Virchows Archiv A Pathol Anat (1993) 422:307–311

Virchows Archiv A
Pathological Anatomy and Histopathology

Foamy spheroid bodies in the globus pallidus and the substantia nigra pars reticulata: an investigation on regional distribution in 56 cases without neurodegenerative diseases

Nobutaka Arai[1], Toshio Mizutani[2], Yoshio Morimatsu[1]

[1] Department of Clinical Neuropathology, Tokyo Metropolitan Institute for Neuroscience, 2–6 Musashidai, Fuchu, Tokyo 183, Japan
[2] Department of Neuropathology, Tokyo Metropolitan Institute of Gerontology, 35-2 Sakae-cho, Itabashi, Tokyo 173, Japan

Received July 7, 1992 / Received after revision and accepted January 11, 1993

Abstract. In order to clarify the sites of predilection for foamy spheroid bodies (FSBs) their regional distribution was studied in 56 persons (30–98 years) without neurodegenerative diseases. Variable amounts of FSBs were observed in approximately 30% of cases and favoured the rostro-ventral parts of the globus pallidus (GP), including the ventral pallidum, and/or the substantia nigra pars reticulata (SNr). The results strongly suggest that FSBs develop during aging and are a hitherto undescribed pathological hallmark for degeneration of the GP and the SNr.

Key words: Foamy spheroid body – Globus pallidus – Ventral pallidum – Substantia nigra pars reticulata – Basal ganglia

Introduction

Studies on foamy spheroid bodies (FSBs) (Arai et al. 1988, 1992), a recently highlighted structure in the human central nervous system, have shown that FSBs are entirely different from axonal swellings (so-called spheroids), although they may have been misinterpreted as a sort of "spheroid"; that FSBs consist of complex ultrastructural profiles which are closely related to astrocytes; and that they are sometimes observed in the substantia nigra (SN) and/or the globus pallidus (GP) in neurodegenerative diseases. Heterogeneous factors, including degeneration, infection, anoxia and injury, may be responsible for the development of FSBs and from a historical standpoint, FSB-like findings seemed to have been described occasionally in the SN and/or the GP as incidental findings of unknown significance. They have been described using various names (Arai et al. 1989) but their true nature remains to be determined.

Correspondence to: N. Arai, Department of Neuropathology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK

The specific aim of this study was to determine the sites of predilection for FSBs in normal brains, in order to see whether FSBs developed during the aging of the human brain and whether the appearance of FSBs represents evidence of system degeneration.

Materials and methods

Histological examination was performed on 56 brains (27 male and 29 female) from persons without neurodegenerative disease. Their ages ranged from 30 to 98 years, as summarized in Table 1. Immediately after autopsy, each brain was fixed in 10% formalin and the following slices were embedded in paraffin blocks: (1) cerebral coronal slices through the frontal pole, the striatal head, the anterior commissure, the mammillary body, the lateral geniculate body, the pulvinar, the posterior horn of the lateral ventricle and the occipital pole; (2) mid-brain slices through the superior colliculus and/or inferior colliculus; (3) slices through the pons (upper, middle or lower); (4) the medulla oblongata (upper and/or lower); and (5) the cerebellum where horizontal or sagittal slices included the dentate nucleus. Each block was cut at a thickness of 8 μm and stained with haematoxylin and eosin, Klüver-Barrera and Bodian stains.

Microscopical observation was performed in whole regions in all cases to spot FSBs (Fig. 1) and, as illustrated in Fig. 2, amounts of FSBs were demonstrated by three degrees of density of dots under a microscope (sparse dots = 1–5/ × 200 fields; dense dots = 6–15/ × 200 fields; black = over 16/ × 200 fields).

Results

Variable numbers of FSBs (Fig. 1) were observed almost exclusively in the GP and/or the substantia nigra pars reticulata (SNr) in 10 of 56 cases examined (28.6%), as demonstrated in Table 1. Representative distributions of FSBs are illustrated in Fig. 2. In the GP, they were observed in both the medial and lateral segments, and particularly favoured the rostro-ventral part of the GP, including the subcommissural part of the GP (sometimes referred to as "ventral pallidum"). In the SN, most FSBs were observed in the ventral part of the SNr,

