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Cortical Atrophy in Senile Dementia of the Alzheimer type is Mainly Due to a Decrease in Cortical Length*

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Summary. A prospective study was undertaken to select mentally normal old subjects and patients with senile dementia of the Alzheimer type (SDAT). The test score of Blessed et al. (1968) (BTS) was used to determine the severity of mental impairment. A pathologic study confirmed the diagnosis of either SDAT or normal brain aging at postmortem examination in 12 cases. The cortical area and the cortical perimeter of the different cerebral lobes were measured on 1-cm-thick coronal sections using a semi-automatic image analyzer. Cortical length and thickness were calculated using perimeter and area values. BTS was significantly correlated with both the area ($r = 0.7695$, $P = 0.003$) and the length ($r = 0.7421$, $P = 0.006$) of the temporal cortex. There was no significant correlation between BTS and thickness of the temporal cortex ($r = 0.559$, $P = 0.059$). These results show that reduction of length is one of the major determinants of cortical atrophy. Although this has to be confirmed by histological study, they favor the hypothesis of a column-selective atrophy in SDAT which should be considered in the interpretation of the microscopic data.

Key words: Senile dementia of the Alzheimer type – Cortical atrophy – Temporal lobe – Morphometry

Introduction

Reduction of the area of the coronal section of the temporal cortex in senile dementia of the Alzheimer type (SDAT) was reported by Hubbard and Anderson (1981). At the same time, other authors (Terry et al. 1981) did not find any significant differences in the thickness of the temporal cortex in normal subjects and demented patients. As the surface reduction noted by Hubbard and Anderson (1981) could be due to a decrease in cortical thickness, total cortical length (on coronal sections), or both these values, we intended to evaluate these two parameters and report the results favoring the second hypothesis.

Methods

Patients

The patients had been involved in a prospective study undertaken in 1983 to evaluate the morphological and biochemical changes in SDAT. Briefly, all of the 115 women over 75 years of age entering long-term care units of a general hospital (Charles Foix Hospital) between June 1983 and April 1984 were submitted to general, neurologic, and psychiatric examination. Seventy-seven patients were initially excluded because of cerebrovascular disease (26), chronic psychiatric syndromes (16), blindness or deafness (11), alcoholism (6), Parkinson's disease (6), or another disabling disease (12). All the other subjects were included in the study and considered either as mentally normal or as affected by SDAT. The test score of Blessed et al. (1968) was used to quantify intellectual efficiency. Lower values of Blessed's test score (BTS) indicate more important mental impairment.

Postmortem Neuropathologic Study

This investigation was performed on one hemisphere; macroscopic and microscopic examination excluded two cases with small cerebral infarcts. The only observed changes were those of SDAT (many plaques and tangles in neocortical areas) or of "normal aging" (a few plaques and tangles mainly confined to the hippocampus) in the 12 brains which were used for this study (four right hemispheres: one control and three demented patients; eight left hemispheres: two control and six demented patients).

Macroscopic Morphometry

Colored marks on the external surface of the hemisphere allowed a precise recognition of the different lobes on the coronal sections. These 1-cm-thick sections, involving the whole hemisphere, were photographed. Area and perimeter of the cortex

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Table 1. General statistics of the four main variables

	Mean	SD	Coeff. Var.	Mini	Maxi	Median
BTS	13.3	9.59	71.96	2	28	11
tA (cm^2)	39.3	11.1	28.16	16.5	59.5	41.5
tT (cm)	0.28	0.02	9	0.21	0.31	0.29
tL (cm)	136	33	24	78	205	135

BTS, test score of Blessed et al. (1968); tA, area of the temporal cortex; tT, mean thickness of temporal cortex; tL, length of temporal cortex; SD, standard deviation; Coeff. Var., coefficient of variation; Mini, minimal value; Maxi, maximal value

were measured with a Leitz-ASM image analyzer on each photographed section. To calculate cortical length and mean thickness, we made the assumption that the cortical ribbon could be viewed as a long rectangle, folded in gyri; the actual perimeter and area of the cortex could then be considered as the corresponding values of a rectangle in which:

$$P = 2L + 2W \quad (1)$$

(P = perimeter; L = length; W = width) and

$$A = L \times W \quad (2)$$

(A = area).

As the length of this theoretical cortical rectangle was much larger than its width, the latter was negligible in the calculation of perimeter values following [1] which could then be estimated as $P \simeq 2L$. To calculate the width of the theoretical cortical rectangle we used the Perimeter/Area ratio: $\frac{2L + 2W}{L \times W}$. Since $P \simeq 2L$, then $\frac{P}{A} \simeq \frac{2L}{L \times W}$ and $W \simeq 2\frac{A}{P}$. We considered that the width of this theoretical cortical rectangle could be taken as an estimation of "mean thickness" of the cortex, while its length corresponded to the "length" of the cortical ribbon.

