Neuroimaging of white matter lesions and ischemia in Göttingen minipigs – a pilot study

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Introduction

In the human brain, cerebral white-matter lesions (WMLs) are seen as areas of high intensity on certain types of magnetic resonance imaging (MRI) scans and are thought to represent small vascular abnormalities. Mild and moderate WMLs are common in healthy elderly people and are of uncertain significance. However, recent brain studies of depressed elderly patients report an excess of white-matter lesions. Furthermore, severe changes may predispose some elderly individuals to depression, and are reportedly associated with poor response to treatment in general. Brain ischemia is a condition of insufficient blood flow to the brain to meet metabolic demands. As a result, the affected areas of the brain cannot function, which might result in permanent neurological damage and death. Risk factors for stroke include old age. Diffusion MRI methods allow the mapping of the diffusion process of water in biological tissues, in vivo and non-invasively. These parameters are altered by brain ischemia. Thus, diffusion MRI's main application has been in the study of neurological disorders, especially for the management of patients who have suffered an acute stroke.

Use of Göttingen minipigs

Both depressive and ischemic disorders affect elderly people. Rodents are commonly regarded as the gold standard in basic research when studying relationships between molecular mechanisms and behaviour. However, while MRI and Positron Emission Tomography (PET) neuroimaging can be carried out in small animals, their small brain size precludes the detection of WMLs and ischemia in the imaging systems designed for humans. To achieve such measurements in an environment that closely resembles the clinical setting, we have specialized in the use of pigs for basic research in neuroimaging. Thus, over the years, we have used different imaging modalities and techniques to explore the neurobiological aspects of ischemic and depressive disorders.

Pilot study

To support our efforts, Ellegaard Göttingen Minipigs donated two old female minipigs for our research efforts. Specifically, our goals were to look for WML and to compare different diffusion MRI techniques in the aging brain during distinct levels of inhaled oxygen. Whole brain and associated structures were scanned with standard three-dimensional, T1-weighted sequences for anatomical details (Figure, part A). This was succeeded by standard clinical T2-weighted sequences aimed at depicting WMLs (Figure, part B). The minipigs were scanned at different oxygen levels (a standard clinical diffusion was weighted and a new experimental MRI sequences was acquired for each level, see Figure, part C). After completing the experiment, the pigs were euthanized. The large cavities of the pig cranium proved to be a challenge for the MRI imaging. Where the T1-weighted images were superior for determining anatomical details, tissue contrast differences were not clear in T2-weighted scans due to a low signal-to-noise ratio. Thus, we could not detect WMLs. Further efforts are needed in the adjustment of MRI parameters and possible injection of an MRI-compatible gel into cranial cavities with the aim of improving the signal-to-noise ratio of the MRI signal. The experimental MRI sequences for imaging of the water diffusion correlated well with the standard clinical sequence. This may indicate that comprehensive and sensitive detection of subtle changes in tissue microstructure due to ischemia will be possible in future minipig models. Such imaging advances could provide better MR diffusion characterization of neural tissues in normal, developmental and pathological states.

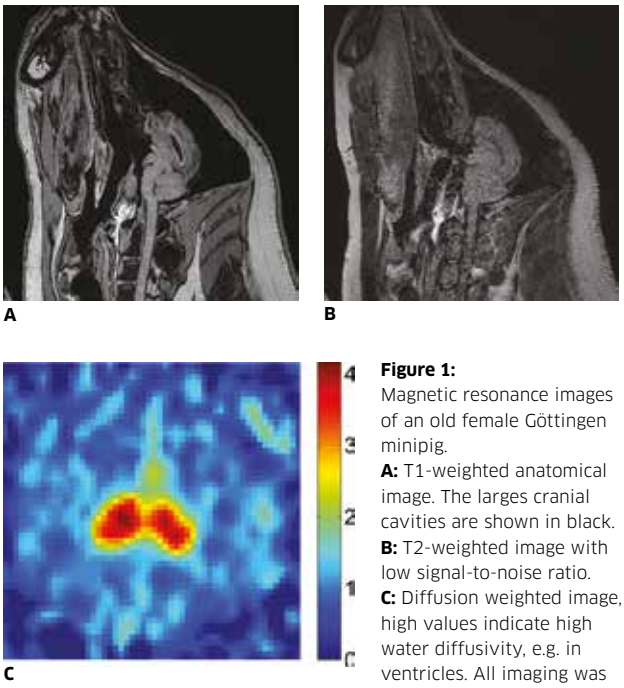

Figure 1:
Magnetic resonance images of an old female Göttingen minipig.
A: T1-weighted anatomical image. The larges cranial cavities are shown in black.
B: T2-weighted image with low signal-to-noise ratio.
C: Diffusion weighted image, high values indicate high water diffusivity, e.g. in ventricles. All imaging was performed with a 3.0 T MR Siemens Trio imaging system.