Table 1. Histological summary

Case no.	Age/sex	Globus pallidus				Substantia nigra		
		Mineralization[a]	Rarefaction with vascular hyalinosis[a]	Astrocytosis[a]	FSB[b]	Depigmentation[a]	Astrocytosis[a]	FSB[b]
1	30/m	−	−	−	−	−	+	−
2	32/m	−	−	−	−	−	−	−
3	44/f	−	−	−	+	−	−	+
4	47/m	−	−	−	−	−	−	−
5	49/f	−	−	−	−	+	−	+
6	51/f	−	−	−	−	+	+	−
7	54/m	+	+	+	−	−	−	−
8	54/m	−	−	−	−	−	+	−
9	55/m	−	−	+	+	+	−	+
10	60/m	+	−	−	−	−	+	−
11	62/f	−	−	−	−	+	−	−
12	64/m	−	−	−	−	−	+	−
13	67/m	−	−	−	−	−	−	−
14	69/m	−	−	−	−	−	−	−
15	69/m	−	−	+	+	+	+	++
16	70/f	+	−	+	+	+	++	++
17	70/f	+	−	−	−	+	+	−
18	72/m	−	−	−	−	−	+	−
19	72/m	++	+	+	−	+	+	−
20	74/f	−	−	−	−	+	+	−
21	76/m	−	−	−	−	+	++	−
22	76/f	−	−	−	−	++	++	−
23	76/f	++	+	+	−	+	++	−
24	77/m	−	++	+	++	++	+	+++
25	78/f	−	−	−	−	+	+	−
26	78/f	−	+	+	−	++	+	−
27	78/f	+	++	+	+	+	+	++
28	79/m	+	−	−	−	++	+	++
29	80/m	−	−	−	−	+	+	−
30	80/f	−	−	−	−	+	−	−
31	81/f	−	−	−	−	+	−	−
32	81/m	+	−	−	−	+	+	−
33	81/m	+	+	+	−	+	+	−
34	82/m	−	−	+	++	+	+	+
35	82/m	−	−	−	−	−	+	−
36	82/f	−	++	++	−	+	+	−
37	82/f	+	−	−	−	−	−	−
38	83/f	+	−	−	−	+	+	−
39	83/f	+	−	−	−	−	+	−
40	83/m	+	−	−	−	+	++	−
41	83/m	−	−	−	−	+	+	−
42	85/m	−	−	−	−	++	+	−
43	86/f	++	++	+	+	+	+	−
44	86/m	−	−	−	−	++	++	−
45	86/f	−	−	−	−	−	+	−
46	87/f	+	+	+	+	+	+	−
47	87/m	+	−	−	−	+	+	−
48	88/m	+	−	−	−	+	+	+
49	88/f	−	−	−	−	−	+	−
50	88/m	−	−	−	−	−	+	−
51	88/f	+	++	+	−	+	+	−
52	88/f	−	+	+	++	+	+	+
53	90/f	−	++	+	−	+	+	−
54	91/f	++	++	+	++	+	++	++
55	96/m	−	++	+	++	+	+	+++
56	98/f	−	+	+	++	+	+	+++

[a] −, almost none; +, mild; ++, moderate to severe

[b] −, none; +, a small number (1–5/×200 field); ++, moderate number (6–15/×200 field); +++, a great number (over 16/×200 field)

