

**Salt-Sensitive Hypertension and Cerebral Circulation  
in Gene-Mutant Mouse and Genetically Stroke Rat**

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**Summary**

Recently, the availability of transgenic mice has enabled us to examine the involvement of specific gene products in various pathological and physiological conditions. Furthermore, we used gene-targeting technology to generate M5 muscarinic acetylcholine receptor-deficient mice ( $M5R^{-/-}$  mice). In the present study, we made a measurement system for blood pressure and cerebral hemodynamics (cerebral blood flow; CBF, vessel diameter; VD) in pial microcirculation in mouse. Using this system, we measured cerebral hemodynamics in gene mutant mice and genetically stroke model rat (stroke-prone spontaneously hypertensive rats; SHRSP) under physiological and pathological condition.

Under anesthetized and automatically ventilated, the animals were fixed in a stereotaxic frame, with the bone overlying the dorsal surface positioned at the center of the left parietal bone. The animals in the stereotaxic frame was placed on the stage of a microscope equipped with a long-working-distance objective, and the cerebral vessels, the branches of the middle cerebral artery, were monitored with a CCD camera and their images captured on a personal computer. A probe with a diameter of 0.5 mm was attached to the point of divergence of the middle cerebral vessel, and CBF in the parietal lobe was measured continuously using a laser-Doppler flow meter and that data were analyzed using a PowerLab system. After a measuring of CBF and vessel diameter, blood samples (30 microL) were obtained from the abdominal aorta to measure levels of arterial blood gases ( $PaO_2$ ,  $PaCO_2$ ) and pH.

We noticed that  $M5R^{-/-}$  mice showed normal peripheral blood pressure (tail-cuff). We determined the diameter of cerebral arterioles and CBF by intravital microscopy through a cranial window in  $M5R^{-/-}$  mice and wild-type mice. Male  $M5R^{-/-}$  mice and SHRSP rats showed a small but significant reduction in the diameter of middle cerebral arterioles (MCA) under resting conditions.  $M5R^{-/-}$  mice and SHRSP rats showed significantly low CBF in a resting state of MCA. Consistent with the observed reduction in the diameter of blood vessels, continuous vasospasm was observed in the posterior cerebral arterioles close to the circle of Wills.