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Age-related Changes of Pyramidal Cell Basal Dendrites in Layers III and V of Human Motor Cortex: A Quantitative Golgi Study

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Summary. Age-related changes of pyramidal cell basal dendrites in layers III and V of human motor cortex (area 4) were analyzed quantitatively in Golgi-impregnated sections by Sholl's method of concentric circles (Sholl 1953). The present data suggested that basal dendrites of the pyramidal cells were decreased in number with advancing age, and that the decrease was more prominent in basal dendrites of layer V pyramidal cells than in those of layer III pyramidal cells.

Key words: Age-related changes – Basal dendrites – Pyramidal cells – Motor cortex – Man

Introduction

Age-related changes of the pyramidal cells in the cerebral cortex have been shown by the Golgi impregnation method in man (Scheibel et al. 1975, 1977; Watanabe 1981) as well as in other animals (Feldman and Dowd 1975; Vaughan 1977; Mervis 1978; Cupp and Uemura 1980; Leuba 1983). According to Scheibel et al. (1975), deterioration of pyramidal cell dendrites in aged human cortex is more prominent in horizontally oriented dendrite components, especially basal dendrites, than in vertically oriented dendrite components. Age-related loss of spines on apical dendrites of layer III pyramidal cells has been observed in the human motor cortex (Watanabe 1981). Thus, the present study was attempted to quantitatively examine age-related loss of basal dendrites of the pyramidal cells in human motor cortex as visualized by the Golgi impregnation method.

Material and Methods

Twenty-eight brains used in this study were obtained from patients of 14–96 years of age, who were neurologically normal and autopsied within 6 h after death. The brains were removed and immediately placed in 10% formalin for more than 5 months. Subsequently, parasagittal regions of the precentral gyrus (area 4) were cut into blocks of 2–3 mm thickness. The tissue blocks were immersed in 2.5% potassium dichromate for 2–3 days at 34.5°C. The tissue blocks were then briefly washed in 1% silver nitrate, and placed in newly prepared 1% silver nitrate for 20 h. Subsequently, the tissue blocks were dehydrated in absolute alcohol for 6 h, embedded in 14% celloidin, and cut serially into sections of 120 μm thickness. The sections were dehydrated in absolute alcohol, cleared in xylene, and mounted in dammar gum without cover-slips.

Sections were judged acceptable for quantitative examination according to the criteria set forth by Rutledge et al. (1974); uniform staining of neuronal processes, absence of precipitated debris, good contrast between cells and background, and relatively uniform tissue thickness. The quantitative analysis was limited to basal dendrites of the pyramidal cells in layers III and V (Fig. 1). For each of the 28 cases, 30 cells were selected in each layer from sections judged acceptable. Drawings of selected cells were made using the drawing attachment Model BH2-DA. Only dendrites entirely contained within a single section of 120 μm thickness were analyzed.

Each of the selected cells was analyzed quantitatively according to Sholl's method of concentric circles (Sholl 1953); concentric spheres were drawn at 20-μm intervals centered on the cell bodies, and dendritic intersections with each sphere were counted (Fig. 2). This procedure provided a measure of dendritic densitiy as a function of distance from the cell body.

The 28 cases were divided into four age-groups, i.e. groups 1, 2, 3, and 4, which respectively included patients of 14–49 years of age (five cases; mean 36.2 years of age), those of 52–69 years of age (ten cases; mean 62.4 years of age), those of 70–79 years of age (six cases; mean 73.3 years of age), and those of 80–96 years of age (seven cases; mean 86.2 years of age). Individual differences in the dendritic density between the young group (group 1) and the other older groups were tested for each sphere by the Mann-Whitney *U*-test.

Results

Basal Dendrites of Layer III Pyramidal Cells (Table 1)

The dendritic densitiy was maximum at the 60-μm sphere in all four age-groups. In group 2, the number of basal dendrites was similar to that in group 1 at the domain from the 40-μm to the 160-μm sphere. On the