Statistics

Mean, standard deviation (SD), ordered statistics, coefficient of correlation (r of Pearson) were computed with Hewlett-Packard "General Statistics Pac" and "Regression Analysis Pac". T probability was calculated using a two-tailed unpaired t-test.

Results

General statistics are given in Table 1. There was no significant correlation between the total surface of the cortex and BTS ($r = 0.447$, $t = 1.58$, $p(t) = 0.145$), between surface of the frontal lobe and BTS ($r = 0.27$, $t = 0.88$, $p(t) = 0.38$), nor between surface of the parietal lobe and BTS ($r = 0.37$, $t = 1.25$, $p(t) = 0.24$).

A strong positive linear correlation was noted between the area of the temporal lobe and BTS ($r = 0.769$, $t = 3.81$, $p(t) = 0.003$). The correlation matrix (Table 2) showed that the length of the temporal cortex was the variable which was highly correlated with BTS, whereas the mean cortical thickness was not significantly correlated with BTS.

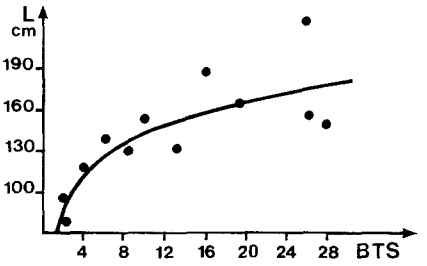

Fig. 1. Correlation between the test score of Blessed et al. (1968) and the length of the temporal cortex (*cm*). $N = 12$

The best fitted correlation curve between BTS and length of the temporal cortex was of the following functional form: $Y = 77.7\ X^{0.234}$ (Fig. 1) ($r = 0.8$).

Discussion

Cerebral atrophy in SDAT is a well-established fact and has been ascertained by weight (Jellinger and Riederer 1983) and volume (Hubbard and Anderson 1981) measurements of the brain.

Our results confirm that selective atrophy of temporal cortex occurs in SDAT and show that this atrophy is related to a decrease in cortical length rather than to a decrease in cortical thickness. Surface reduction is in agreement with the data of Hubbard and Anderson (1981) which showed a selective temporal atrophy (as evaluated by area measurement on coronal section) in demented subjects over 80 years of age. The absence of significant reduction of cortical thickness also concords with the results of Terry et al. (1981) which demonstrated that the thickness of the coronal section of the midfrontal and superior temporal cortex was not statistically different in normal subjects and demented patients. As yet, the pathologic mechanism underlying cortical atrophy remains unknown. Cortical atrophy could be considered as the consequence of a great number of elementary microscopic changes. If these were occurring randomly, the reduction of surface would involve both length and thickness in the same proportion. As the reduction of length appeared much more important than the reduction of thickness, one should admit that atrophy is not a random process. If affected elements were distributed in specific layers, reduction of thickness would be expected to be prominent; on the contrary, if they were organized in a columnar pattern, thickness would remain normal, while length would be expected to be diminished. Our data favor the second hypothesis.

Only microscopic studies could allow to find out which elements are affected (cells or neuropil) and whether changes are actually distributed in a columnar pattern. Published data have regularly shown a reduction of cell density which would not be present if

Table 2. Correlation matrix

	tA			tT			tL		
	r	*t*	*p(t)*	*r*	*t*	*p(t)*	*r*	*t*	*p(t)*
BTS	0.77	3.81	0.003**	0.55	2.13	0.059^{ns}	0.74	3.5	0.006**
tA				0.73	3.35	0.007**	0.98	18.17	0.0000***
tT							0.6	2.39	0.019*

r, coefficient of correlation; *t*, two-tailed unpaired *t*-test; *p(t)*, probability of a deviation greater than *t*; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; ns, not significant

shrinkage of the neuropil was the major cause of atrophy. Cellular loss was of nearly equal importance in all layers of the cortex (Terry et al. 1981; Mountjoy et al. 1983); this does not support the laminar hypothesis and could be in accordance with loss of columns of cells. Other studies have mentioned a "disruption of the normal cytoarchitecture" (Brun and Englund 1980; Hyman et al. 1984) but the type of disruption observed was not defined according to the present criteria of length or width atrophy; thus, further quantitative studies seem necessary to investigate whether loss of neurons does actually occur in columns.

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