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Parkinson's Disease: Distribution of Lewy Bodies and Monoamine Neuron System*

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Summary. A systematic study of the central and peripheral nervous systems in 3 cases of Parkinson's disease has demonstrated that Lewy bodies are present in 27 nuclei. Of these 20 nuclei (12 pigmented and 8 unpigmented) are involved in 2 or all 3 cases.

It is noticed that the distribution of Lewy bodies in Parkinson's disease described here corresponds surprisingly well to that of monoamine (dopamine, noradrenaline and serotonin) cell bodies demonstrated in rats by the histochemical fluorescence method. This correlation is similar to that of Alzheimer's neurofibrillary changes in postencephalitic Parkinsonism as described by Ishii. Inasmuch as these viewpoints are also in agreement with previously reported biochemical data on Parkinsonism, it is suggested that Parkinsonism (idiopathic and postencephalitic) should represent a system degeneration of monoamine neuron systems.

Key words: Parkinson's disease — Lewy bodies — Monoamine neuron system.

Lewy bodies were first described by Lewy [23] in 1912 in the substantia innominata and the dorsal vagal nucleus in Parkinson's disease. They were first seen in the substantia nigra by Trétiakoff [32] who called them Lewy bodies. Subsequent observations on Parkinson's disease confirmed the almost constant occurrence of numerous Lewy bodies in the pigmented brainstem nuclei [5, 6, 19, 24], although they have also been found in various other conditions; postencephalitic Parkinsonism [20, 24, 28], Parkinsonism-dementia complex [21], Alzheimer's disease [33], senile dementia [20, 24], Hallervorden-Spatz syndrome [9], striato-nigral degeneration [35], progressive supranuclear palsy [34], other conditions [20, 26], and the aging brain [5, 17, 20, 24]. This has suggested a relationship between Lewy bodies and the pathogenesis of Parkinson's disease. This study was intended to investigate the exact distribution of Lewy bodies in Parkinson's disease and to help to clarify their significance.

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MATERIAL AND METHOD

Three autopsy cases of Parkinson's disease were examined: case 1, 59 year old male; case 2, 61 year old male; case 3, 45 year old male.

Multiple sections were prepared from various parts of both the central and peripheral nervous systems. They consisted of frontal, parietal, occipital and temporal lobes including Ammon's horn with hippocampal gyrus, putamen, caudate nucleus, globus pallidus, thalamus, hypothalamus, subthalamic nucleus, mammilllary body, substantia innominata, amygdaloid nucleus, midbrain, pons, medulla oblongata, cerebellar hemisphere with dentate nucleus, spinal cord, trigeminal ganglion, spinal root ganglion, and paravertebral and celiac sympathetic ganglia.

All sections were stained with hematoxylin and eosin, and occasionally using the Bodian, Periodic acid-Schiff and Azan methods when these were considered necessary. The tissues were subjected to a systematic cell-by-cell examination at a magnification of 400 diameters. The designation of the brainstem nuclei followed that of Olszewski and Baxter [27].

RESULTS

The anatomical location and number of Lewy bodies (Fig. 1) in each case are shown in Figure 2 and Table 1. Although the number of Lewy bodies varied considerably from site to site and from case to case, the distribution was essentially similar in each case. At least one nerve cell with a Lewy body was found in 27 nuclei. Of these, 20 nuclei were involved in 2 or all 3 cases. These nuclei are:

1. Hypothalamus, lateral nucleus, 2. Hypothalamus, posterior nucleus, 3. Substantia innominata, 4. Griseum centrale mesencephali, 5. Nucleus substantiae nigrae, 6. Nucleus parabrachialis pigmentosus, 7. Nucleus supratrochlearis, 8. Nucleus tegmenti pedunculopontinus, subnucleus compactus, 9. Nucleus tegmenti pedunculopontinus, subnucleus dissipatus, 10. Nucleus locus coeruleus, 11. Nucleus subcoeruleus, 12. Nucleus pontis centralis oralis, 13. Nucleus centralis superior, subnucleus medialis, 14. Processus griseum pontis supralemnis-

