

Department of Internal Medicine

Division of Neurology

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General Summary

Our research in 2018 consisted of the following areas: (1) cerebrovascular disease and (2) neurodegenerative disease. We have performed studies of clinical and basic neurology.

Research Activities

Cerebrovascular disease

First, we have played a leading role in a multicenter study to investigate the clinical characteristics of juvenile stroke and have taken part in a multicenter study to clarify the characteristics of patients with stroke who are taking oral anticoagulants. Second, we have worked to establish an intrahospital system to treat patients with hyperacute stroke, consisting of stroke coordinate nurses who support the hyperacute treatment, including thrombolysis, and a new smartphone application (JOIN[®]) that can share texts, neuroimages, photographs, and videos among the stroke team. By using this application, we can evaluate stroke volume and the site of occlusion with the same quality as with the monitor of a personal computer. Third, we have performed several prospective and retrospective studies from our stroke care unit registry.

The main themes of our clinical studies are as follows:

- 1) To survey the current status of diagnosing deep vein thrombosis (DVT) via ultrasonographic examination of leg veins for patients with acute stroke and DVT
- 2) Right-to-left shunt evaluation with a novel probe (pasteable soft ultrasound probe)
- 3) To investigate whether the JOIN[®] application would shorten the time from admission to thrombolysis and mechanical thrombectomy in patients with hyperacute ischemic stroke
- 4) To investigate the relationship of cerebral microbleeds and functional outcomes in patients with a noncardiogenic transient ischemic attack and minor ischemic stroke
- 5) To investigate the proportion and explored factors for patients who have acute ischemic stroke with a poor outcome 90 days after onset but a good outcome at hospital discharge
- 6) To investigate the prevalence of DVT and pulmonary embolism in patients with a cryptogenic stroke and to investigate the clinical features of cryptogenic stroke in relation to the location of a DVT

Neurodegenerative disease

1. Parkinson's disease

We have continued clinical studies of cardiovascular autonomic dysfunction in patients with Parkinson's disease (PD). We investigated the association of cardiovascular autonomic dysfunction and cognitive impairment in patients with PD. We also evaluated the effect of a dopamine agonist (rotigotine) on nocturnal hypotension observed with a 24-hour ambulatory blood pressure monitoring test. Second, we compared the correlation with assessments of dopamine transporter scan, myocardial ^{123}I -meta-iodobenzylguanidine scintigraphy, and orthostatic hypotension between depression and anhedonia in patients with drug-naïve PD. Third, we investigated whether the characteristics of white and red blood cells are associated with clinical symptoms in patients with drug-naïve PD. Fourth, we developed a simple smell identification test to aid the diagnosis of PD and compared this test with standardized olfactory tests for Japanese patients. Finally, we examined the patterns and trends in anti-PD drug prescriptions in 20,936 patients (aged ≥ 30 years with newly diagnosed PD) using nationwide registry data from 2008 through 2016.

2. Multiple system atrophy

We investigated the association of dysphagia and vocal cord palsy in multiple system atrophy to assess the optimum timing of percutaneous endoscopic gastrostomy.

Basic research

1. PD

Mutations of the retromer component vacuolar protein-sorting protein 35 is linked to autosomal dominant forms of familial PD, PARK17. We analyzed the movement and function of the retromer in neurons differentiated from induced pluripotent stem cells from patients with PARK17.

2. Amyotrophic lateral sclerosis

Reduced expression of the survival of motor neuron gene is suggested to be a risk factor for amyotrophic lateral sclerosis. We have investigated the role of survival of motor neuron protein in the pathogenesis of amyotrophic lateral sclerosis. We are also developing induced pluripotent stem cells introduced mutation in transactive response DNA-binding protein.

3. Peripheral neuropathy

We investigated the pathogenesis of hypothyroidism-related neuropathy. We generated a mouse model of adult-onset hypothyroidism and analyzed in these mice hormonal status, mechanical thresholds, electrophysiological properties, and voltage-gated potassium channel protein levels of sciatic nerves.

Publications

Oka H, Nakahara A, Umehara T. Rotigotine Improves abnormal circadian rhythm of blood pressure in Parkinson's disease. *Eur Neurol.* 2018; **79**: 281-6.

Kono Y, Nishioka K, Li Y, Komatuzaki Y, Ito Y,

Yoshino H, Tanaka R, Iguchi Y, Hattori N. Heterozygous *HTRA1* mutations with mimicking symptoms of CARASIL in two families. *Clinical Neurology and Neurosurgery.* 2018; **172**: 174-6.