FSB, Foamy spheroid body

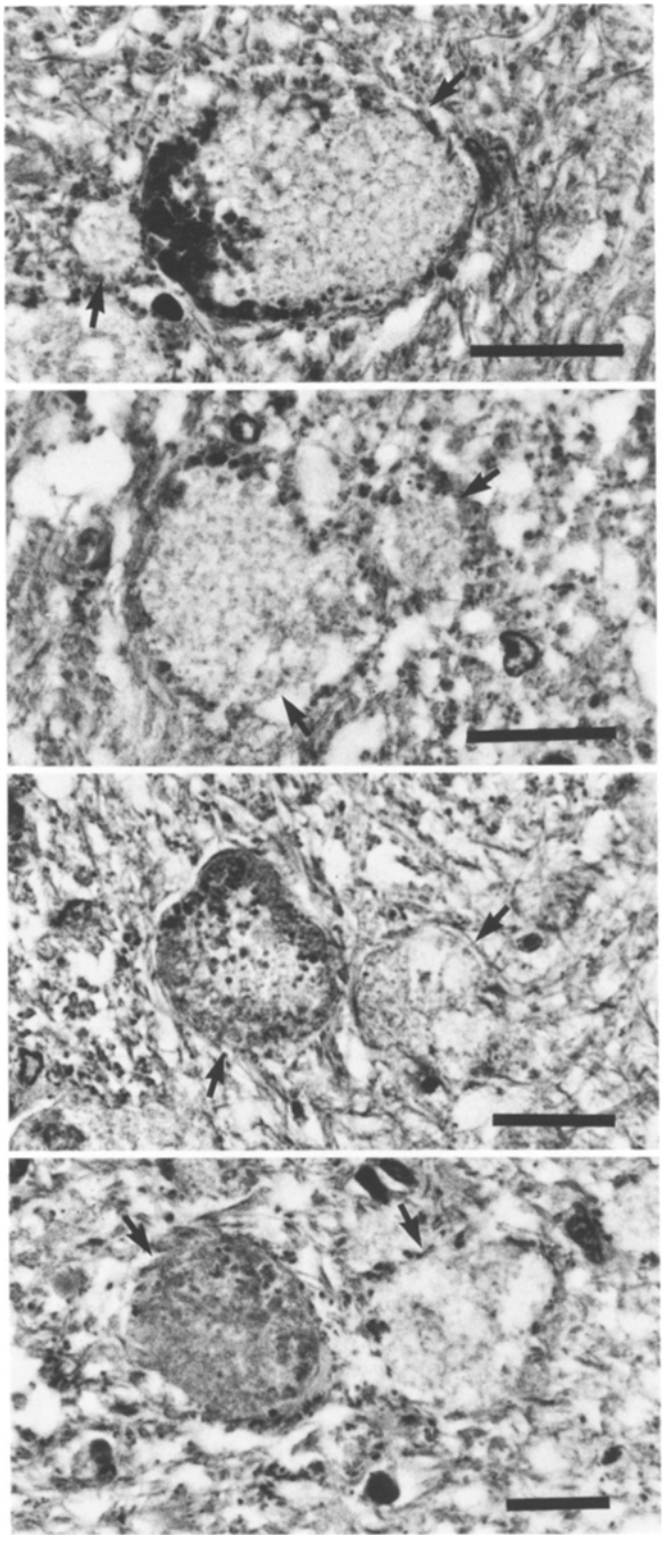


Fig. 1. Various microscopical findings of foamy spheroid bodies as indicated by *arrows*. Some of them were faintly stained pale by H&E stain, showing amorphous and foamy appearances. The others occasionally contained varying numbers of eosinophilic and rather coarse granules in their periphery. *Bar* = 20 μm

especially in the rostral SNr. In addition to the GP and the SNr, however, a very small number of FSBs were noticed less frequently in the striatum in 2 cases (3.6%). No FSBs appeared in the SN pars compacta (SNc). In summary, FSBs favoured the rostro-ventral parts of both the GP and the SNr (Fig. 3).

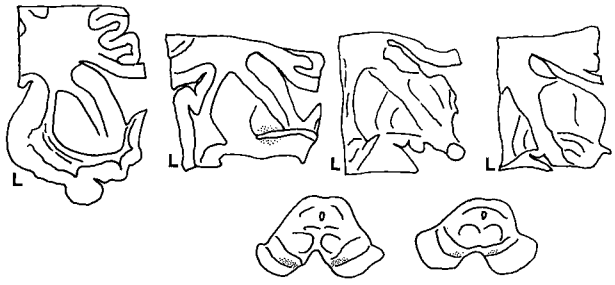
The appearance of FSBs seemed to be independent of degrees of other histological changes such as mineralization (pseudocalcification), rarefaction with vascular hyalinosis and astrogliosis in the GP, or loss of pigmented neurons and astrogliosis in the SN (Table 1). In some cases, however, a number of FSBs were observed in association with severe arterial hyalinosis and infarction (case 54) and with old cystic infarction (case 56).

Discussion

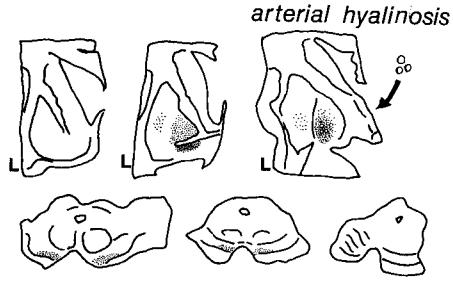
This study clearly demonstrates that FSBs favour the rostro-ventral parts of the GP and/or the SNr in approximatelly 30% of cases without neurodegenerative diseases. In the GP, FSBs favoured (1) the rostral parts of both the inner and the external segments of the GP and (2) the ventral pallidum, which is a part of the GP extending ventrally and rostrally beneath the anterior commissure, defined in rats (Heimer and Wilson 1975), man (Haber and Watson 1985; Haber 1987) and monkeys (Haber 1987), and considered to be closely related to the limbic system (for a review, see Nauta 1986). In addition to the GP, FSBs were seen in the SN, and of great interest is that the appearance of FSBs was almost confined to the SNr within the SN.