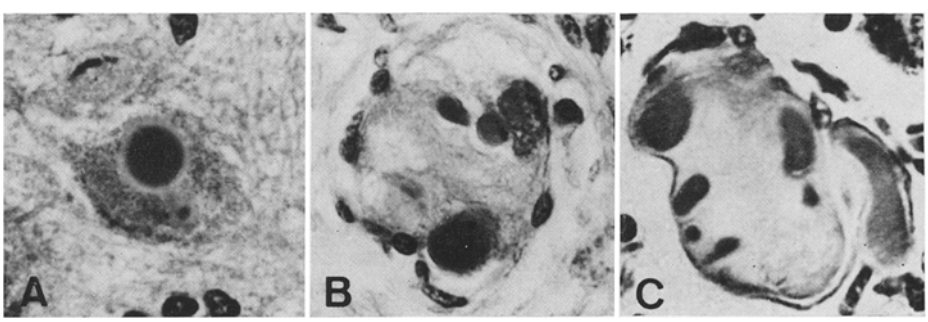

Fig. 1. (A) A Lewy body with a deeply eosinophilic core. Case 1, Nucleus centralis superior, subnucleus medialis (hematoxylin-eosin, ×640). (B) A neuron from stellate ganglion containing 3 Lewy bodies and eccentric nucleus. Case 2. (hematoxylin-eosin, ×640). (C) A neuron of coeliac ganglion containing several intracytoplasmic Lewy bodies of various sizes and shapes. An "extracellular" Lewy body of elongated shape is present immediately adjacent to the neuron. Case 2. (Bodian, ×640)

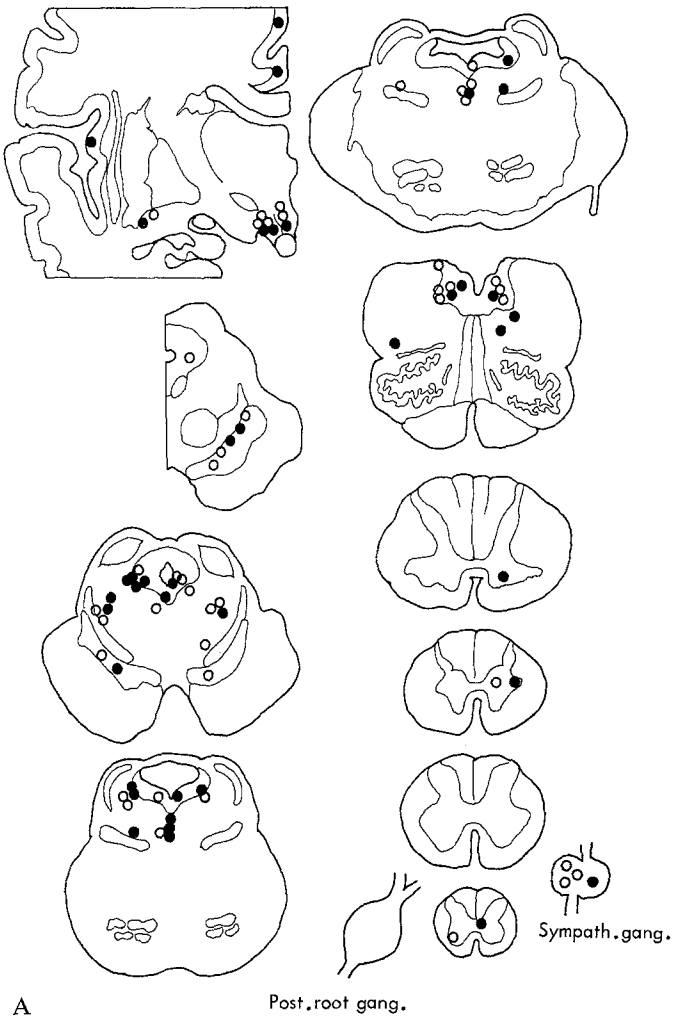

Fig. 2 A–C. Schematic drawing of distribution of Lewy bodies in 3 cases of Parkinson's disease. • = 1 to 3 intracytoplasmic Lewy bodies. ○ = 1 to 3 "extracellular" Lewy bodies. (A) case 1; (B) case 2; (C) case 3

calis, 15. Nucleus dorsalis motorius nervi vagi, 16. Nucleus gigantocellularis, 17. Nucleus paragigantocellularis lateralis, 18. Nucleus medullae oblongata centralis, subnucleus ventralis, 19. Intermediolateral nucleus of spinal cord, 20. Sympathetic ganglia; paravertebral and celiac. The involvement of these nuclei is illustrated in Figure 3.

Lewy bodies were not observed in the Ammon's horn, amygdaloid nucleus, putamen, caudate nucleus, globus pallidus, thalamus, red nucleus, inferior olive, dentate nucleus or Purkinje cells of the cerebellum.

A total of 120 sections from cervical, thoracic and lumbar spinal root ganglia failed to show any inclusions.

