Magnetic Resonance Imaging, Histology, and Sensorimotor Analysis of a Novel Ischemic Stroke Pig Model

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Stroke is the leading cause of long-term disability among adults in the United States. Despite hundreds of drugs going to clinical trials, only one has been approved by the Food and Drug Administration. One explanation for the high rate of translational failure is the lack of preclinical testing in a gyrencephalic animal model. The vast majority of stroke therapies are developed and verified in lissencephalic rodent models. Pigs possess a gyrencephalic brain and are more similar to humans than rodents with respect to gray-white matter composition and size. We hypothesized that cauterization of the middle cerebral artery (MCA) in pigs would lead to ischemic infarction and functional neurological deficits. Our objective was to develop a pig middle cerebral artery occlusion (MCAO) ischemic stroke model to address the need for a robust and repeatable gyrencephalic animal stroke model.

A right fronto-temporal craniectomy was performed on 8 adult male Yucatan miniature pigs. The MCA was permanently occluded with bipolar electrocautery. Magnetic resonance imaging (MRI) was performed 1 and 90 days post-MCAO surgery. A computational video capture system was used to assess changes in motor function pre- and post-stroke. Histological analysis was performed 90 days following MCAO surgery.

Diffusion weighted and apparent diffusion coefficient MRI images confirmed stroke damage 1 day post MCAO. T1-FLAIR MRI analysis showed a loss of 59.17 ± 10.06 cc of tissue from day 1 to day 90. Histological examination of the brain demonstrated severe atrophy of the affected right hemisphere. The white matter in the affected cortex could not be defined due to loss of normal elements, glial proliferation, and infiltration of gitter cells. Motor function analysis showed loss of gait symmetry and changes in stride length and maximum hoof height of the contralateral limbs.

MCA occlusion in pigs led to structural and sensorimotor changes that are compatible with an ischemic stroke injury. MRI and histological analysis demonstrated the evolution of a significant structural lesion that was repeatable and consistent between MCA occluded animals. Corresponding motor function analysis consistently confirmed a loss of gait symmetry in all MCA occluded animals.

The development of a pig MCAO model will allow stringent assessment of efficacy and safety of novel stroke therapies in an animal model that shares important neuro-anatomical and physiological features with humans.