In vivo visualization of cerebral microvasculature using BOLD contrast microscopic MRA

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Introduction

Emerging evidences indicate that the cerebral microvasculature may be critical in the pathogenesis of various brain diseases. Hence, assessment of small cerebrovasculature may give clue to diagnosis, to provide indicator of disease progression and to evaluate therapeutic efficacy. Current magnetic resonance angiography (MRA) methods, i.e. Time-of-flight-MRA (TOF-MRA) or contrast enhanced-MRA (CE-MRA), offer techniques for imaging large vessels, but have limited values in the imaging of smaller vessels such as arterioles and venules. A previously proposed method, 3D ΔR_2 microscopic magnetic resonance angiography (3D ΔR_2 mMRA), utilizes the administration of iron oxide contrast agent to visualize microvasculature [1]. However, the potential side effects and less availability of contrast agent limit the application of the method in the clinical setting. An alternative technique to visualize cerebral microvasculature was based on the intrinsic blood oxygen level-dependent (BOLD) contrast [2]. In present study, we proposed a new 3D gas challenge ΔR2* mMRA (3D gas ΔR2* mMRA) method that used intrinsic BOLD contrast manipulated by carbogen challenge to directly visualize cerebral microvasculature. In this context, carbogen challenge augmented cerebral blood flow and altered BOLD contrast of cerebral vessel and thus acts as a physiological contrast agent.

Materials and Methods

MRI experiments were performed on a 7-T PharmaScan 70/16 MR scanner (Bruker, Germany) with an active shielding gradient using a birdcage transmitter coil and a separated quadratic surface coil for signal detection. Four Sprague–Dawley rats were initially anesthetized with 5% isoflurane flowed in air at 2L/min. When fully anesthetized, the animal was placed in a prone position and fitted with a custom-designed head holder inside the magnet. 2% isoflurane was used to maintaine the anesthesia via a nose piece throughout the experiments. Body temperature was maintained with warm air and water circulation system, monitored by rectal thermometer. Heart rate and arterial SO_2 were continuously monitored with pulse oximeter. To determine ΔR_2*, T_2*-weighted images (T_2* WI) under the inhalation of air followed by carbogen were performed. The second T_2* WI was delayed by 15 minutes to allow complete gas exchange. T_2* WI was acquired using 3D gradient-echo with flow compensation (3D-GEFC) sequence with parameters: matrix size = 256×256×96 (zero-padded to 512×512×192), FOV = 2.56×2.56×1.4cm^3, TR = 90ms, TE = 25ms, FA = 15°, bandwidth = 9kHz, NEX = 2, and total acquisition time of 73 min. 3D ΔR2*-mMRA images was obtained by first coregistration of pre-challenge and post-challenge images, followed by segmentation of the brain, ΔR_2* map calculation $(1/TE)\ln(S_{O2}/S_{Air})$, and 3D volume-rendering using a commercial 3D visualization platform, Avizo software (TGS, San Diego, CA). Vascular photographs of a normal rat brain were acquired after perfusion.

Results and discussion

Fig. 1 shows normal rat brain T_2* WI images of pre-challenge (Fig. 1A) and post-challenge image (Fig. 1B) and ΔR_2* map (Fig. 1C), which was calculated using the abovementioned equation in horizontal plane, clearly delineated the cerebral microvasculature. 3D gas ΔR_2* mMRA was generated by volume-rendering of ΔR_2* map. Fig. 2 shows the 3D gas ΔR_2* mMRA images and corresponding vascular photographs of rat brain. The dorsal view and magnified sections of the data sets (Fig. 2A), lateral view (Fig. 2B) of 3D gas ΔR_2*-mMRA in Fig. 2A clearly revealed major venous sinuses and their ramifications on the brain surface. These vessels were further validated and identified as follows: superior sagittal sinus (double-arrow), superior cerebral veins (arrow), and rhinal vein (arrowhead). These vessels on the brain surface were well correlated with vascular photographs. Fig. 3 shows 3D gas ΔR_2*-mMRA images in three orthogonal views and their respective positions. Intracortical vessels were depicted in the axial view (Fig. 3A), horizontal view (Fig. 3B) and sagittal view (Fig. 3C) of 3D gas ΔR_2* mMRA. These results demonstrated the potential of 3D gas ΔR_2* mMRA as a high resolution non-invasive MRA techniques.

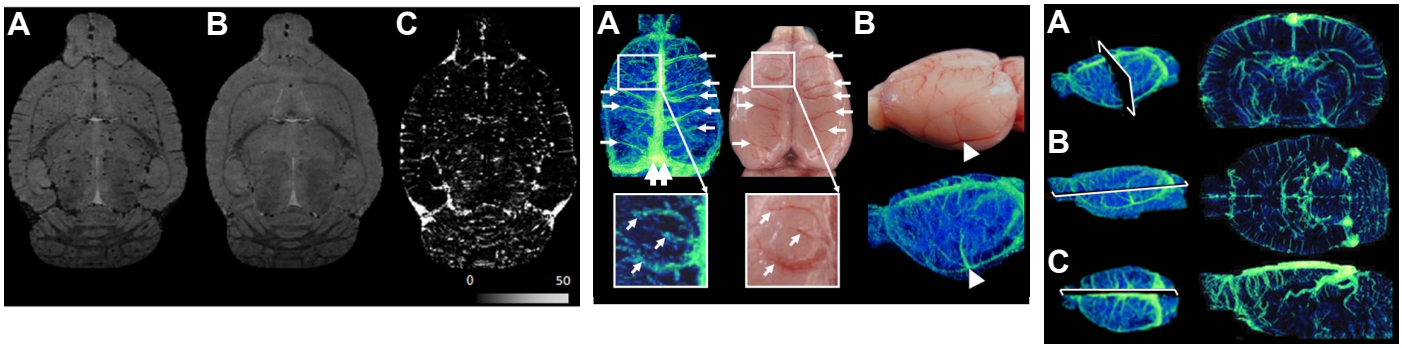

Fig 1. Segmented high resolution T_2* WI images and computed ΔR2* image of a rat brain. (A) air breathing pre-challenge image, (B) carbogen breathing post-challenge image, and (C) computed ΔR_2* image.

Fig 2. 3D ΔR_2* mMRA images and corresponding vascular photographs of a normal rat. (A) Dorsal view and magnified sections of the data sets (B) Lateral view.

Fig 3. 3D ΔR_2* mMRA images of a normal rat in three orthogonal views and their positions: (A) axial; (B) horizontal; (C) sagittal slice plane.

Reference: 1) Lin CY et al. *Neuroimage*, 2009;45. 2) Reichenbach JR et al. *Radiology*, 1997;204