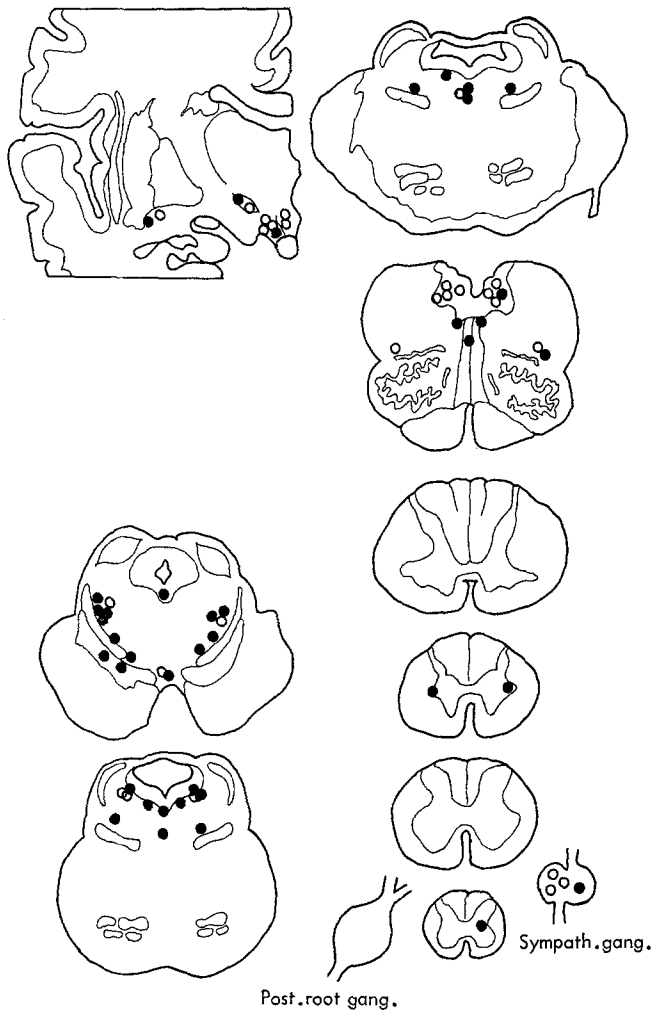

Fig. 2B

So-called extracellular Lewy bodies, which have been attributed to Lewy body type cellular degeneration by den Hartog Jager and Bethlem [13], are found frequently in almost the same distribution as that of intracytoplasmic Lewy bodies, especially in the hypothalamus, dorsal vagal nucleus and sympathetic ganglia.

DISCUSSION

Despite numerous reports concerning Lewy bodies [5, 6, 12—14, 17, 19—21, 24, 28, 31—33], little information is available regarding their exact distribution in Parkinson's disease. In the present study, Lewy bodies were found in 27 different nuclei, of which 20 were common to 2 or all 3 cases. Only the nucleus parabrachialis pigmentosus was not noted by den Hartog Jager and Bethlem (1960)

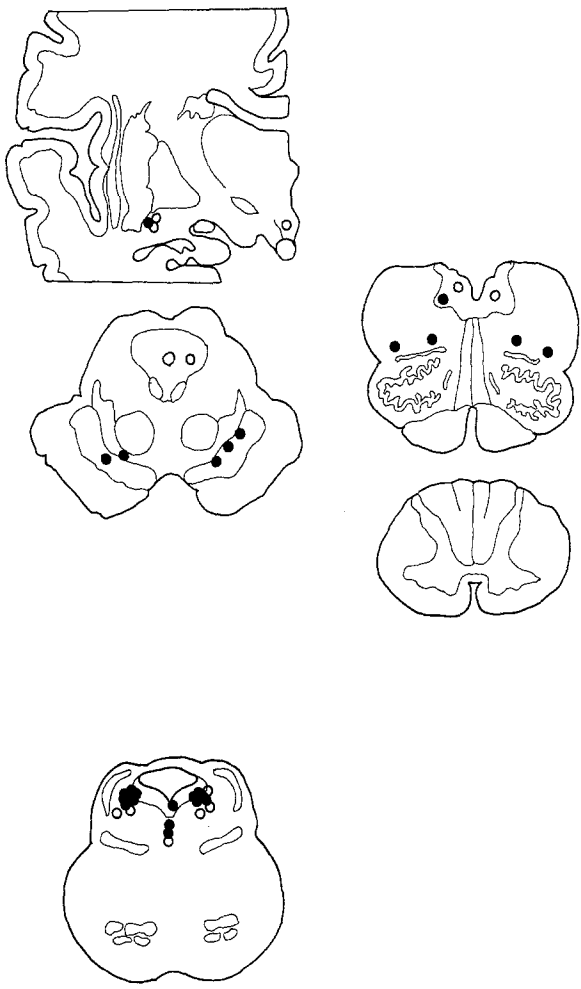

Fig. 2 C

when they studied Lewy bodies in serial sections in one case of Parkinson's disease [13]. Hence, the results of the present study and those reported by den Hartog Jager and Bethlem reveal that these 20 nuclei are the common sites for Lewy bodies in Parkinson's disease.

