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The somatosensory cortex in multiple system atrophy

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Abstract

In multiple system atrophy (MSA), it has been accepted that the motor-related cortical area may degenerate. However, there have been few investigations of the postcentral cortex of the somatosensory area. For this reason, we investigated the effects of MSA on both the precentral and the postcentral cortex and were able to demonstrate degenerative changes in each. Furthermore, our study showed that degeneration of the postcentral cortex preceded that of the precentral cortex. In addition, we showed that the Betz cells were not selectively lost, but merely depleted like other neurons of the deep cortical layers. Therefore, the effects of MSA are apparently related to selective loss of the small-sized myelinated fibers in the corticospinal tract.

Keywords: Multiple system atrophy; Somatosensory cortex; Primary motor area; Neuronal loss; Pyramidal tract; Putamen; Pontine nuclei

1. Introduction

Approximately one century after Dejerine and Andre-Thomas published the first article on olivo-ponto-cerebellar atrophy in 1900, the discovery of glial cytoplasmic inclusions (GCIs) [1,2] was an epoch-making event in neurological science. It has become apparent that the distribution of GCIs corresponds closely to the topography of the pathological lesions of this disease [3,4]. It has become apparent that multiple system atrophy (MSA) is more widespread system degeneration than previously expected. Now it has been accepted that degeneration of the motor-related areas is the primary lesion and one of the essential pathologies of MSA. Since in cases of MSA, this area showed laminar astrocytosis [5], atrophy [6–8], neuronal loss [9], neuronal degeneration of the cortex [10], and the GCIs were distributed from the deep white matter through the subcortical areas into the cerebral cortex [3]. Furthermore, it has been suggested that the degeneration of white matter in MSA is closely related to the pathological changes occurring in the adjacent gray matter [11]. Betz cells have been used as one of the hallmarks of various pathological conditions of the motor cortex. In MSA, however, it is controversial whether the Betz cells are preserved or depleted, because there have been opposing reports demonstrating either loss [12] or preservation of the Betz cells [5,6].

The postcentral cortex, including the somatosensory area, connects closely to the primary motor area (MI) [13]. Unfortunately, in comparison with studies of the precentral cortex [5–10,12], we have little knowledge on the pathology of the postcentral cortex in MSA.

Thus, we analyzed cases of MSA to clarify the pathology of the somatosensory area besides MI, and behavior of the Betz cells.

2. Materials and methods

We examined 5 cases of MSA, donated to the Tokyo Metropolitan Neurological Hospital between 2004 and 2006 and 3 controls (mean ages 78 years) of non-neurological disorders. In all cases the clinical diagnosis of MSA was confirmed neuropathologically [1,14,15].

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The brain and spinal cord specimens were fixed with formalin and embedded in paraffin, and then were stained with hematoxylin and eosin, Klüver–Barrera (KB), Bodian, and Gallyas-Braak stains. Selected specimens were immunostained with α-synuclein (1:200, Santa Cruz biotechnology), glial fibrillary acidic protein (GFAP) (1:100, Novocastra), and CD-68 (KP-1) (1:400, Novocastra) by the labeled streptavidin-biotin method.

The degrees of neuronal cell loss and gliosis were estimated visually in areas indicated in Table 1. Counting of the GCIs was performed manually using an eye-piece micrometer by Gallyas–Braak staining.

Morphometry of the precentral and postcentral cortex at the vertex region was performed using 10 μm thicknesses of the parasagittally sectioned preparations stained with KB method. According to Brody's method [16], the neurons in an area surrounded by a rectangle (0.125 × 0.25 mm) of an eye-piece micrometer were counted manually. This procedure was repeated contiguously from the surface of the cortico-medullary junction. Counting was repeated in the next area eight times. As a whole, the area used for counting neurons was 2 mm the width of the cortex. The cortical surface for the counting area faced toward the central sulcus and was located parallel with the cortico-medullary border. The counting of neurons was performed in the MI, area 4 of Brodmann in the precentral cortex and primary somatosensory area (SI), and area 3b of Brodmann in the postcentral cortex.

Data were expressed as histograms. Each bar shows the number of the neurons at the point of the certain depth from the surface of the cortex. Statistical analyses were carried out for comparing cortical thickness and neuronal numbers of the MSA group with those of the control group using the Mann–Whitney *U* test.

3. Results

3.1. Clinical features

The duration of disease ranged from 4.3 to 18 years (mean 8.3 years). Table 1 shows the cases in order of the length of the duration of disease. Cases 1 and 2 were MSA-P in which Parkinsonism was the primary clinical finding, while the other cases were MSA-C in which cerebellar signs were clinically predominant [17]. All patients gradually developed the need for help in walking secondary to parkinsonism, cerebellar signs and/or autonomic dysfunctions at various points from 2 to 4 years from the onset of the disease. Case 2, 3 and 4, after the bedridden stage, showed forced laughing/crying, dystonia, cognitive dysfunction, and action myoclonus. Case 5, who survived far longer than the mean MSA duration (7.3 years [18]), developed dementia and then akinetic mutism. None of the cases showed severe corticospinal dysfunction.

Table 1
Neuropathological findings

Case no. (age at onset, gender)	Duration of disease (years)	Brain weight (Brain atrophy)	Putamen		Substantia nigra		Inferior olives		Pontine nuclei		Cerebellar white matter		Pyramid of medulla oblongata		Precentral cortical deep layer		Postcentral cortical deep layer	
			Loss of Ns or Fs	GCIs	Loss of Ns or Fs	GCIs	Loss of Ns or Fs	GCIs	Loss of Ns or Fs	GCIs	Loss of Ns or Fs	GCIs	Loss of Ns or Fs	GCIs	Gliosis	GCIs	Gliosis	GCIs
1 (57, F)	4.3	1296 g (−)	++	++	++	−	++	−	+	++	+	++	+	+	+	++	+	++
2 (48, F)	6	1310 g (−)	+	++	++	−	+	−	+	+	+	+	++	−	++	++	++	++
3 (63, M)	6	1225 g (−)	+	++	+	−	++	−	++	+	++	+	++	+	++	++	++	−
4 (53, F)	7	1230 g (−)	++	+	++	−	+++	−	++	+	++	+	++	+	+++	++	++	++
5 (57, M)	18	1127 g (+++)	+++	−	+++	−	+++	−	+++	−	+++	−	+++	−	+++	++	+++	++

Loss of Ns or Fs: Loss of neurons or fibers, +: mild or uncertain, ++: moderate; +++: severe GCIs, −<100/mm^2, 100/mm^2 ≦+<300/mm^2, 300/mm^2 ≦++.