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General Summary

Our research in 2009 was conducted in the following areas: 1) sexual dysfunction in Parkinson disease (PD), 2) autonomic dysfunction in neurodegenerative disease, 3) neurophysiological studies of the visual information processing functions and diabetic polyneuropathy, 4) neuroradiological studies with nuclear medicine, 5) ultrasonolographical studies of cerebrovascular disease, and 6) basic research in motor neuron disease and in the axonal plasticity of the central nervous system.

Research Activities

Sexual dysfunction in PD

Sexual dysfunction often occurs in PD. In this study, we used the Beck Depression Inventory, Second Edition, to evaluate depression. The relations of the degree of sexual debility to depression and autonomic disorders were studied. We concluded that the degree of sexual debility in PD is associated with the severities of depression and autonomic disorders.

Autonomic dysfunction in neurodegenerative disease

We studied the cardiovascular autonomic dysfunction in patients with Lewy body disease, such as PD or dementia with Lewy bodies. The autonomic function was evaluated using cardiac metaiodobenzylguanidine (MIBG) scintigraphy, hemodynamic function test by Valsalva maneuver and orthostatic tolerance test. Using these methods, we estimated the characteristics of subclinical autonomic nervous dysfunction in de novo PD without orthostatic hypotension (OH). We also studied the relation of olfactory dysfunction to cardiovascular dysautonomia in patients with PD. Olfactory dysfunction in PD was thus significantly related to both cardiac sympathetic and parasympathetic dysfunction, as well as vascular sympathetic dysfunction. As nonmotor symptoms of PD, olfactory dysfunction and autonomic network failure appear to be closely related in PD.

Cliniconeuropathological evaluation of the olfactory bulb in PD

We investigated the incidence and extent of Lewy body-related alpha-synucleinopathy (LBAS) in the olfactory bulb in 320 consecutive patients examined at autopsy. Paraffin-embedded sections were immunostained with antibodies against phosphorylated alpha-synuclein, tyrosine hydroxylase, phosphorylated tau, and amyloid-β. LBAS was

found in the central nervous system of 102 patients and in the olfactory bulb of 85 patients. All 35 patients who showed LBAS with pigmentation loss in the substantia nigra had LBAS in the olfactory bulb. LBAS in the amygdala was more strongly correlated with LBAS in the anterior olfactory nucleus than with that in the periphery of the olfactory bulb. These results indicate a high incidence of LBAS in the aging human olfactory bulb; they also suggest that LBAS extends from the periphery to the anterior olfactory nucleus and results in the clinical manifestations of Lewy body disease.

Neurophysiological studies of the visual information processing functions and diabetic polyneuropathy

Visual information processing functions were compared by means of visual and auditory event-related potentials in patients with PD, dementia with Lewy bodies, and Alzheimer's disease (AD).

The clinical utility of nerve conduction studies and neurological examination of the feet with newly established techniques was assessed, in collaboration with the Department of Diabetes, Metabolism and Endocrinology, in patients with diabetes mellitus but no sensory symptoms in the feet. The findings of the study suggest that 34% of patients with diabetes mellitus have subclinical polyneuropathy.

Neuroradiological studies with nuclear medicine

Brain perfusion images were compared using statistical imaging methods, such as 3-dimensional stereotactic surface projection of ^{123}I-isopropyliodoamphetamine single-photon emission computed tomography (SPECT) and easy Z-score imaging system of ^{99m}Tc-ethylcysteinate dimer SPECT, among patients with dementing and parkinsonian disorders. These novel methods demonstrated the spectrum of pathological involvement of the cholinergic and dopaminergic projections of AD and PD, suggesting their usefulness in routine clinical practice.

Amyloid imaging has recently emerged as a promising tool that enables us to evaluate the progression of disease objectively by assessing in vivo accumulation of amyloid-β in the brains of patients with AD. The purpose of this study was to directly compare the characteristics of 2 amyloid probes, [^{11}C] Pittsburgh Compound-B (PIB) and [^{11}C] BF-227, in the same patients with AD. The sensitivity of [^{11}C] PIB for detecting amyloid-β accumulation may be much higher than that of [^{11}C] BF-227. However, the difference in the distribution of the 2 probes presumably reflects the difference in the specificity to amyloid-β, or the difference in the affinity to the different stage of amyloid-β aggregation in the senile plaque generation process, or both. Therefore, these differences may provide additional pathophysiological information about amyloid cascade in AD.

Ultrasonolographical studies of cerebrovascular disease

Cerebrovascular ultrasonography is useful for evaluating cerebral hemodynamics rapidly and in real time for patients with acute ischemic stroke. We evaluated the occlusion of intracranial arteries using transtemporal and suboccipital window by transcranial color flow imaging with thrombolysis in brain ischemia flow-grading system and monitored

residual flow in real time every 15 minutes until 120 minutes after a bolus injection of tissue plasminogen activator (tPA). We monitored complete recanalization within 60 minutes after bolus injection of tPA in 2 of the 3 patients who had a good echo window. We conclude that real-time ultrasound monitoring is useful for evaluating the thrombolytic effect of t-PA.

Physiological role of monocarboxylate transport in the maintenance of hypoglossal motor neuron activity

In hypoglossal motor neurons, monocarboxylate transported by monocarboxylic acid transporter does not play a major role in maintaining the resting potential, which is likely to be maintained by ATP of other origins and makes a major contribution to the maintenance of excitatory synaptic transmission. The energy from monocarboxylate is mainly consumed at synapses.

Assessment of functional recovery and axonal plasticity in paired immunoglobulin-like receptor B-deficient mice after traumatic brain injury

The myelin-associated proteins Nogo, myelin-associated glycoprotein, and oligodendrocyte myelin glycoprotein inhibit axonal plasticity. Each protein interacts with both the Nogo receptor and paired immunoglobulin-like receptor B (PirB). We examined whether blocking PirB activity enhances axonal reorganization and functional recovery after cortical injury. However, our results suggest that blocking the function of PirB is not sufficient to promote axonal reorganization or functional recovery after cortical injury.

Publications

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