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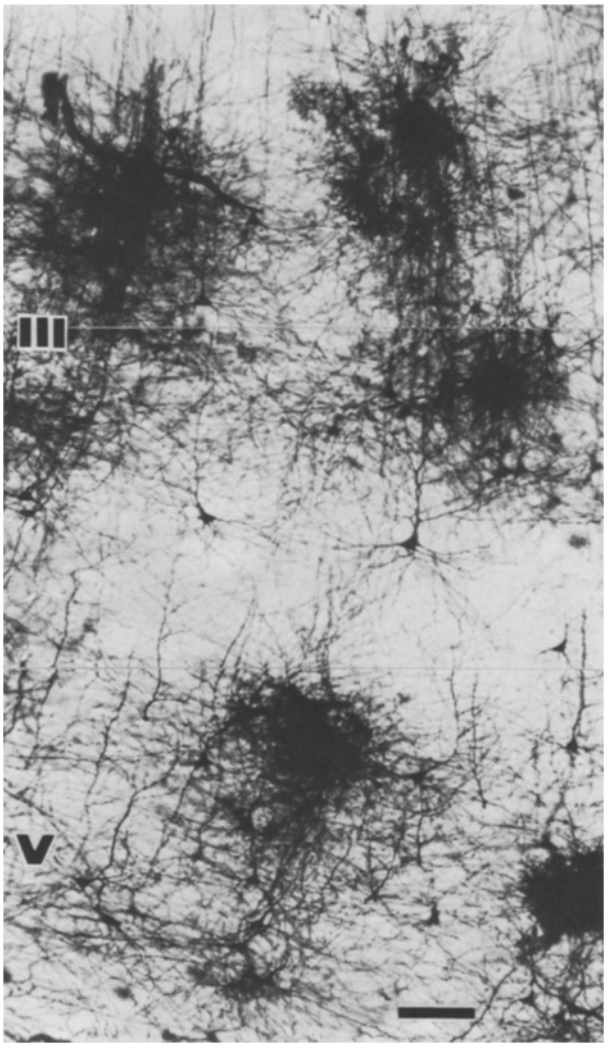

Fig. 1. Pyramidal cells in layers III and V of the motor cortex. Scale bar: 100 μm

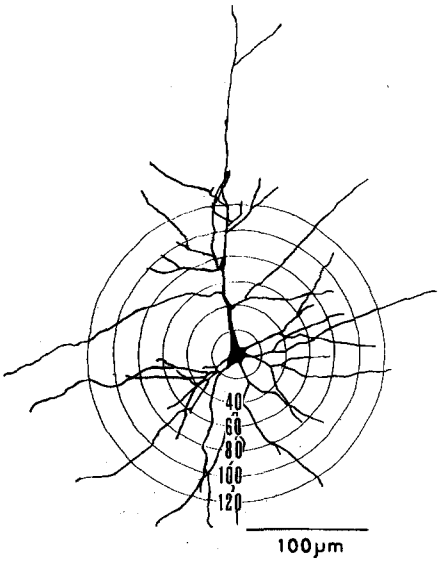

Fig. 2. Sholl's method of concentric circles. The number of basal dendrites intersected with each sphere was counted. This provides a measure of dendritic density as a function of distance from the cell body

other hand, the numbers of basal dendrites at the 180-μm and the 200-μm spheres in group 2 were smaller than those in group 1; the difference between the two groups was statistically significant.

In group 3, the number of basal dendrites at the 100-μm and the 120-μm spheres was smaller than that in group 1; the difference between the two groups was statistically significant. On the other hand, between group 3 and group 1 no significant differences were found in the number of basal dendrites at the 140-μm, 160-μm, and 180-μm spheres. The number of basal dendrites at the 200-μm sphere in group 3 was smaller than that in group 1; the difference was statistically significant.

In group 4, the number of basal dendrites was the smallest among the four groups. At the 40-μm, 60-μm, and 80-μm spheres, the number of basal dendrites in group 4 was similar to that in group 1. However, the number of basal dendrites at the domain from the 100-μm to the 200-μm sphere was smaller in group 4 than in group 1.

Basal Dendrites of Layer V Pyramidal Cells (Table 2)

Age-related decrease of basal dendrites was more marked in layer V pyramidal cells than in layer III pyramidal cells. In group 2, the number of basal dendrites was smaller than that in group 1 at the whole domain from the 40-μm to the 200-μm spheres; the difference was statistically significant. In group 3, the number of basal dendrites was slightly smaller than that in group 2, and significantly smaller than that in group 1. The number of basal dendrites in group 4 was the smallest among the four groups.

