Feasability of Using Clinical T3 MRI to Monitor Infarct Zone and BBB Disruption in a Rat Model of Stroke

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Introduction

Stroke is the third leading cause of death and the leading cause of long-term disability. Experimental models of stroke are essential to study the pathophysiology of brain ischemia and the effects of novel therapeutic approaches. Magnetic resonance imaging (MRI) is an invaluable non-invasive tool for evaluating the location, volume, and the nature of stroke lesions. Until now, purpose-dedicated, small-bore, and very high-field-strength (up to 11.7 T) MRI systems were required in most rat stroke model studies. The purpose of the present study was to report the feasibility of using clinical magnetic resonance (MR) imaging devices for the depiction of stroke in a rat model. To validate our approach, we compared our MRI results with histological analysis.

Materials and Methods

40 Wistar rats were randomly assigned into one of 4 groups, with10 rats in each group. 2 groups were subjected to middle cerebral artery occlusion (MCAO, stroke groups), and 2 other groups were sham-operated (control groups). All rats were examined at 24h after surgery, using a clinical MRI 3T scanner (Ingenia, Philips Medical Systems, Best) to investigate the infarcted zone and blood brain barrier (BBB) disruption. The MRI protocol consisted of diffusion weighted imaging (DWI), fluid attenuated inversion recovery (FLAIR) and T2-weighted images. For the measurement of BBB breakdown, k-^{trans} technique with contrast agent (gadolinium) was used. Immediately after the MRI study, rats were sacrificed and their brains were removed for histological examination. Infarct volume was determined using TTC staining and BBB permeability was evaluated by measuring Evans' Blue extravasations. The size of brain injury was measured by using image analysis software (Image J 1.37; National Institutes of Health). A linear regression model between MRI and histological results was established in order to validate the new MRI technique.

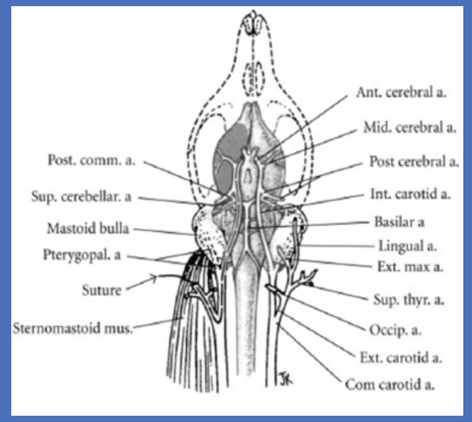

Figure 1: MCAO Procedure

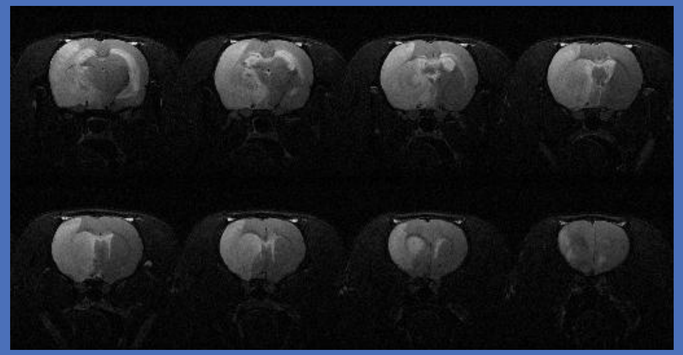

Figure 2: T2 MRI 24 hours after MCAO

Results and Conclusions

- The focal cerebral ischemia lesions were distinguishable in all stroked rats.
- No pathological changes were detected in sham-operated control animals.
- The infarct zone volume was 8.4%±4 in T2 technique, 6.9%±3.2 in Flair technique and 10.2% ±5.1 in DWI technique.
- The infarct zone volume by histological examination was 12.4% ±6.3.
- There was a strong positive correlation with all techniques and histological examination (r= 0.81346, r= 0.833, r= 0.741681 respectively), $p<0.01$.
- BBB breakdown k-^{trans} extravasations index was 2.5 ±1.3 versus Evans blue extravasations index-3.11±1.48, representing a satisfactory positive correlation (r=0.468), $p<0.01$.

- Ischemic lesions were well distinguished on MR images as validated with postmortem standard- of-reference techniques.
- The results revealed notable and striking correlations between the two methods, both quantitatively and qualitatively.
- This setup offers advanced MR imaging of small animals