

Characterization of neuronal damage by iomazenil binding and cerebral blood flow in an ischemic rat model

Hiroshi TOYAMA,*¹ Kaname MATSUMURA,*² Hiromichi NAKASHIMA,*² Kan TAKEDA,*² Akira TAKEUCHI,*¹ Sukehiko KOGA,*¹ Toshimichi YOSHIDA*³ and Masanori ICHISE*⁴

*¹Department of Radiology, Fujita Health University, Toyoake, Japan

*²Department of Radiology, and *³First Department of Pathology, Mie University, Tsu, Japan

*⁴Department of Nuclear Medicine, University of Toronto, Toronto, Canada

I-123-iomazenil is a SPECT probe for central benzodiazepine receptors (BZR) which may reflect intact cortical neuron density after ischemic insults. We evaluated whether neuronal damage in rats could be characterized by iomazenil as compared with cerebral blood flow (CBF). Serial changes in I-125-iomazenil for BZR and I-123-IMP for CBF were analyzed after the unilateral middle cerebral artery occlusion in rats by using an *in vivo* dualtracer technique. Uptake ratios of affected to contralateral regions were calculated. The iomazenil as well as IMP were decreased in all regions except for the cerebellum (remote area). Both iomazenil and IMP increased over time except in the temporal region (ischemic core). The iomazenil uptake was higher than IMP except in the ischemic core between 1 and 3-4 wk when iomazenil was lower than IMP. Iomazenil showed a moderate decrease in the proximal and middle parietal regions (peri-infarct areas) at 3-4 wk. The triphenyl-tetrazolium-chloride (TTC) stain at 1 wk demonstrated unstained tissue in the temporal region indicating tissue necrosis. With hematoxylin-eosin (HE) stain at 1 wk, widespread neuronal necrosis with occasional intact neurons were found in the proximal parietal region, and isolated necrotic neurons were represented in the distal parietal region. Iomazenil correlated well with the neuron distribution and the finding of a discrepancy between iomazenil and IMP might be useful in evaluating the neuronal damage.

Key words: ischemic penumbra; benzodiazepine receptor; cerebral blood flow, iomazenil; neuronal damage