Arch. Psychiat. Nervenkr. 227, 89—95 (1979)

Archiv für Psychiatrie und Nervenkrankheiten
Archives of Psychiatry and Neurological Sciences

The Course of Brain Atrophy in Parkinson's Disease

E. Schneider*, H. Becker, P.-A. Fischer, H. Grau, P. Jacobi, and R. Brinkmann

Department of Neurology (Head: Prof. Dr. P.-A. Fischer) and
Department of Neuroradiology (Head: Prof. Dr. H. Hacker),
University Clinic, Frankfurt a. M., Federal Republic of Germany

Summary. In 110 parkinsonian patients (53 men, 57 women) aged 38—81 years, computer-tomographic follow-up investigations were done to assess the development of brain atrophy. The control examinations were done after an average of 28 months. At that time an increase in brain atrophic changes of different localization could be observed in 23% of the patients. In addition, it could be demonstrated that the increase in pathologic CT findings is to be observed especially in patients with higher age, a more marked impairment in psycho-organic capacity, more pronounced handicaps in the fine-motorial performances at the beginning of the study. From the neuroradiological point of view, patients with more marked pathologic CT findings upon the first examination, be these ventricular enlargement and/or cortical atrophy, more often showed a progression of brain atrophy.

Key words: Parkinson's disease – Cerebral atrophy – Follow-up study – Computed tomography.

Zusammenfassung. Bei 110 Parkinson-Kranken (53 Männer, 57 Frauen) im Alter von 38—81 Jahren wurden computertomographische Verlaufsuntersuchungen zur Entwicklung der Hirnatrophie durchgeführt. Die Kontrolluntersuchung erfolgte nach durchschnittlich 28 Monaten. Zu diesem Zeitpunkt konnte bei 23% der Kranken eine Zunahme hirnatrophischer Veränderungen unterschiedlicher Lokalisation festgestellt werden. Darüber hinaus zeigte sich, daß von dieser Zunahme die Kranken betroffen waren, die im Beginn der Studie älter waren, eine stärkere psychoorganische Alteration aufwiesen und auch in den feinmotorischen Leistungen stärker behindert waren. Aus neuroradiologischer Sicht sind es die Kranken, die bereits bei der Erstuntersuchung stärkere CT-Veränderungen, gekennzeichnet durch Ventrikelerweiterung und/oder kortikale Atrophie, aufwiesen.

Schlüsselwörter: Parkinsonsyndrom – Hirnatrophie – Verlaufsuntersuchung – Computertomographie.

Corresponding author: Prof. Dr. E. Schneider, Abt. für Neurologie, Klinikum der Universität, Schleusenweg 2—16, D-6000 Frankfurt a. M., Federal Republic of Germany

0003-9373/79/0227/0089/$ 01.40

Introduction

Brain atrophic changes are a frequent accompanying symptom in Parkinson's disease. Among 250 patients investigated pneumencephalographically Selby (1968) found cortical atrophy in 57.2% and an enlargement of the ventricular system in 30% of the cases. Svennilson et al. (1960) observed a ventricular enlargement in 51% of their patients. Gath et al. (1975) saw cortical atrophy in 46.7% and ventricular enlargement in 77.8% of their patients. In our investigations utilizing computed tomography in 173 patients, we had a pathologic CT finding in 51.4% of patients, in most cases a combination of cortical atrophy and ventricular enlargement (Becker et al., 1976, 1979). Ventricular enlargement proved to be age dependent, whereas cortical atrophy was related to age as well as to the duration of the illness. Extranigral lesions of different localization, including cortical areas, were also seen in pathologic-anatomical investigations (Adams et al., 1964; Earle, 1968; Alvord et al., 1974). Alvord et al. were able to demonstrate that cortical degenerative lesions are more pronounced in parkinsonian patients than in an age-matched control group. Based on pneumencephalographic (Schwab et al., 1959; Selby, 1968) as well as computer-tomographic findings (Fischer et al., 1976; Schneider et al., 1979) it has been shown that brain atrophic changes influence the degree of specific parkinsonian symtoms and psychopathologic disturbances and that they are also important with regard to the results of basal ganglia surgery (Selby, 1968) and the response to levodopa treatment (Schneider et al., 1978). In several follow-up studies, it was shown that the favorable effect of levodopa declines after a 2—3 year treatment period (for literature see: Birkmayer and Hornykiewicz, 1976; Schneider et al., 1977; Fischer et al., 1978). The reasons for this loss of therapeutic efficacy are not yet completely clear. The factor of brain atrophy certainly must be considered. Thus, within the scope of this clinico-computer-tomographic follow-up study, we tried to clear up the following questions:

(1) Is there an increase in brain atrophy as assessed by computed tomography (CT) during a limited time of about 2 years?
(2) Are there differences between patients with and without increase in brain atrophy with regard to clinical, psychological test, and CT findings even at the beginning of the study?

Subjects and Methods

Our study is based on 110 parkinsonian patients (53 men, 57 women) whose mean age at the time of the first CT (CT I) was 64.1 years (range 38—81 years). The duration of the disease until the time of the CT was 6 years (range 1—22 years). The control CT (CT II) was carried out about 28.2 months later (range 13—38 months). At the beginning CT was performed with the prototype of the Siretom (image matrix 80×80) and the control investigations with the Siretom[1] (image matrix 128×128). Therefore certain limitations in the comparability were unavoidable. Evaluation of the CT findings was done without knowledge of the clinical and psychological test data. At first, a general evaluation into normal, light, moderate, and severe atrophic changes, independent of its respective localization, was made. In addition, the degree and extent of

1 Financed by Volkswagenwerk Foundation

cortical atrophy (localized/diffuse), and the existence of isolated ventricular enlargement or isolated cortical atrophy were assessed. Linear measurements were made to assess the width of the sulci and the width of the ventricular system (anterior horn tips, cella media, and third ventricle). Additional details on the radiological procedure may be found in Becker et al. (1976).

In each patient, data concerning the neurological, psychopathological, and psychological test status with regard to the state of well being, intelligence, fine-motorial performance, and visual reaction times were available (for methodology see Fischer et al., 1973). Seventy-seven patients were treated with levodopa, and 43 were untreated.

Results

1. Computer-Tomographic Findings

The essential CT data are given in Table 1, in which only shifts to clear-cut pathological changes were considered, thus omitting borderline findings. A worsening of brain atrophic changes was found in 25 patients (23%), including ventricular enlargement as well as cortical atrophy. As far as the measurement values are concerned, an increase in all parameters was observed. The increase in sulci width is due to changes in eight patients; the increase in cella media and

Table 1. Course of cerebral atrophy as assessed by computed tomography in parkinsonian patients ($n = 110$)

a) Aspectual scoring	CT I number of patients	CT II number of patients
Overall grading		
normal and light pathologic	53	48
medium and severe pathologic	57	62
Isolated ventricular enlargement of moderate and severe degree	4	5
Isolated cortical atrophy of moderate and severe degree	9	9
Cortical atrophy of moderate and severe degree	28	32
Ventricular enlargement of moderate and severe degree	39	42
Localization of cortical atrophy: diffuse/localized	60/24	63/23

b) Measuring values	CT I mean values	CT II mean values
Sulcus width (mm)	6.2	6.4*
Cella media width (mm)	26.5	28.4**
Anterior horn width (mm)	38.9	39.5**
Third ventricle width (mm)	6.2	6.5**

* $P < 0.05$; ** $P < 0.01$ using Student's t-test

anterior horn width is due to changes in 23 and 15 patients, respectively. As in cases with uncertainties in the measurement procedure, a decision was made not to accept any worsening; the figures in Table 1 thus indicate a lower limit in the increase of pathological findings.