It has been well documented that Lewy bodies occur frequently in the pigmented nuclei of the brainstem in Parkinson's disease [5, 6, 19, 24, 32]. A comparison of the distribution of these bodies in the 20 nuclei with their distribution in the pigmented cells of the central and peripheral nervous systems [4, 25] reveals that 8 of the 20 nuclei containing these bodies are not pigmented. These are the hypothalamus, substantia innominata, griseum centrale mesencephali, nucleus supratrochlearis, nucleus centralis superior, processus griseum pontis supralemniscalis, and intermediolateral nucleus of the spinal cord.

Table 1. Distribution of Lewy bodies in 3 cases of Parkinson's disease

	Case		
	1	2	3
Cerebral cortex	+	-	-
Hypothalamus, lateral nucleus	+	+	-
Hypothalamus, posterior nucleus	+	+	+
Substantia innominata	+	+	+
Subthalamic nucleus	-	+	-
Griseum centrale mesencephali	+	+	+
Nucleus substantiae nigrae	+	+	+
Nucleus parabrachialis pigmentosus	+	+	+
Nucleus paranigralis	-	+	-
Nucleus supratrochlearis	+	+	/
Nucleus tegmenti pedunculopontinus, subnucleus compactus	+	+	/
Nucleus tegmenti pedunculopontinus, subnucleus dissipatus	+	+	/
Griseum centrale pontis	+	-	-
Nucleus locus coeruleus	+	+	+
Nucleus subcoerleus	+	+	+
Nucleus pontis centralis oralis	+	+	+
Nucleus centralis superior, subnucleus medialis	+	+	+
Processus griseum pontis supralemniscalis	+	+	+
Nucleus dorsalis motorius nervi vagi	+	+	+
Nucleus of Roller	/	+	/
Nucleus gigantocellularis	/	+	+
Nucleus paragigantocellularis lateralis	/	+	+
Nucleus medullae oblongatae centralis, subnucleus ventralis	+	+	/
Spinal cord, intermediolateral nucleus	+	+	/
Spinal cord, intermediomedial nucleus	+	-	-
Spinal cord, anterior horn	+	-	-
Sympathetic ganglia; paravertebral & coeliac	+	+	/

Nomenclature of brainstem nuclei is according to Olszewski and Baxter [27]
+ = Lewy body present, - = no Lewy body detectable, / = not examined

Recent biochemical studies on idiopathic and postencephalitic Parkinsonism [7,15,16,29,30] have shown a decrease in the content not only of dopamine but also of noradrenaline and serotonin. Dahlström and Fuxe (1964) have demonstrated the exact distribution of the monoamine cell bodies in the brainstem of the rat by the histochemical fluorescence method [10]. In the brainstem, there is a striking similarity between the distribution of Lewy bodies here described and that of the monoamine cell bodies described by Dahlström and Fuxe. In other words, of the 15 nuclei containing Lewy bodies which are located in the brainstem, 11 are pigmented and, as pointed out by Bazelon et al. [4], correspond to the catecholamine (dopamine and noradrenaline) cell bodies of Dahlström and Fuxe, and the remaining 4 unpigmented nuclei are located in the raphe and their distribution is identical with that of the serotonin cell bodies. The only nucleus among the 20

which has been demonstrated not to contain monoamine cell bodies is the intermediolateral nucleus of the spinal cord.

Ishii [22] has studied, in detail, the distribution of Alzheimer's neurofibrillary changes in 8 cases of postencephalitic Parkinsonism and pointed out its striking similarity to that of the monoamine cell bodies described by the authors mentioned above. In fact, marked similarity is noted between the distribution of Lewy bodies in idiopathic Parkinsonism as described in this paper and that of Alzheimer's neurofibrillary changes in postencephalitic Parkinsonism as described by Ishii [22], although some difference is to be noted in that Alzheimer's neurofibrillary changes are also described in the caudate nucleus and putamen in 6 out of 8 cases of postencephalitic Parkinsonism. Neurofibrillary changes also seem to occur more frequently in the serotonin cell bodies rather than in the catecholamine cell bodies in the brainstem, contrary to the disposition of Lewy bodies in idiopathic Parkinsonism.

It seems quite important that both Lewy bodies and Alzheimer's neurofibrillary changes, which have been regarded as characteristic of idopathic and postencephalitic Parkinsonism respectively, show a similar distribution to that of the monoamine cell bodies, suggesting that degeneration of monoamine cell bodies causes a reduction of the content of monoamines in idiopathic and postencephalitic Parkinsonism.

Another significant fact bearing on this point is that the monoamine cell bodies give rise to ascending and descending axons to various areas of the central nervous system, and thus form a large number of monoamine neuron systems which produce and store the dopamine, noradrenaline and serotonin respectively and which, in all probability, function by releasing the amines as neurotransmitters from their synaptic terminals [1–3, 8, 10, 11, 18]. These results in agreement with biochemical data [7, 15] suggest that degeneration of numerous monoamine neuron systems other than the nigro-neostriatal dopamine neuron system also occur in Parkinsonism.

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