Discussion

According to the previous Golgi impregnation studies, pyramidal cells of the aging human cortex seem to undergo a sequence of histopathologic events (Scheibel et al. 1975, 1976, 1977; Watanabe 1981). Although Watanabe (1981) observed age-related loss of spines on apical dendrites of layer III pyramidal cells in the human motor cortex, Scheibel et al. (1975) reported that deterioration of pyramidal cell dendrites was more prominent in basal dendrites than in apical dendrites. Thus, in the present study, the number of basal dendrite was estimated in Golgi-impregnated pyramidal cells in layers III and V of the human motor

Table 1. Basal dendrites of pyramidal cells in layer III

Group	Distance from soma (μm)								
	40	60	80	100	120	140	160	180	200
I	7.3	9.3	8.8	7.5	6.2	4.7	3.6	2.7	2.0
II	7.6	9.1	8.5	7.0	5.4	4.0	2.9	2.0*	1.4*
III	7.8	8.7	7.9	6.4*	5.0*	3.8	2.9	2.1	1.4**
IV	7.8	8.4	7.8	6.3**	4.8**	3.4**	2.3**	1.5***	1.0***

Data presented as mean number of basal dendrites which were intersected with each sphere
Statistical analysis was by Mann-Whitney *U*-test
* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

Table 2. Basal dendrites of pyramidal cells in layer V

Group	Distances from soma (μm)								
	40	60	80	100	120	140	160	180	200
I	9.1	12.1	12.2	11.0	9.3	7.8	6.4	4.9	3.8
II	8.5*	10.5***	10.3***	9.2***	7.6***	6.1***	4.7***	3.6**	2.6**
III	7.6***	9.5***	9.5***	8.7***	7.3***	5.9***	4.5***	3.6**	2.8**
IV	7.5***	8.2***	7.4***	6.0***	4.7***	3.5***	2.6***	1.9***	1.3***

Data presented as mean number of basal dendrites which were intersected with each sphere
Statistical analysis was by Mann-Whitney *U*-test
* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

cortex (area 4), using the method of concentric circle (Sholl 1953) which provides a measure of dendritic density as a function of distance from the cell body (Fig. 2).

All of the 28 cases which were examined in the present study were neurologically normal and divided into four groups according to their ages. The Golgi-impregnated sections were used for the quantitative examination of basal dendrites of pyramidal cells only when they fulfilled the criteria set forth by Rutledge et al. (1974).

As evidenced in Tables 1 and 2, the number of basal dendrites of pyramidal cells in the human motor cortex was smaller in the older groups (groups 2–4; 52–96 years of age) than in the youngest group (group 1; 14–49 years of age), and the difference between the number of basal dendrites in the older groups and that of the youngest group was more marked in basal dendrites of layer V pyramidal cells than in those of layer III pyramidal cells. Thus, the present data suggest that in the human motor cortex, basal dendrites of layer V pyramidal cells are more susceptible to the aging process than those of layer III pyramidal cells.

In accordance with the present data, Leuba (1983) observed in the visual cortex of the mouse that age-related loss of dendrites around the cell bodies of the pyramidal cells was 25% in layer III and 34% in layer V. On the other hand, Scheibel et al. (1975) reported that senile changes of basal dendrites in the human neocortex were most marked in layer III pyramidal cells of the prefrontal and superior temporal gyri. The data of Scheibel et al. (1975), however, were not quantitative, and Scheibel et al. (1977) actually observed marked senile changes in layer V pyramidal cells of the motor cortex; by the eighth decade of life, 75% or more of Betz cells and less than 30% of non-Betz pyramidal cells showed age-related changes, such as shortening, disruption, and progressive disappearance of basal dendrites.

According to a quantitative Golgi analysis of layer II pyramidal cells in the prefrontal cortex of the rhesus monkey (Cupp and Uemura 1980), pyramidal cell basal dendrites are preferentially lost at the distal tips and undergo a distal-proximal degenerative process with advancing age. The present data suggest that the age-related loss of basal dendrites of layer III pyramidal cells in the human motor cortex initially occurs at their distal portions (Table 1).

In regard to the mechanism of the loss of dendrites with advancing age, Scheibel et al. (1975) hypothesized that during aging, neurofibrillary material accumulates within the cell bodies at the base of the dendrites to such an extent that cytoplasmic transport along dendrites is disrupted and finally occluded. In the

present study, however, no findings suggesting the accumulation of neurofibrillary material or the disturbance of cytoplasmic transport were obtained.

On the basis of a Golgi study in the cerebral cortex of the rabbit, Globus and Scheibel (1967) assumed that vertical dendrite systems received presynaptic inputs of extracortical origin, while horizontal dendrite systems, including basal dendrites, were recipient to afferents of intracortical origin. If this assumption remains valid in the human motor cortex, the decrease of pyramidal cell basal dendrites may result in a deficiency of cortical regulatory influences upon the output systems of the motor cortex.

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