

Evaluation of rCBF in Excitotoxic Neuronal Injury Using FAIR Technique

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Introduction

Regional cerebral blood flow (rCBF) is an important indicator for monitoring pathological alterations of cerebral function in a given brain region. In the central nervous system, nitric oxide (NO) is proved to be an important mediator in the regulation of normal blood flow. It has been hypothesized that NO plays a key role in the pathogenesis of excitotoxic neuronal injury. Flow-sensitive alternating inversion recovery (FAIR) technique (1), employing tissue water as an endogenous contrast agent, is a powerful tool for sequential measurements of CBF. In the present study, we used the excitotoxin 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) treated rats as an experimental model to determine the regional alteration of CBF using FAIR technique.

Method

Four to five-month-old male Sprague-Dawley rats ($n=7$) were anesthetized i.p. with a mixture of urethane and α -chloralose. A bolus injection of MPTP (15 mg/kg, Sigma) was administered intravenously.

MRI experiments were performed on a 4.7 Tesla spectrometer with an active shielding gradient at 5.6 G/cm in 500 μ s. A 20 cm birdcage coil was used for RF excitation, and a 2 cm diameter surface coil was placed directly over the skull for receiving signals. The rat was placed in a prone position with a custom-designed head-holder. The FAIR experiment was implemented with two IR images with and without slice-selective gradients during an inversion pulse. The inversion pulse was hyperbolic secant pulse with a pulse length of 8 ms. After an inversion pulse and a subsequent inversion recovery time (TI), RARE images were acquired with a matrix size of 256 \times 128 and a FOV of 4 cm. A slab thickness of 5 mm was inverted for the slice-selective IR images. Images were collected with a TI of 1.5 s, TR of 3 s, TE of 20 ms, NA of 2 and an echo train length of 4. Images were processed by using commercially available image analysis software (MRVision, MRVisionCo., Menlo Park, CA, USA).

Results

FAIR images shown in Fig. 1 indicate the CBF changes within the brain region before and at the indicated time-points after MPTP injection. Fig. 2 shows the relative CBF changes as a function of time in the cortical and striatal regions. After MPTP administration, relative CBF in both cortical and striatal regions progressively increased. After 73 mins post MPTP injection, CBF in the cortical region reached its maximum and then progressively returned to control level at 175 mins. CBF in the striatal region reached its maximum level at 107 mins post MPTP injection and decayed to control level at 209 mins. CBF in the cortical region decayed to control level faster than in the striatal region. DWI showed no observable lesions during the course of the experimental period.

Discussion

The temporal changes of relative CBF induced by MPTP in rat brains were measured. It has been suggested that NO plays an important role in MPTP toxicity (2). NO is an endothelial factor and a potent vasodilator that causes an increase in CBF. Therefore, our findings of increased CBF may be ascribed to the effects of NO. In the cortex, CBF elevated earlier and decayed faster than in the striatum. This may indicate that MPTP metabolizes at a higher rate within the endothelium of cortical vessels. Previous studies (3) have shown that the cerebral cortex contains less NO than the hypothalamus, cerebellum, or pituitary. This may explain why the increased CBF was sustained over a longer period in the striatal region than in the cortical region. Our data demonstrates that changes of CBF and brain damage induced by MPTP are correlated. No lesions were observed in the DWIs during the course of the experimental period. CBF measurements may prove to be invaluable for early detection of brain damage.

References

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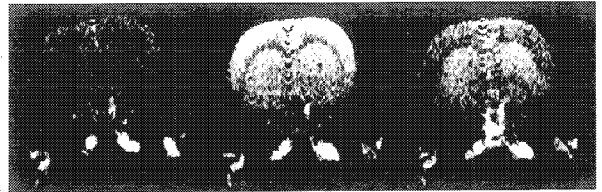


Fig. 1: Representative FAIR images: (a) control, (b) 73 mins and (c) 175 mins after MPTP injection.

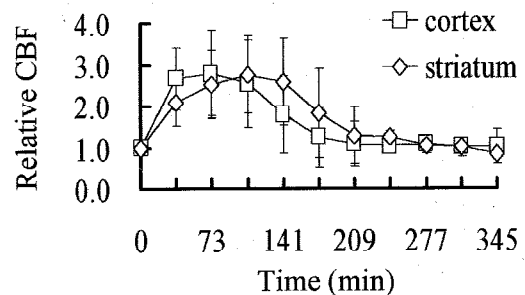


Fig. 2: Temporal relative CBF in cortical and striatal regions.