Temporal profile of T2-weighted MRI allows discrimination between pannecrosis and selective neuronal death following focal cerebral ischemia in the rat

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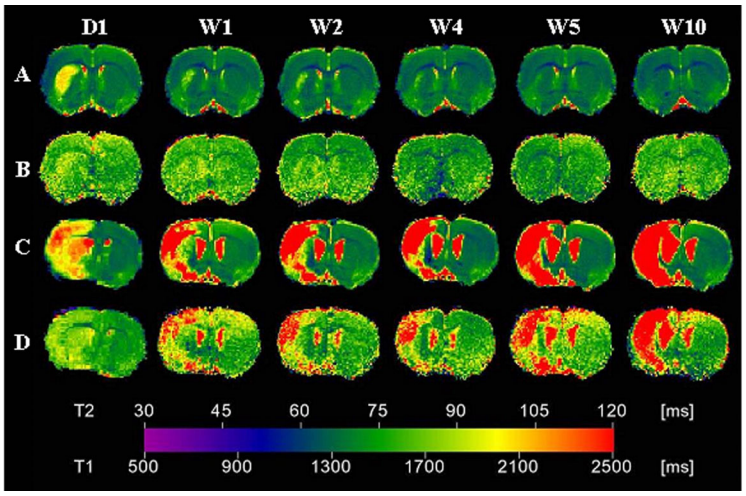
Introduction: In the Wistar rat strain two different lesion types were consistently induced by transient (60min) occlusion of the middle cerebral artery (MCA) on Magnetic Resonance Imaging (MRI): one restricted to the caudoputamen (with focus on the dorsolateral striatum; "cp") and one involving both caudoputamen and cortex ("cp+"). These lesion types led to distinctly different behavioral patterns: while animals with lesions encompassing also the cortex presented with significant sensorimotor deficits, sensorimotor function was preserved in animals with exclusively subcortical lesions. We therefore investigated whether the exclusively subcortical lesions represent a different kind or degree of ischemic damage, and whether this would be discernible by a specific pattern on follow-up MRI. By addressing these questions we wanted to assess the widely accepted MRI parameters T_1 and T_2 for their reliability of detection and demarcation of chronic ischemic lesions.

Methods: MCAO was induced in male Wistar rats (260-300g) for 60 min. Animals received follow-up T_1- and T_2-weighted MRI from day 1 until week 10. MRI measurements were performed on a 4.7T BioSpec animal scanner with a 30 cm bore magnet (Bruker BioSpin, Ettlingen, Germany), equipped with actively shielded gradient coils (100 mT/m; rise time < 250 µs). Rf transmission was achieved with a Helmholtz coil (diameter 12 cm) and the signal was detected with a 22 mm diameter surface receiver coil. Separate groups of animals were analyzed histologically after 2, 6 and 10 weeks. Histology included immunohistochemistry for neuronal and astrocytic markers as well as hematoxylin-eosin and luxol-fast-blue/cresyl violet staining.

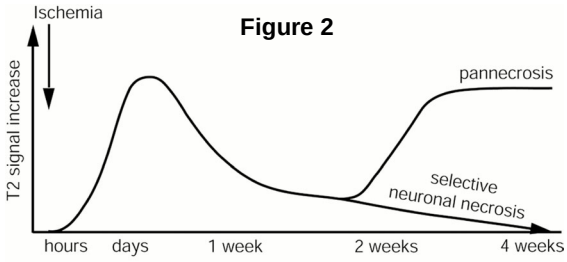
Results: In cp+ lesions (Figure 1C and D) cortical T_2 values kept rising from day 1 to 10 weeks after the MCAO, while T_2 values of the subcortical lesion area slightly decreased during the first two weeks but then increased again towards week 10. Cortical and subcortical T_1 relaxation times remained elevated to the final observation time point, when the whole infarct was sharply demarcated on both parameter maps. In contrast to lesions involving the cortex, exclusively subcortical infarctions were characterized by a complete resolution of initially increased relaxation times T_1 and T_2 by 10 weeks after stroke induction (Figure 1A and B). On histological analysis, most of the infarcted tissue, as characterized on T_2-weighted images at day 1, had undergone necrotic degeneration in cp+ animals, while there was no such degeneration detected in cp animals. Inflammatory infiltrate, loss of neurons, and gliosis were found within cp lesions (analyzed 2, 6 and 10 weeks after MCAO) as well as at the border zone of cp+ lesions. While staining for myelin sheaths (luxol fast blue) indicated loss of fiber tracts at the border zone of cp+ lesions, axonal fibers passing through cp lesions appeared intact.

Figure 1



Follow-up MRI of an animal with exclusive caudoputaminal lesion (cp, panels A and B) and of an animal with a lesion involving caudoputamen and cortex (cp+, panels C and D). Parameter maps of T_1 (B, D) and T_2 (A, C) at day 1 (D1) and 1-10 weeks (W1-W10) after MCAO.

Figure 2



Schematic temporal profile of T_2 relaxation time changes upon MCAO

Conclusions: In the exclusively subcortical ischemic lesions described in our study the initial signal increase on T_1 and T_2maps following 60 min MCAO rapidly diminished within one week and had completely resolved at 10 weeks. This normalization of imaging findings was not paralleled by tissue recovery, since neuronal necrosis and gliosis with a pronounced inflammatory reaction were observed. However, cystic degeneration of tissue and loss of fiber tracts, a characteristic trait of cp+ animals, were not part of the histological picture in the cp group at any observation time point. This might explain why sensorimotor function is less disturbed in animals with cp lesions.At chronic observation time points, MRI allows discrimination of selective neuronal death and pannecrosis (normalization vs. continuous or secondary increase of relaxation times; Figure 2).