Shoji R, Kono Y, Furuhashi H, Nakano M, To-

- risu Y.** Foix-Chavany-Marie Syndrome Induced by a Unilateral Brain Abscess. *Intern Med.* 2019; **58**: 581-3. Epub 2018 Sep 12.
- Mitsumura H, Arai A, Sato T, Komatsu T, Sakuta K, Sakai K, Terasawa Y, Kubota J, Iguchi Y.** A novel probe attached to the neck can accurately detect a large patent foramen ovale. *J Neurol Sci.* 2018; **392**: 122-5.
- Murakami H, Yamamoto K, Yasumoto T, Kimura A, Sakae Y, Nomoto S, Kubota S, Watanabe D, Watanabe K, Saito Y, Yano S, Ono K.** Cerebrospinal fluid 5-HIAA concentrations correlate with cardiac uptake of 123I-MIBG during myocardial scintigraphy in drug naïve Parkinson's disease. *J Neural Transm* 2018; **125**: 1511-4.
- Murakami H, Kimura A, Yasumoto T, Miki A, Yamamoto K, Ito N, Momma Y, Owan Y, Yano S, Ono K.** Usefulness differs between the Visual Assessment and Specific Binding Ratio of 123I-ioflupane SPECT in assessing clinical symptoms of drug-naïve Parkinson's disease patients. *Frontiers in Aging Neuroscience.* 2018; **10**: 412.
- Omoto S, Hayashi T, Matsuno H, Higa H, Kamemaya S, Sengoku R, Takahashi-Fijigasaki J, Murayama S, Iguchi Y.** Neuronal intranuclear hyaline inclusion disease presenting with childhood-onset night blindness associated with progressive retinal dystrophy. *J Neurol Sci.* 2018; **388**: 84-86.
- Terasawa Y, Arai A, Sakai K, Mitsumura H, Iguchi Y.** Transcranial color-coded sonography findings of patients with reversible cerebral vasoconstriction syndrome. *J Clin Neurosci.* 2019 Mar; **61**: 290-2.
- Umehara T, Oka H, Nakahara A, Matsuno H, Toyoda C.** High norepinephrine orthostatic hypotension in early Parkinson's disease. *Parkinsonism Relat Disord.* 2018; **55**: 97-102.
- Sakuta K, Sato T, Sakai K, Komatsu T, Sakai K, Terasawa Y, Mitsumura H, Iguchi Y.** The NAG scale : Noble Predictive Scale for Hematoma Expansion in Intracerebral Hemorrhage. *J Stroke Cerebrovasc Dis.* 2018; **27**: 2606-12.
- Komatsu T, Matsushima S, Kaneko K, Fukuda T.** Perivascular enhancement in anti-MOG antibody demyelinating disease of the CNS. *J Neurol Neurosurg Psychiatry.* 2019; **90**: 111-2.
- Komatsu T, Iguchi Y, Arai A, Sakuta K, Sakai K, Terasawa Y, Mitsumura H, Matsushima M.** Large but Nonstenotic Carotid Artery Plaque in Patients With a History of Embolic Stroke of Undetermined Source. *Stroke.* 2018; **49**: 3054-6.
- Onda A, Miyagawa S, Takahashi N, Gochi M, Takagi M, Nishino I, Suzuki S, Oishi C, Yaguchi H.** Pembrolizumab-induced Ocular Myasthenia Gravis with Anti-titin Antibody and Necrotizing Myopathy. *Intern Med.* 2019; **58**: 1635-8. Epub 2019 Feb 1.
- Sato T, Terasawa Y, Higa H, Matsuno H, Arai A, Omoto S, Mitsumura H, Toyoda C, Koike H, Iguchi Y.** Nerve Ultrasound, Electrophysiological, and Clinical Changes in Treatment-Naive Chronic Inflammatory Demyelinating Polyneuropathy: A Case Report. *J Clin Neurophysiol.* 2019; **36**: 82-4.
- Koga M, Iguchi Y, Ohara T, Tahara Y, Fukuda T, Noguchi T, Matsuda H, Minatoya K, Nagatsuka K, Toyoda K.** Cerebrovascular imaging of cerebral ischemia in acute type A aortic dissection. *Gen Thorac Cardiovasc Surg.* 2018; **66**: 439-45.
- Tokuda N, Koga M, Ohara T, Minatoya K, Tahara Y, Higashi M, Miyazaki Y, Kajimoto K, Matsubara S, Makita N, Sakamoto Y, Iguchi Y, Mizuno T, Nagatsuka K, Toyoda K.** Urgent detection of acute type A aortic dissection in hyperacute ischemic stroke or transient ischemic attack. *J Stroke Cerebrovasc Dis.* 2018; **27**: 2112-211.
- Matsubara S, Koga M, Ohara T, Iguchi Y, Minatoya K, Tahara Y, Fukuda T, Miyazaki Y, Kajimoto K, Sakamoto Y, Makita N, Tokuda N, Nagatsuka K, Ando Y, Toyoda K.** Cerebrovascular imaging of cerebral ischemia in acute type A aortic dissection. *J Neurol Sci* 2018; **388**: 23-7.
- Takagi D, Moriwaki M, Katayama N, Katagiri N, Yaguchi H, Fujishima I.** A case of severe dysphagia caused by glossopharyngeal and vagus nerve palsy due to ANCA-associated vasculitis. *Deglutition.* 2019; **9**: 91-8.
- Seki M, Uruha A, Ohnuki Y, Kamada S, Noda T, Onda A, Ohira M, Isami A, Hiramatsu S, Hibino M, Nakane S, Noda S, Yutani S, Hanazono A, Yaguchi H, Takao M, Shiina T, Katsuno M, Nakahara J, Matsubara S, Nishino I, Suzuki S.** Inflammatory myopathy associated with PD-1 inhibitors. *J Autoimmun.* 2019; **100**: 105-13. Epub 2019 Mar 10.

Reviews and Books

- Suzuki M, Yogo M, Morita M, Terashi H, Iijima M, Yoneyama M, Takada M, Utsumi H, Okuma Y, Hayashi A, Orimo S, Mitoma H.** A proposal for new algorithm that defines gait-induced acceleration and gait cycle in daily parkinsonian gait disorders. In: Ortiz JH, editor. *Wearable Technologies.* London: IntechOpen; 2018. p. 25-48. doi: 10.5772/intechopen.75483. Available from: <https://www.intechopen.com/books/wearable-technologies/a-proposal-for-new-algorithm-that-defines-gait-induced-acceleration-and-gait-cycle-in-daily-parkinson>