2. Relation Between Progression in Brain Atrophy and the Basic Clinical, Psychological Test and CT Findings

Irrespective of the kind and degree of brain atrophy, it is important to know in which patients the progression occurs. Table 2 depicts differences between patients with and without an increase in brain atrophy with regard to clinical and psychological test data. Accordingly, older patients, or those with a more pronounced impairment in cerebro-organic capacity and more marked handicap in their daily activities, are affected. This is also indicated by the clearly worse performances on the fine-motorial tests (Perdue Pegboard and Minnesota Rate of Manipulation Test) in this group of patients. In contrast, the differences concerning the degree of the specific parkinsonian symptomatology are less obvious and of statistical relevance only for tremor and the overall score of the neurological symptomatology. But it must be mentioned that we are dealing with a mixed group of patients (treated or not treated with levodopa) who demonstrate differences in relation between CT findings and clinical symptomatology (Schneider et al., 1979). Nevertheless, it can be said that patients neurologically more severely affected demonstrate a progression in brain atrophic changes. Of equal importance was the question of whether there are differences in the basic CT

Table 2. Comparison between patients with and without increase in cerebral atrophy. Mean values of clinical and psychological test basic data

Clinical and psychological test variables	Patients with increase in cerebral atrophy ($n = 25$)	Patients without increase in cerebral atrophy ($n = 85$)
Age in years	69.3	62.6**
Duration of illness until CT I (years)	5.8	6.1
Akinesia	9.7	7.7
Rigidity	5.3	3.9
Tremor at rest	4.1	2.3*
Overall score of neurological symptomatology	15.0	11.6*
Handicap in daily activities	13.9	11.0**
Cerebro-organic impairment	1.8	1.2**
Purdue Pegboard Bimanual performances	10.7	15.5**
Minnesota Rate of Manipulation Test Bimanual performances	17.6	21.7**
Simple visual reaction time (s)	19.7	17.1
Complex visual reaction time (log) (s)	1.79	1.73

* $P < 0.05$; ** $P < 0.01$ using Student's t-test

Table 3. Comparison between patients with and without increase in cerebral atrophy: Relation to basic CT findings

a) Aspectual scoring		With increase in CT findings ($n = 25$)	Without increase in CT findings ($n = 85$)
Overall grading			
normal and light pathologic		5	43**
moderate and severe pathologic		20	42
Marke cortical atrophy	yes	8	20
	no	17	65
Localization of cortical atrophy			
diffuse		18	42
localized		2	22

** $P < 0.01$ in χ^2 test

b) Measurement values	With increase in CT findings ($n = 25$)	Without increase in CT findings ($n = 85$)
Sulcus width (mm)	7.3	6.2*
Cella media width (mm)	29.1	25.9*
Anterior horn width (mm)	41.6	38.1*
Third ventricle width (mm)	7.0	6.0

* $P < 0.05$ using Student's t-test

findings. The results of this analysis are given in Table 3. It is obvious that patients with a progression in brain atrophy more often had signs of brain atrophy (20 of 25 patients), larger sulcus widths, and a larger ventricular system at the beginning of the investigation.

Discussion

Up to now, investigations concerning the course of brain atrophy in Parkinson's disease have not been feasable. The painfulness of pneumencephalography and the danger of complications (Potthoff, 1970) did not allow use of this method to clarify this special problem. Also, with CT, no systematic investigations have yet been published. Our results demonstrate that during the very limited time of 28 months in about 23% of the patients, an increase of brain atrophy is observable. An even faster worsening of brain atrophy during only 1 year, accompanied by a marked worsening of the psycho-organic symptomatology has been demonstrated in single cases (Fischer et al., 1976), and this increase of brain atrophy can take place centrally or cortically. It is noteworthy that mainly a certain group of patients is affected. These patients are older and have a more marked psycho-organic impairment and worse results in fine-motorial perform-

