## 論 文 内 容 要 旨

Blood pressure variability in acute ischemic stroke: Influence of infarct location in the insular cortex (色性期影響の面互亦動、自己所の博塞如信

(急性期脳梗塞の血圧変動:島皮質の梗塞部位 による影響)

European Neurology, 2017, in press.

主指導教員:丸山 博文教授 (医歯薬保健学研究科 脳神経内科学) 副指導教員:粟井 和夫教授 (医歯薬保健学研究科 放射線診断学) 副指導教員:細見 直永 准教授 (医歯薬保健学研究科 脳神経内科学)

## 北村 樹里

(医歯薬保健学研究科 医歯薬学専攻)

**Background**: High blood pressure (BP) in acute ischemic stroke is associated with poor outcome, and increased BP variability has been suggested as a prognostic factor for poor outcomes. Circadian rhythms in the autonomic nervous system play a crucial role in intra-individual BP variability. Thus, impairment of the autonomic nervous system could affect the BP fluctuations. The insular cortex plays an important role in the central autonomic network. Functional neuroimaging studies have reported different autonomic roles based on the laterality and the parts of the insular cortex. Several studies reported effects on autonomic impairments due to insular infarction. However, the findings were conflicting. The aim of this study was elucidate the influence of insular infarction on BP variability and outcomes according to the infarct location in the insular cortex and infarct volume.

**Methods**: The participants in this study were patients diagnosed with first-ever acute ischemic stroke of the unilateral middle artery territory within 48 hours of symptom onset. The BP was measured every 3 hours for 72 hours after admission. BP variability during the first 24 hours after admission (hyperacute phase) and during 2-3 days after admission (acute phase) was calculated using the difference between the maximum and minimum BP ( $\Delta$ BP), standard deviation (SD), coefficient of variation (CV), and successive variation (SV) of systolic and diastolic BPs. The locations of infarctions and their volumes were evaluated using magnetic resonance imaging (MRI) on the day of admission and 2 weeks later. When patients were unable to undergo MRI, lesions were evaluated by computed tomography performed on the first and second days of admission and 2 weeks after admission. Patients were classified into three groups of right insular cortex, left cortex, and no insular cortex infarction. Furthermore, the infarct areas involving with the insular cortex were divided into four groups (right anterior, right posterior, left anterior, and left posterior). We analyzed the differences of variables among these groups.

**Results**: Ninety patients fulfilled with criteria were enrolled in this study. Of the 90 patients, 33 showed infarction involving insular cortex. Patients with insular infarction showed a significantly larger infarct volume, higher mRS scores than patients without insular infarction (P < 0.01, P < 0.01, respectively). The  $\Delta$ BP, standard deviation SD, and CV of systolic BP in the hyperacute phase were lower in patients with insular cortex infarction than in those without insular cortex infarction (P = 0.04, P = 0.02, P = 0.03, respectively). Significant differences were observed in age, NIHSS score on admission, infarct volume, and mRS score at 2 weeks after admission among the three groups (P < 0.05, P < 0.001, P < 0.001, P < 0.001, respectively). The SD and CV of systolic BP in the hyperacute phase showed significant differences among the three groups with right insular infarction, with left insular infarction, and without insular infarction (P < 0.05, P < 0.05,

respectively). The systolic BP variability tended to be smaller in patients with right anterior insular cortex infarction than in the other area of insular cortex infarction in the hyperacute phase and in the acute phase. The neurological outcomes 2 weeks after admission appeared poorer in the groups with right anterior and with right posterior insular infarctions.

**Conclusion**: In our study, the early neurological outcomes appeared to be worse in patients with insular cortex infarction than in without insular cortex infarction, even though their systolic variability was less in the hyperacute phase. The BP variability might not be associated with early outcomes, and prognosis might be regulated by other factors.

This study showed the systolic BP variability in the hyperacute phase was decreased in patients with right insular cortex infarction. In addition, there was a tendency for the systolic BP variability to be lower in patients with right anterior insular infarction than in patients with infarcts in other areas. A meta-analysis of human neuroimaging studies suggested that the right anterior insular cortex is the only area that affects both sympathetic and parasympathetic functions. Based on previous findings, we suggest that the patients in the present study with ischemic stroke involving the right anterior insular cortex might have had impairments in both the sympathetic and parasympathetic nervous systems, thus resulting in a decreased systolic BP variability.