En ce qui concerne les cellules mammotropes les résultats de notre étude concordent donc avec les études biochimiques effectuées chez l'animal et chez l'homme, qui indiquent que dans plusieurs espèces existent une augmentation de la sécrétion de prolactine chez les sujets porteurs de cancer mammaire.

Le rôle de cette perturbation et le mécanisme de contrôle de la sécrétion de la prolactine sont encore mal connus. Mais des arguments parlent en faveur d'une altération primaire de la fonction thyroïdienne qui serait abaissée. La baisse du taux des hormones thyroïdiennes, d'une part sensibiliserait les cellules mammaires à l'égard de la prolactine, et d'autre part entraînerait une hyperproduction de TRH qui agît aussi comme «releasing factor» de la prolactine. C'est ce mécanisme d'hyposécrétion de thyroxine–hypersecrétion de prolactine qui serait responsable du développement de dysplasies puis de néoplasies des tissus mammaires[16].

L'étude morphométrique au microscope électronique effectuées ici confirme l'existence d'une hyperactivité des cellules à prolactine chez la souris C3H (MTV +) porteuse de tumeur mammaire. Mais elle souligne aussi l'importance des cellules somatotropes qui témoignent d'une hyperactivité fonctionnelle parallèle à celle des cellules mammotropes. La signification et le rôle de ces perturbations méritent d'être précisés.

Synaptic vesicles and other organelles of human mossy fibre endings. A morphometric study[1]

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Summary. The mossy fibre ending organelles of 6 men were studied, using morphometric methods. The numerical densities of agranular, coated and dense core vesicles, as well as the number of agranular vesicles per μm^2 of the synaptic surface and per synapse were calculated.

Recently, Dyson and Jones[2] have pointed out that, apart from the variations that can be found in the synaptic contacts of under-nourished rats[3], there are significant differences in the synaptic vesicular population of these animals. However, the absence of an accurate determination of correcting factors for form and size distribution of synaptic contacts[4], which are needed for the calculation of their numerical densities[5], has not allowed us to establish a numerical relationship between synaptic vesicles and synapses. Since the accurate determination of such factors appears to be even more difficult in man that in experimental conditions, it seems advisable, in quantitative studies concerning human terminals, to use a procedure that can avoid such difficulty. We have studied human mossy fibre endings with a morphometric method[6] that allows their quantitative ultrastructural characterization without having to take into consideration the factors cited above.

Material and methods. Observations were made on the granular layer of the cerebellar cortex of 6 men (males of 9, 15, 33, 34, 39 and 41 years old). Tissue fragments of the posterior lobe of the cerebellar hemispheres of 5 men were obtained during surgery for removal of acoustic neuromas of the cerebello-pontine angle. In the 6th man, tissue fragments were removed from the pyramid of the cerebellar vermis during brain surgery for removal of a medulloblastoma of the 4 ventricle. The ethical principles of the Helsinki Declaration of 1964, concerning human experimentation, were followed. In all cases, blocks were fixed according to the Kanaseki and Kadota[7] method; details of the procedure were described in a previous study[8].

1 This work was granted by INIC: Centro de Morfologia Experimental (MbP1) e Centro de Anatomia Patológica e Oncologia (MbP3).

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Summary of the ultrastructural morphometric study of mossy fibre ending organelles in 6 men

	Observation No.	Agranular vesicles N_V (No./μm^3)	Coated vesicles N_V (No./μm^3)	Dense core vesicles N_V (No./μm^3)	Mitochondria V_V (μm^3/100 μm^3)	Multivesicular bodies V_V (μm^3/100 μm^3)	Smooth endoplasmic reticulum S_V (μm^2/100 μm^3)
Man	I	840 ± 80*	12.4 ± 2.1*	1.85 ± 0.39*	22.0 ± 2.4*	0.22 ± 0.08*	47.5 ± 5.4*
	II	1015 ± 45	11.9 ± 2.0	0.95 ± 0.42	17.4 ± 0.8	0.15 ± 0.08	37.7 ± 2.9
	III	854 ± 27	10.9 ± 1.6	2.58 ± 0.52	20.9 ± 1.0	0.20 ± 0.07	40.3 ± 3.0
	IV	973 ± 32	9.4 ± 2.1	1.50 ± 0.31	19.9 ± 1.4	0.10 ± 0.05	39.6 ± 6.3
	V	850 ± 74	10.4 ± 0.9	2.33 ± 0.51	18.2 ± 1.8	0.36 ± 0.16	39.2 ± 3.2
	VI	954 ± 100	9.0 ± 1.2	0.96 ± 0.40	21.8 ± 2.0	0.10 ± 0.05	57.3 ± 8.2
	Interindividual mean ± SE	914 ± 31	10.7 ± 0.5	1.70 ± 0.28	20.0 ± 0.8	0.19 ± 0.04	43.6 ± 3.1

