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General Summary

Our research in 2011 was conducted in the following areas: 1) abnormalities of movement and posture in patients with Parkinson's disease (PD), 2) autonomic dysfunction in neurodegenerative diseases, 3) neurophysiological studies of diabetic polyneuropathy and visual information processing functions in neurodegenerative diseases, 4) neuroradiological studies with nuclear medicine, 5) ultrasonographic studies of cerebrovascular disease, 6) cerebral infarctions in clear cell carcinoma of the ovary, and 7) basic research on motor neuron disease and axonal plasticity of the central nervous system.

Research Activities

Abnormalities of movement and posture in patients with PD

Zonisamide is an antiepileptic agent that has been used, on the basis of the results of clinical and experimental studies, to manage tremor in patients with PD in Japan since 2009. In the present study, we quantitatively evaluated the effectiveness of zonisamide for parkinsonian tremor with an actigraph, an instrument that can sense motion and record motor counts. Actigraphy was performed before and after treatment with zonisamide in patients with PD. The motor count after treatment with zonisamide was significantly lower with that before treatment, objectively showing that zonisamide is effective for treating tremor in PD. We conclude that zonisamide is promptly effective for controlling tremor in patients with PD.

We also surveyed antecollis, camptocormia, and other postural deformities in PD and related disorders as part of a multicenter investigation.

Autonomic dysfunction in neurodegenerative diseases

We studied cardiovascular autonomic dysfunction in patients with Lewy body diseases, such as PD and dementia with Lewy bodies. Autonomic nervous function, including cardiac sympathetic gain, was evaluated on the basis of cardiac uptake of radioiodinated metaiodobenzylguanidine, the response to the Valsalva maneuver, and the orthostatic tolerance test. Using these methods, we examined the characteristics of subclinical autonomic nervous dysfunction in de novo PD. We also studied the relation of olfactory dysfunction to cardiovascular dysautonomia in patients with PD. Olfactory dysfunction in PD was thus found to be significantly related to both cardiac sympathetic and parasympathetic dysfunction, as well as to vascular sympathetic dysfunction. As nonmotor

symptoms of PD, olfactory dysfunction and autonomic network failure appear to be closely related.

Our present study demonstrated marked impairment of olfactory sensation in Japanese patients with PD, as assessed with the simple, inexpensive, and noninvasive Odor Stick Identification Test for the Japanese. This test could be clinically useful for detecting olfactory dysfunction in PD and for differentiating PD from multiple system atrophy and progressive supranuclear palsy.

We investigated the volume of the olfactory bulb in PD and PD-related diseases, including multiple system atrophy, progressive supranuclear palsy, corticobasal degeneration, and other neurodegenerative diseases. The olfactory bulb volume in PD was smaller than that in other PD-related diseases. These results are compatible with those of our study of the olfactory bulb in autopsy cases. Magnetic resonance may be a useful tool for the differential diagnosis of PD and PD-related diseases. We plan to carry out further examinations.

We used the Parkinson Fatigue Scale (PFS-16) to compare fatigue and various clinical features of PD subtypes. We divided patients with PD into 2 groups: those with tremor-dominant PD and those with akinetic rigid PD. Using PFS-16, we compared the patient groups in terms of age, disease duration, Unified Parkinson's Disease Rating Scale, postural changes in systolic blood pressure, cardiac metaiodobenzylguanidine uptake, and coefficient variation of RR intervals. We further divided patients with tremor-dominant PD and those with akinetic rigid PD into subgroups—the F+ subgroup (PFS-16≥3.3), and the F– subgroup (PFS-16<3.3)—and investigated the differences between the 4 subtypes. Patients with akinetic rigid PD and fatigue had severe motor impairment and orthostatic hypotension. Therefore, akinetic rigid PD differs from tremor-dominant PD in terms of motor impairment, fatigability, and autonomic failure.

Neurophysiological studies of visual information processing functions in neurodegenerative diseases and of diabetic polyneuropathy

Visual information processing functions were compared in patients with PD, dementia with Lewy bodies, and Alzheimer's disease, by means of visual and auditory event-related potentials. The findings of the study suggest that in patients with PD and in patients with dementia with Lewy bodies with visual hallucinations, but not in patients with Alzheimer's disease, visual information processing functions are selectively impaired, compared with auditory functions.

Nerve conduction studies and neurological examination of the feet with newly established techniques in patients with diabetes mellitus who had no sensory symptoms in the feet were performed in collaboration with the Department of Diabetes, Metabolism and Endocrinology. The findings of the study suggest that 34% of these patients have subclinical polyneuropathy.

Neuroradiological studies with nuclear medicine

Neuroradiological studies were performed in patients with neurodegenerative disorders, including dementia and parkinsonism. Brain perfusion images were compared by means of statistical imaging methods, such as 3-dimensional stereotactic surface projection

analysis of isopropyliodoamphetamine single-photon emission computed tomography (SPECT) images and the easy Z-score imaging system of ethyl cysteinate dimer SPECT images, among patients with dementia and parkinsonian disorders. These novel methods demonstrated the spectrum of pathological involvement of cholinergic and dopaminergic projections of Alzheimer's disease and PD, suggesting their usefulness for routine clinical practice.

Ultrasonographic studies of cerebrovascular disease

Cerebrovascular ultrasonography was useful for evaluating cerebral hemodynamics rapidly and in real time for patients with acute ischemic stroke. We evaluated the occlusion of intracranial and extracranial arteries with ultrasonography and monitored residual flow in real time every 15 minutes until 120 minutes after bolus administration of tissue plasminogen activator (t-PA). Two patients treated with t-PA had insufficient echo windows. In the first patient internal carotid artery occlusion was diagnosed with carotid ultrasonography. Because the occlusion persisted after t-PA therapy, endovascular therapy was considered. The second patient had ischemic stroke caused by cholesterol crystal embolism, which was indicated by a microembolic signal at the posterior cerebral artery. Monitoring of the microembolic signal with ultrasonography was useful for evaluating the therapeutic effect in this case of cholesterol crystal embolism. Real-time ultrasonographic monitoring is useful for evaluating the early thrombolytic effect of t-PA associated with early clinical recovery.

Cerebral infarctions in clear cell carcinoma of the ovary

Clear cell carcinoma of the ovary is a well-known cause of thrombosis and embolism. Clear cell carcinoma is reportedly complicated by pulmonary embolism more often than are other ovarian cancers. In this study we examined the complication of cerebral infarction in cases of ovarian cancer. We found that clear cell carcinoma was complicated by cerebral infarction more often than were other ovarian cancers.

The mechanism underlying the selective vulnerability of motoneurons

Amyotrophic lateral sclerosis is a fatal neurodegenerative disease characterized by progressive loss of motoneurons. Data suggest that selective vulnerability of motoneurons is due to an imbalance between excitatory and inhibitory innervation. Therefore, realizing the function and the development of inhibitory inputs on motoneurons is important for understanding selective vulnerability. We have performed experiments to study the plasticity of glycinergic synaptic inputs. We recorded the glycine synaptic membrane current from control mice and glycine receptor α3-deficient mice. Our findings suggest that glycine inputs increase with age and that glycine receptors (α3) induce presynaptic plasticity.

Publications

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Reviews and Books

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