ances as assessed by special tests. From the neuroradiological aspect, it is this group of patients which is characterized by pathologic CT findings such as larger sulci widths and a larger ventricular system in the area of the anterior horn tips and cella media and to a certain extent also the third ventricle. The only weak relation between the course of brain atrophy and the specific neurological symptomatology can be explained by the preponderance of levodopa-treated patients. As shown previously, the relation between brain atrophy and a more marked neurological symptomatology is found mainly in untreated patients (Schneider et al., 1979). Irrespective of the demonstrated relations in this context, one must question whether there are any causative factors influencing the course of brain atrophy. At first, age must be mentioned, as we know that ventricular enlargement is correlated with increasing age in normal subjects (Barron et al., 1976; Hahn and Rim, 1976; Gyldensted, 1977; Haug, 1977) as well as in parkinsonian patients (Becker et al., 1976, 1979). In contrast, cortical atrophy in parkinsonian patients is also influenced by the illness itself; patients with a longer duration of the illness more often have—independent of their age—a more marked cortical atrophy (Schneider et al., 1979; Becker et al., 1979). This observation is supported by the pathologic-anatomical investigations of Alvord et al. (1974). Since among our patients, there is an increase in brain atrophy in the higher age group, age must play an important role. An influence of the duration of the illness on the progression of brain atrophy could not be ascertained during the observation period. Finally, arteriosclerosis as a causative factor must be discussed. The influence of arteriosclerosis on the pathogenesis of parkinsonism, which has been discussed by Brissaud (1890), Lewy (1913), and Critchley (1929) cannot, in our opinion, be determined for sure. Scott and Netzky (1961) have pointed out that both diseases may appear at the same time. Eadie and Sutherland (1964) did not find signs of arteriosclerosis more often in parkinsonian than in age-matched patients treated for orthopedic reasons. In our investigations, it has been demonstrated that there is no relationship between signs of arteriosclerosis and brain atrophy in Parkinson's disease (Schneider et al., 1977). Therefore the worsening of brain atrophy cannot be easily explained by circulation disturbances.

References

Adams, R. D., van Bogaert, L., van der Eecken, H.: Striato-nigral degeneration. J. Neuropathol. Exp. Neurol. **23**, 584—608 (1964)

Alvord, E. C., Forno, L. S., Kusske, J. A., Kaufmann, R. J., Rhodes, J. S., Goetowski, Ch. R.: The pathology of parkinsonism: A comparison of degenerations in cerebral cortex and brainstem. Adv. Neurol. **5**, 175—193 (1974). New York: Raven Press 1974

Barron, S. A., Jacobs, L., Kinkel, W. R.: Changes in size of normal lateral ventricles during aging determined by computerized tomography. Neurology **26**, 1011—1013 (1976)

Becker, H., Grau, H., Schneider, E., Fischer, P.-A., Hacker, H.: CT examination series of parkinsonian patients. In: Cranial computerized tomography, W. Lanksch, E. Kazner (eds.), pp. 249—254. Berlin-Heidelberg-New York: Springer 1976

Becker, H., Schneider, E., Hacker, H., Fischer, P.-A.: Cerebral atrophy in Parkinson's disease —represented in CT. Arch. Psychiat. Nervenkr. (in press, 1979)

Birkmayer, W., Hornykiewicz, O. (eds.): Advances in parkinsonism. Basel: Editiones Roches, 1976

Brissaud, E.: Leçon sur les maladies nerveuses. (Salpétrière 1893—1894). Recueillis et publiées par H. Meige. Paris: Masson 1895

Critchley, M.: Arteriosclerotic parkinsonism. Brain **52**, 23—83 (1929)

Eadie, M. J., Sutherland, J. M.: Arteriosclerosis in parkinsonism. J. Neurol. Neurosurg. Psychiat. **27**, 237—240 (1964)

Earle, K. M.: Studies on Parkinson's disease including x-ray fluorescent spectroscopy of formalin fixed brain tissue. J. Neuropath. Exp. Neurol. **27**, 1—14 (1968)

