time of CT (6.4 years versus 6 years). Schneider et al. [6] found that cortical atrophy increases with duration of illness.

Age of patients at the beginning of the illness is more interesting. The beginning of illness is definitely later in parkinsonian patients with frontal cortical atrophy only (mean age 63.1 years) than in parkinsonian patients with normal CT scans (mean age 53.8 years).

The duration of dopatherapy until the time of CT seems to be of no great significance. For Fischer et al. [5] dopatherapy was more effective in patients with normal CT scans.

We must note that in the CT group with mixed atrophy, just as cortical atrophy is the most pronounced (three grading 3 and three grading 2), so it is with mean duration of illness (8.3 years) and with mean duration of dopatherapy (5.8 years).

There is no difference according to the parkinsonian clinical triad between the group of parkinsonian patients with normal CT scans and the group of parkinsonian patients with frontal cortical atrophy only. One can see marked parkinsonism and a normal CT scan; conversely, one can see frontal cortical atrophy and only slight symptomatology. Tremor was graded 2 for all patients with frontal cortical atrophy.

Fischer et al. [5] found that rigidity was more pronounced in patients with abnormal CT scans. For Schneider et al. [6] the global clinical symptomatology of parkinsonian patients was more marked when CT showed abnormalities. This statement implies that there is a relation between nigrostriate lesions and cortical lesions. On the contrary, our results appear to show a dissociation between nigrostriate lesions and prefrontal cortical lesions.

In our work there was no significant difference by psychometric testing between the CT group with normal CT scan and the CT group with frontal cortical atrophy only. One can see a normal CT scan and a frontal score between 50% and 75% (seven of 10 patients). But no patient with frontal cortical atrophy only had a frontal score above or equal to 90% and four of these patients had frontal scores less than or equal to 50%. No statistically significant relation between brain atrophy and intelligence was found by Schneider et al. [6].

Bès et al. (unpublished data) studied cerebral blood flow by ^{133}Xe inhalation technique in young subjects, older patients free of any mental or cerebrovascular disease, and parkinsonian patients. In parkinsonian patients, they showed the disappearance of the hyperfrontal distribution noted in the young subjects and to a lesser degree in the subjects of comparable age.

One is tempted to correlate this hemodynamic situation with clinical CT signs, which indicate prefrontal lobe damage in parkinsonian patients. This correlation will be the subject of further investigations.

There seem to be two Parkinson diseases: a disease beginning before 65 years of age and damaging the nigrostriate system, and another disease beginning after 65 years and damaging both the nigrostriate system and the cortex.

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