The GP and the SNr organize the innermost tier of the basal ganglia, the tier III described by Nauta (1979). Interestingly, the distributional topography of FSBs was very similar to that region, which has close cytoarchitectural and neurochemical similarities throughout (Nauta 1986). Taking these into account, it could be assumed that FSBs represent degeneration of the innermost part of the basal ganglia (tier III) and our study could support the idea that the GP and the SNr behave as a unitary aggregate, fortuitously separated by the internal capsule (De Long and Georgopoulos 1979). No FSBs have been observed in cases with degeneration of the SNc associated with idiopathic Parkinson's disease or in cases with combined degenerations of both the GP and the Luy's body, as seen in dentato-rubro-pallido-luysial atrophy or Machado-Joseph disease (Arai et al. 1992). The present topographical data confirm that the development of FSBs depends not on dysfunction of the SNc-striatal dopaminergic system nor on that of the pallido-luysial (or luysio-pallidal) system, but on that of the GP-SNr unitary system.

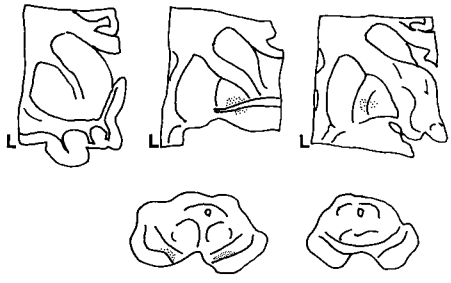
The cases examined were mainly obtained from elderly persons who had neither neurological symptoms nor significant pathological changes. It is believed that our data represent the ordinary pattern of the appearance of FSBs in frequency and topography during aging, and we suggest that aged persons have relatively more FSBs, although a quantitative analysis was not undertaken.



