Evolution of diffusion tensor parameters after permanent experimental stroke in rats

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Introduction

Brain ischemia causes structural damage to the tissue that give rise to a loss of organization and structure at the cellular level. The changes in water apparent diffusion coefficient (ADC) are related to changes in brain water content while the changes in anisotropy are linked to changes in tissue microstructure. In the present work, in a rat model of permanent middle cerebral artery occlusion (MCAO), we measured the temporal evolution of the diffusion tensor imaging (DTI) parameters (fractional anisotropy (FA) and rotationally invariant ADC). Furthermore we compared whether different brain regions have characteristic behavior after permanent ischemia. There are no studies that have systematically followed the evolution of DTI parameters after ischemia over long periods with repeated MR imaging.

Material and methods

Wistar rats (n=9) were subjected to focal cerebral ischemia by permanent suture MCAO (1). They were imaged at 2 and 3.5 hours, 1, 2, 3, and 4 days, 1, 2, 4, 6, and 8 weeks. Sham-operated rats were used as healthy controls (n = 8). The MRI measurements were performed with a 4.7 T MR Scanner (PharmaScan, Bruker BioSpin, Germany). The temporal evolution of diffusion tensor indices (FA and ADC) was measured.

Result and Discussion

When we compared between the brain tissues (cortex vs. subcortex, cortex vs. corpus callosum, and subcortex vs. corpus callosum), FA showed a significant difference between the tissues ($p < 0.001$), and ADC no significant difference between the tissues ($p > 0.05$).

Figure 1 and 2 show how FA reduces strongly in the acute and subacute phase after permanent MCAO in all ischemic tissues (cortex, subcortex, and corpus callosum). As FA decreased and the tissue became more isotropic, the darker it appeared. However, FA reduced more rapidly and under longer period in subacute and chronic phase in gray matter (GM) regions (cortex) than in white matter (WM) regions (corpus callosum). As we found more pronounced decrease of diffusion anisotropy in GM, it can be thought that GM is more vulnerable to ischemia than WM (2). However, in the chronic phase, FA normalized. Increased organization of the extracellular space and movement of water into the more restricted environment of the intracellular space may both occur with cytotoxic edema, and these result an increased FA (3).

ADC decreased strongly after MCAO and became significantly different ($p < 0.05$) from the normal brain regions as seen in the figure 2. After the decrease, ADC increased steadily and normalized 2-4 weeks after MCAO. Afterwards, ADC increased steadily up to 6 weeks in all tissues (figure 2). The general trend of ADC evolution (over the 8 weeks observation period) was similar in all tissues. However, different tissues normalized in different time points. As seen in the figure 1, when ADC normalized, T2 and FA can be used for defining the lesion area.

This study showed that, after permanent MCAO, there are differences in the temporal evolution of FA in different brain tissues. Differences in neuronal structure between WM and GM make it likely that the mechanism of ischemic injury and strategies for protection will vary. This way in the future, FA may enable separate evaluation of the treatment response of WM and GM to neuroprotective therapy.

References

(1) Koizumi et al., 1986, Jpn J Stroke. 8, 1-8., (2) Arakawa et al., 2006, Stroke. 37, 1211–1216., (3) Green et al., 2002, Stroke. 33, 1517-1521.

Fig 1. *The evolution of FA, ADC, and T2 after MCAO.*

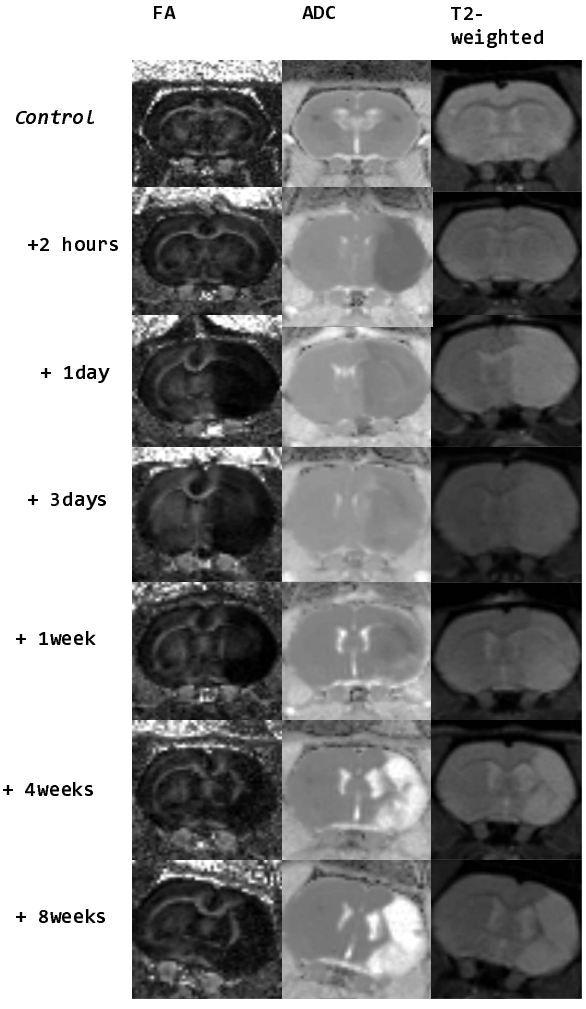

Fig 2. *The evolution of DTI indices, rFA and rADC, over 8 weeks (2 hours – 8 weeks), is presented for subcortex, cortex, and corpus callosum. Normal presents the ratio between healthy right and left hemisphere in healthy animals. Time points that are significantly different from the normal are marked with an asterisk (*).*