Fischer, P.-A., Schneider, E., Jacobi, P., Maxion, H.: Langzeitstudie zur Effektivität der L-Dopa-Therapie bei Parkinsonkranken. Nervenarzt **44**, 128—135 (1973)

Fischer, P.-A., Jacobi, P., Schneider, E., Becker, H.: Correlation between clinical and CT-findings in Parkinson's syndrome. In: Cranial computerized tomography, W. Lanksch, E. Kazner (eds.), pp. 246—248. Berlin-Heidelberg-New York: Springer 1976

Fischer, P.-A., Schneider, E., Jacobi, P.: Die Langzeitbehandlung des Parkinsonsyndroms. Befunde und Probleme. In: Langzeitbehandlung des Parkinsonsyndroms, P.-A. Fischer (Hrsg.), pp. 87—103. Stuttgart-New York: Schattauer 1978

Gath, I., Jörgensen, A., Sjaastad, O., Berstad, J.: Pneumencephalographic findings in parkinsonism. Arch. Neurol. **32**, 769—773 (1975)

Gyldensted, C.: Measurements of the normal ventricular system and hemispheric sulci in 100 adults with computed tomography. Neuroradiology **14**, 183—192 (1977)

Hahn, F. J. Y., Rim, K.: Frontal ventricular dimensions on normal computed tomography. Am. J. Roentgenol. **126**, 593—596 (1976)

Haug, G.: Age and sex dependence of the size of normal ventricles on computed tomography. Neuroradiology **14**, 201—204 (1977)

Lewy, F. H.: Paralysis agitans. In: Handbuch der Neurologie, M. Lewandowsky (ed.), p. 920. Berlin: Springer 1912

Potthoff, P. C.: Psychoorganic syndromes following pneumencephalography in parkinsonian patients. In: Abstracts of Papers Presented, Part I, 5th International Symposium on Stereoencephalotomy, 1970, Freiburg i. Br., p. 21, T. Riechert, F. Mundinger, R. Hassler, H. T. Wyers, E. A. Spiegel (eds.). International Congress Series No. 217. Amsterdam: Excerpta Medica Foundation 1970

Schneider, E., Fischer, P.-A., Jacobi, P.: Zur Konstanz der L-Dopa-Wirkung beim Parkinsonsyndrom. Ergebnisse einer 4-Jahres-Langzeitstudie. Nervenarzt **48**, 205—210 (1977)

Schneider, E., Fischer, P.-A., Becker, H., Hacker, H., Pencz, A., Jacobi, P.: Relationship between arteriosclerosis and cerebral atrophy in Parkinson's disease. J. Neurol. **217**, 11—16 (1977)

Schneider, E., Fischer, P.-A., Jacobi, P., Becker, H.: Zur Relevanz extranigraler Hirnläsionen bei Parkinsonkranken. In: Langzeitbehandlung des Parkinsonsyndroms mit L-Dopa, P.-A. Fischer (Hrsg.), pp. 115—129. Stuttgart-New York: Schattauer 1978

Schneider, E., Fischer, P.-A., Jacobi, P., Becker, H., Hacker, H.: The significance of cerebral atrophy for the symptomatology of Parkinson's disease. J. Neurol. Sci. (in press, 1979)

Schwab, R. S., England, A. C., Peterson, E.: Akinesia in Parkinson's disease. Neurology (Minneap.) **9**, 65—72 (1959)

Scott, T. R., Netsky, M. G.: Parkinson's syndrome: a critical review. Int. J. Neurol. **2**, 51—60 (1961)

Selby, G.: Cerebral atrophy in parkinsonism. J. Neurol. Sci. **6**, 517—559 (1968)

Svennilson, E., Torvik, A., Lowe, R., Leksell, L.: Treatment of parkinsonism by stereotactic thermolesions in the pallidal region. Acta Psychiatr. Scand. **35**, 358—377 (1960)

Received December 27, 1978