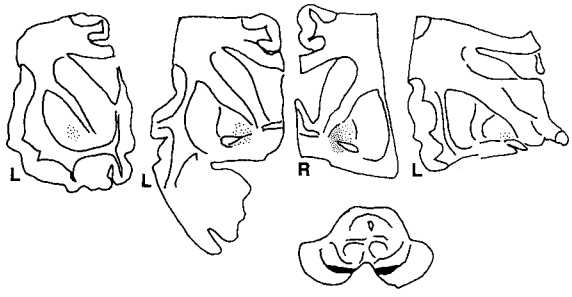
Case-15 69/male



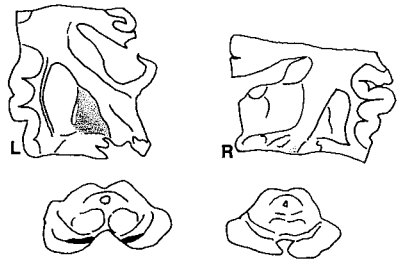
Case-54 91/female



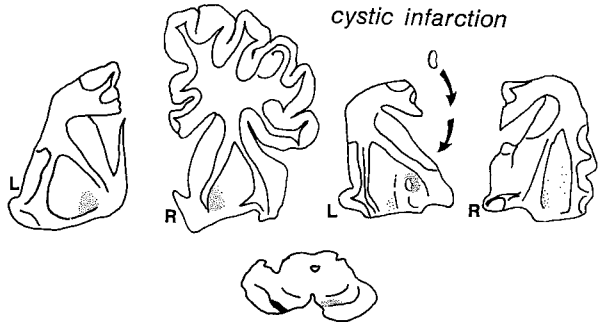
Case-16 70/female



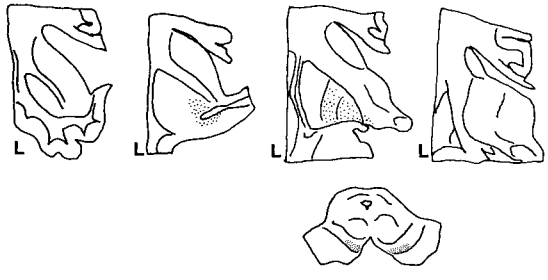
Case-55 96/male



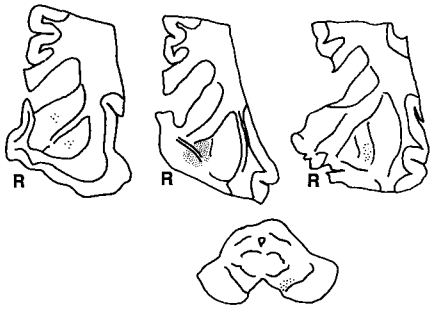
Case-24 77/male



Case-56 98/female



Case-27 78/female



Case-34 82/male

Fig. 2. Representative distributional patterns of foamy spheroid bodies (FSBs) in nine cases. Density of dots represents amount of FSBs. In general, FSBs favoured the rostro-ventral parts of the globus pallidus and the substantia nigra pars reticulata. FSBs rarely appeared in the striatum of relatively aged persons, as shown in cases 34, 54 and 56. Although FSBs were almost independent of other histological changes, as summarized in Table 1, a number of FSBs were seen around infarction or arterial hyalinotic lesions in some cases (cases 54 and 56); (▪) 1–5/ × 200 field; (▪) 6–15/ × 200 field, (▬) 16 < / × 200 field

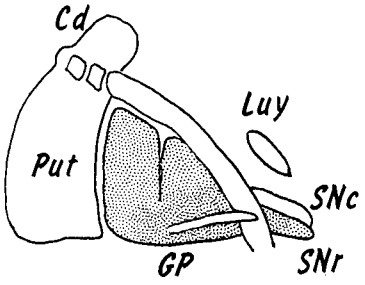


Fig. 3. Schematization of the sites of predilection of FSBs (modified from Nauta's schema, 1986). As indicated by dot-like appearances, FSBs favoured the globus pallidus (including the subcommissural pallidum) and/or the substantia nigra pars reticulata. *Cd*, Caudate nucleus; *Put*, putamen; *GP*, globus pallidus; *Luy*, Luy's body; *SNc*, substantia nigra pars compacta; *SNr*, substantia nigra pars reticulata

It is not clear, however, whether the development of FSBs is caused by aging processes of the nervous system alone. It is possible that the development of FSBs depends on age-related vulnerability to various medical complications in the GP and the SNr, such as anoxia. However, with the exception of 2 cases (nos. 54 and 56) with infarctions, there was no obvious relationship between the appearance of FSBs and degrees of other common histological changes such as mineralization (pseudocalcification), rarefaction with arterial hyalinosis and astrocytosis. This strongly suggests that FSBs are not produced secondary to such factors but through hitherto unknown pathological processes.

References

Arai N, Honda Y, Amano N, Yagishita S, Misugi K (1988) Foamy spheroid bodies in the substantia nigra: report of an unusual case with recurrent attacks of peculiar twilight state. J Neurol 235:330–334

Arai N, Yagishita S, Amano N, Iwabuchi K, Misugi K (1989) "Grumose degeneration" of Trétiakoff. J Neurol Sci 94:319–323

Arai N, Yagishita S, Misugi K, Oda M, Kosaka K, Mizutani T, Morimatsu Y (1992) Peculiar axonal debris with subsequent astroyctic response (foamy spheroid body): a topographic, light microscopic, immunohistochemical and electron microscopic study. Virchows Arch [A] 420:243–252

DeLong MR, Georgopoulos (1979) Motor functions of the basal ganglia as revealed by studies of single unit activity in the behaving primate. Adv Neurol 24:131–140

Haber S (1987) Anatomical relationship between the basal ganglia and the basal nucleus of Meynert in human and monkey forebrain. Proc Natl Acad Sci USA 84:1408–1412

Haber SN, Watson SJ (1985) The comparative distribution of enkephalin, dynorphin and substance P in the human globus pallidus and basal forebrain. Neuroscience 14:1011–1024

Heimer L, Wilson RD (1975) The subcortical projections of the allocortex. Similarities in the neural associations of the hippocampus, the piriform cortex, and the neocortex. In: Santini (eds) Golgi Centennial Symposium: perspectives in neurology. Raven Press, New York, pp 177–193

Nauta HJW (1979) A proposed conceptual reorganization of the basal ganglia and telencephalon. Neuroscience 4:1875–1881

Nauta HJW (1986) The relationship of the basal ganglia to the limbic system. In: Vinken PJ, Bruyn GW, Klawans HL (eds) Handbook of clinical neurology, vol 5. Extrapyramidal disorders. Elsevier, Amsterdam, pp 19–31