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STEREOLOGICAL QUANTITATION OF BRAINS FROM DEMENTED AND NONDEMENTED OLD FEMALES

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ABSTRACT

Neocortical volume, surface, and thickness and the volume of the ventricular system was estimated using unbiased stereological methods on brains from 28 old females (mean age 81.8 yrs) with increasing degree of senile dementia and compared with the same parameters on brains from 13 age-matched (mean age = 82.7 yrs) nondemented controls. Brains from the demented patients had decreased cortex volume. Neocortical thickness was significantly reduced in the demented patients with the highest degree of reduction in the most demented patients, while surface area not was changed. Furthermore ventricular volume was significantly increased in the demented patients.

KEY WORDS: Cavalieri estimate, dementia, neocortical volume, stereology, surface, thickness.

INTRODUCTION

While many earlier studies have been concerned with correlating different neurodegenerative changes like neuritic plaques and neurofibrillary tangles with clinical symptoms and severity of dementia, only few studies have been concerned with quantitating gross cerebral atrophy in senile dementia and Alzheimer's disease.

In these earlier studies atrophy of the temporal and parietal regions have been most often reported with concomitant ventricular enlargement. The results have, however, been somewhat conflicting. For example reductions of total hemispheric volume in patients with Alzheimer's disease was reported by Miller et al. (1980) and De la Monte (1991) using image analyzing systems. They found no change in the ratio between grey and white matter. Global cortical atrophy in Alzheimer brains with the temporal lobe most affected was reported by Mann (1991). Using a point counting method Hubbard and Anderson (1981) found global cortical atrophy in younger Alzheimer patients while in older patients (>80 yrs) only the temporal lobe was affected. Finally, Duyckaerts et al. (1985) using an image analyzing system reported a selective atrophy of the temporal cortex in Alzheimer patients, and found that this atrophy was related to a decrease in cortical length rather than to a decrease in cortical thickness.

In the present study unbiased stereological methods have been used for the estimation of the neocortical volume, surface and thickness, and the volume of the ventricular system, in old females with increasing degree of dementia compared with age-matched nondemented controls.

MATERIAL

Brains from 28 senile demented women (mean age = 81.8 yrs) with varying degrees of dementia were compared with brains from 13 age-matched non-demented and neurologically sound women (mean age = 82.7 yrs), see Tbl.1.

Table 1. The material is subdivided in four groups (group 0-3) according to severity of dementia: Group 0 = controls, group 1 = mild to moderate dementia, dementia score 1-3; group 2 = marked dementia, score 4-5; group 3 = severe dementia, score 6-7.

Mean and Coefficient of Variation (CV = SD/mean) are indicated.

	Dementia score	Age (yrs)	Body height (cm)	Body weight (kg)	Fix.brain weight (gr)	Number of cases
0	-	82.7 (0.08)	157.8 (0.04)	55.4 (0.18)	1201 (0.11)	13
1	2.9 (o.13)	80.9 (0.01)	154.5 (0.03)	56.5 (0.21)	1077 (0.08)	7
2	4.6 (0.11)	82.0 (0.03)	155.5 (0.04)	55.5 (0.23)	1052 (0.08)	11
3	6.2 (0.07)	82.3 (0.03)	157.1 (0.04)	48.0 (0.19)	1030 (0.10)	10

All the demented patients were from a chronic psychogeriatric ward in Copenhagen, Denmark, and had all been prospectively evaluated with a psychometric dementia test and neurologic examination once a year during their last years. The tests assessed a wide range of cognitive functions (intelligence, orientation, psychomotor performance, language, visuospatial abilities and various types of memory). Performances on the different psychological subtests were scored on a 7 point scale, and a general score was obtained from one to seven, with a high score indicating severe dementia. The control patients had all died from non-neurologic illnesses in general surgical and medical wards. Although the control patients had not been assessed psychologically during life, all had been living a normal, independent life at home up to a few days before death. Brains from the demented patients were collected in the period from 1971-76 and the controls from 1979-87. Brains showing any sign of infarction or other lesions that could contribute to dementia were excluded.

METHOD

All brains were fixed in 0.1M sodium phosphate buffered formaldehyde for at least five months. Right or left hemispheres were chosen at random. The hemispheres were embedded in 6% agar, sliced coronally at 7 mm intervals and the volumes of neocortex, white matter, central grey structures and ventricles were estimated by the Cavalieri method (Gundersen et al.,1988; Regeur and Pakkenberg,1989). Neocortical surface was estimated by counting the total number of intersections between test lines and neocortical surface.
For statistical evaluation the material was subdivided into four subgroups according to severity of dementia and the brain data evaluated in these four groups using Kendall's tau.

RESULTS

The fixed brain weight was statistically significantly reduced by 17% in the severe demented group (mean 1201 g, CV = 0.11) compared to controls (mean 1030 g, CV = 0.10), p = 0.004.

Neocortical volume was decreasing with increasing dementia, Kendall´s tau = - 0.24, p = 0.07 which did not reach statistical significance. Neocortical surface did not change with dementia, Kendall´s tau = - 0.092, p = 0.50. Neocortical thickness was significant reduced by in the demented patients compared with controls, Kendall´s tau = - 0.46, p = 0.0007. Ventricular volume increased significantly with increasing degree of dementia, Kendall´s tau = + 0.31, p = 0.018. The volumetric data are given in Table 2. For further details on the material, see Regeur, in preparation.

Table 2. Volumetric data: Neocortical volume (NE V), neocortical surface (Ne S), neocortical thickness (Ne t) and ventricular volume (Ve V) given in mean values and CV for the four groups of patients

Patient group	Ne V (cm^3)	Ne S (cm^2)	Ne t (mm)	Ve V (cm^3)
0	200.8 (0.18)	763 (0.16)	2.58 (0.09)	12.19 (0.65)
1	186.9 (0.13)	760.1 (0.06)	2.46 (0.10)	13.81 (0.54)
2	181.3 (0.13)	752.1 (0.12)	2.39 (0.08)	14.8 (0.35)
3	169.5 (0.13)	751.2 (0.08)	2.25 (0.09)	16.73 (0.38)

DISCUSSION

Using unbiased stereological methods we found that neocortical thickness had the closest relationship with dementia of the four different volumetric data estimated. Furthermore, neocortical thickness was the most stabile estimator with less variation (CV 8-10%) compared with the other parameters.

The estimation of neocortical surface was not unbiased as the estimator/equation requires an isotropic design, which is not the case in this study. However, as shown earlier by Oster et al.(1993) the bias in estimating the neocortical surface in a non-isotropic design is minimal and negligible compared to the biological variation. The neocortical surface was normal in the demented patients.

Neocortical volume decreased with increasing degrees of dementia but did not reach significance. A similar result was reported for this age group by Hubbard and Anderson (1981). Possible regional changes has not been evaluated, but are under preparation (Regeur, in preparation).

In this material the ventricular volume increased significantly with increasing dementia, but with a wide variation (CV's 35-65%). As pointed out by Hubbard and Anderson (1981) ventricular enlargement is not an accurate diagnostic marker for cerebral atrophy.

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