Diffusion Tensor Imaging of Renal Ischemia/Reperfusion Injury

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Introduction

Renal ischemia/reperfusion injury (IRI) is a major cause of acute renal failure (ARF) in native and in transplanted kidneys, associating with a high mortality and morbidity [1]. IRI in kidney associated with transplantation may also influence early graft function and late changes [2]. However, noninvasive technique to assess renal function and microstructure has been limited. Diffusion weighted imaging (DWI) has been used to assess renal function in various disease states by means of diffusion coefficient [3,4]. Recently, anisotropy measurement with diffusion tensor imaging (DTI) has been found to provide additional information about functional and structural status of kidney [5,6]. In this study, we aim at characterizing diffusion properties of kidney by means of mean diffusivity (MD) and fractional anisotropy (FA) in an experimental rat model of renal IRI.

Methods

Animal Procedures: Diffusion tensor imaging was performed in five normal Sprague-Dawley (SD) rats (200-250 g) and five SD rats (200-250 g) that had undergone renal IRI. The employed rodent model of unilateral renal IRI was performed as described previously [7]. The animals were anesthetized with an intraperitoneal (i.p.) injection of 100 mg/kg ketamine, and 10 mg/kg xylazine. The abdomen was shaved and a midline incision was made. The right renal pedicle was clamped using a vascular clamp. The right kidney was inspected for ischemia for 2 minutes. After 60 minutes of renal ischemia, the clamp was removed initiating renal reperfusion. The kidney was again inspected for restoration of blood flow, and then the abdomen was closed. Animals were scanned with DTI at about 5 hours after IRI.

MRI: All MRI experiments were performed on a 7 Tesla MRI scanner (70/16 PharmaScan, Bruker, Germany) with a 60 mm quadrature resonator for RF transmission and receiving. Each rat was anesthetized with isoflurane/air using 1.0-1.5 % for maintenance. Body temperature was maintained at about 36.5°C by circulating warm water in a heating pad with respiratory monitoring. Diffusion tensor imaging (DTI) was performed on one oblique coronal slice passing through both kidneys with respiratory-gated single-shot spin-echo echo-planar imaging (SE-EPI) sequence using TR ≈ 2.0-2.5 s (2 respiratory cycles), TE = 33 ms, FA = 90º, two b-values were used (0 and 300 s/mm^2) for 6 diffusion gradient directions, FOV = 5.12×5.12 cm, slice thickness = 2 mm, acquisition matrix = 64×64, voxel size = 0.8×0.8×2 mm^3, NEX = 10, and total scan time of ~3 min. DW images were first co-registered using AIR5.2.5 [8]. MD and FA maps were generated using DTIStudio [9]. Region of interests (ROIs) were drawn in renal cortex and medulla of both kidneys for MD and FA measurements based on the marked contrast between the less anisotropic cortex and anisotropic medulla on the FA maps. Paired t-test was employed to compare the differences in MD and FA values between right cortex/medulla and left cortex/medulla. P values less than 0.05 were considered statistically significant.

Results and Discussion

Fig. 1a and 1b show the typical MD and FA maps of kidneys in a normal rat respectively. Fig. 2a and 2b show the MD values and FA values in right cortex (RL), left cortex (LC), right medulla (RM), and left medulla (LM) of normal rats (N = 5) respectively. Higher FA values in medulla (0.37 ± 0.03) than in cortex (0.17 ± 0.01) were observed due to the radially oriented structures in medulla, which is consistent with the findings in human kidney [5,6]. The MD and FA differences between right cortex/medulla and left cortex/medulla were not statistically significant, demonstrating the reproducibility of the DTI sequence. Typical MD and FA maps of kidneys at 5 hours after renal IRI are shown in Fig. 3a and 3b respectively. Fig. 4a and 4b show the MD values and FA values in right (injured) and left (non-injured) kidneys after injury (N = 5) respectively. The MD values of right cortex/medulla were significantly lower ($P < 0.05$) than that of left cortex/medulla after IRI. Moreover, the FA values of right medulla were significantly lower ($P < 0.05$) than that of left medulla after injury. MD decrease in both injured cortex and medulla after renal IRI could arise from the decreased extracellular space caused by cytotoxic edema [4,7]. This could be also due to the disturbances of microcirculation caused by microvascular coagulation [10]. FA decrease in medulla is likely due to the necrosis of tubular epithelial cells, which are most susceptible to hypoxia [4,11]. Histological study is currently underway to correlate with the MRI findings in this study.

Conclusion

The experimental results demonstrated that DTI is useful in identifying renal IRI by characterizing the changes in MD and FA. Anisotropic measurement in addition to diffusion coefficient measurement using DTI may provide additional information in various renal diseases.

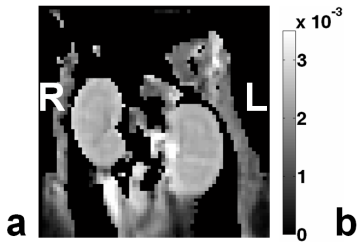

Fig. 1. Typical (**a**) MD map (in mm^2/s) and (**b**) FA map of kidneys in normal rat. R: right, L: left.

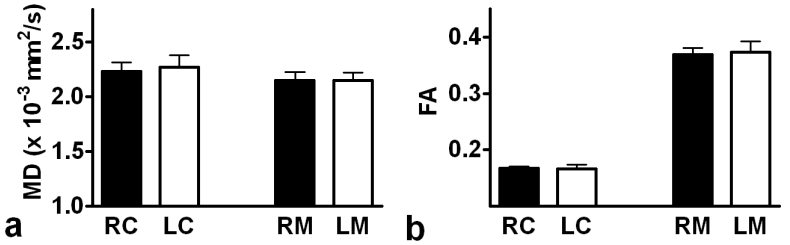

Fig. 2. (**a**) MD and (**b**) FA values (N = 5) in normal rats. RC: right cortex, LC: left cortex, RM: right medulla, LM: left medulla.

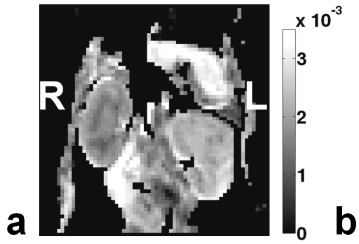

Fig. 3. Typical (**a**) MD map (in mm^2/s) and (**b**) FA map of kidneys at 5 hrs after renal IRI in right kidney.

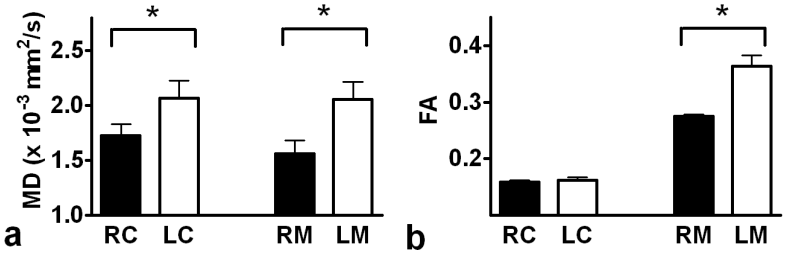

Fig. 4. (**a**) MD and (**b**) FA values (N = 5) in rats at 5 hrs after injury. * $P < 0.05$.

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