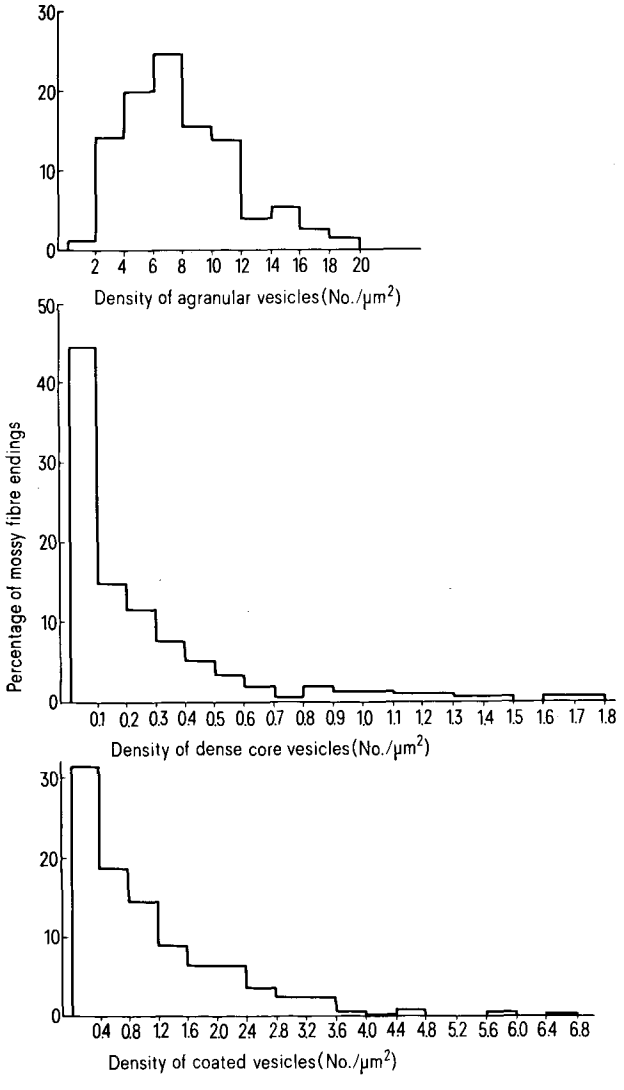
* Mean and SE of the mean of 5 blocks (10 micrographs from each block).

From each man, 5 tissue blocks were selected at random. From each block, a silver ultrathin section was double stained with uranyl acetate and lead citrate and microphotographed at a primary magnification of × 10,000. The exact final magnification for each set of electron micrographs was calibrated by means of a carbon grating replica; as an extreme variation of less than 5.0% of the mean was found, only the mean value for the final magnification (× 30,000) was used in the calculation of the morphometric parameters. From each ultra-thin section, 10 electron micrographs of different mossy fibre endings chosen at random were recorded. A double quadratic lattice test system of 400 points and 225 cm^2 of area was used to calculate the volumes of mitochondria and multivesicular bodies per unit volume of mossy fibre endings (Vv), the surface of smooth endoplasmic reticulum per unit volume of mossy fibre endings (Sv) and the numbers of agranular, coated and dense core vesicles per unit volume of mossy fibre endings (Nv). In order to determine Nv, the formula of DeHoff and Rhines[9] modified by Haug[10] was used $Nv = Na/\bar{D} + T - 2h$), in which Na is the number of vesicles, T is the section thickness and h is the smallest recognizable cap section of the vesicles. Na of dense core vesicles was calculated through the counting of their profiles in all the area of mossy fibre endings profiles while the counting of agranular and coated vesicles was made on a square of approximately 1.56 μm^2 (25 points of the quadratic lattice), that was chosen at random on each mossy ending profile. $\bar{D}$ of the agranular vesicles was calculated measuring 100 profiles of agranular vesicles in each man and the mean diameters of coated and dense core vesicles were calculated, measuring 50 profiles from each type of vesicles in each man. T was estimated to be 50 nm in all the electron micrographs and h was calculated measuring the smallest profile of each type of vesicle. In order to determine all the other morphometric parameters, the techniques described by Weibel[6] were used. No corrections were made in what concerns Holmes effect.

To calculate the number of agranular vesicles per μm^2 of synaptic contacts, the numerical density of vesicles was divided by the synaptic surface per unit volume of mossy fibre endings. The value of this synaptic surface was calculated by multiplying the previously determined surface-to-volume ratio of the terminals by the fraction of the terminal neurolema with synaptic contacts[11]. To calculate the number of agranular vesicles per synapse, we considered, as did Vrensen and DeGroot[12], that the synaptic contacts could be compared to flat circular surfaces; this assumption makes possible to use the average length of the synaptic contacts, previously determined[11], in the calculation of the area of the referred synaptic circles ($A = (0.5L_{syn})^2$). The multiplication of this area by the number of agranular vesicles per μm^2 of the synaptic contacts, gives the number of vesicles per synapse. Individual morphometric data were averaged and the SD and the SE were calculated. The values obtained were submitted to an analysis of variance. 2 means were considered significantly different if the probability of error (p) was smaller than 0.05.

Results and discussion. The results obtained are summarized in the table. The results obtained in the 6th man, whose tissue blocks were removed from the cerebellar vermis, were similar to those found in the other 5 men, except in what concerns the surface density of smooth endoplasmic reticulum which, for unknown reasons, is higher in the 6th man than in the other ones (table). The number of agranular vesicles per μm^2 of the synaptic surface was found to be 2135 ± 78, and the number of vesicles per synapse 131 ± 5, assuming that the area of synaptic contacts is 0.0616 μm^2.

The mean diameter of agranular vesicles was found to be 45.5 nm, while those of coated and dense core vesicles were found to be 73.3 nm and 97.0 nm, respectively. In what concerns the vesicular densities, it was possible to disclose a Gaussian distribution for agranular vesicle density and a Poisson distribution for coated and dense core vesicle densities (figure). We think that this method not only gives a reliable determination of the parameters concerning synaptic surface and synaptic vesicles but also allows the calculation of the number of vesicles per synapse.



Histogramatic distribution of numerical densities of agranular, dense core and coated vesicles.

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