MRI of congenital arteriovenous malformation in Wistar rats: the effect of altering diffusion tensor imaging in accessing white matter integrity

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Introduction

Congenital hydrocephalus was accidentally found in the baseline scan of Wistar rats[1] (N=36) used in the traumatic brain injury (TBI) study. Over a period of 6 months, we have observed 60% female rats obtained from two vendors were abnormal in their ventricular and vascular systems, which may influence the interpretation of TBI findings. MRI techniques were performed including: MR angiography (MRA), susceptibility weighting imaging (SWI), and diffusion tensor imaging (DTI), to diagnose central nervous system (CNS) abnormalities including arteriovenous malformation (AVM) in these rats. Significant differences in the MRI results exist between the normal and AVM rats, indicating that a baseline scan is critical to exclude animals with the AVM abnormality to ensure a consistent and reliable animal model of CNS disease.

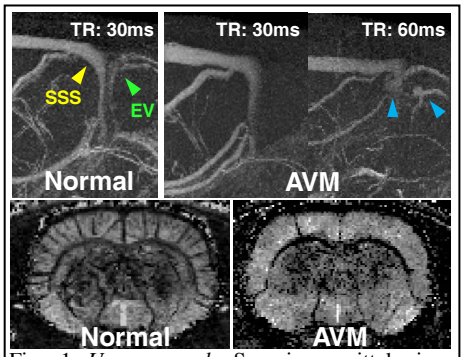

Fig. 1 *Upper panel:* Superior sagittal sinus (SSS) and emissary vein (EV) were clearly seen in the normal rat using TR=30ms in MRA. EV is not observed in the AVM rats using the same TR. The tangled EV appears when TR is increased to 60ms suggesting slower blood flow in these vessels (blue arrows). *Lower panel:* SWI images reveal that the cerebral vasculature is remarkably scarce in the AVM rats.

Material and Methods

Animal

Twelve female 10-week-old Wistar rats purchased from Charles River and Harlan Laboratories were used in this study. Congenital hydrocephelous were found in half of the animals (N=6) by anatomical MRI. The animalswithout hydocephalus served as normal control rats.

MRI

MRI data were acquired in vivo using a Dolty quadrature coil on a Bruker 7T spectrometer. 3D time-of-flight MRA and SWI were used to examine the CNS vasculature. Parameters for the FLASH time-of-flight MRA: TR 30ms, TE 3.2 ms, FOV 1.4 × 2.56 × 1.8 (cm), voxel size 90 (μm, isotropic); NEX 3. Scan time was 30 min. Gradient echo SWI: TR 60ms, TE 3.2 ms, FOV 3.5 × 2.56 × 1.4 (cm), voxel size 200 (μm, isotropic); NEX 2. Scan time was 17 min. Diffusion data were acquired using 3D spin echo EPI: TR 700ms, TE 37 ms; segment 4, Δ 15 ms; δ 5 ms; *b*-value 0 and 800 s/mm^2 with 15 encoding directions. FOV and the voxel size are the same with SWI. Scan time was 55 min. Fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) were derived to inspect the white matter integrity at the corpus callosum (CC). All imaging data were processed by in house Matlab scripts. Following euthanasia rats were perfused with radiopaque Microfil for the micro CT imaging of vasculature (resolution: 10 μm isotropic). Behavioral observations were also obtained.

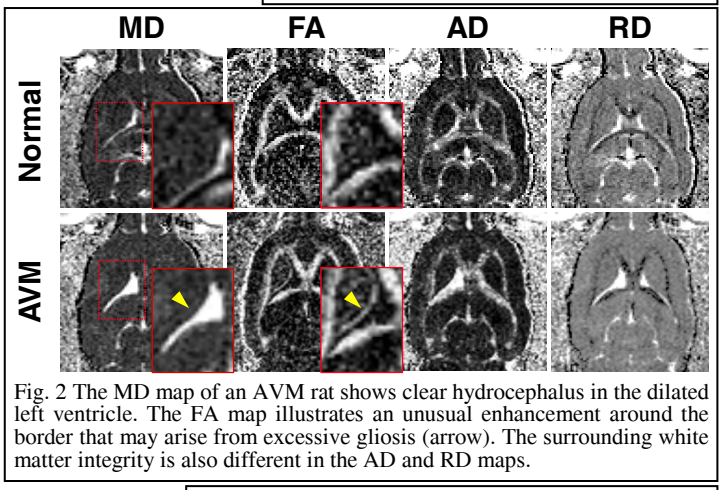

Fig. 2 The MD map of an AVM rat shows clear hydrocephalus in the dilated left ventricle. The FA map illustrates an unusual enhancement around the border that may arise from excessive gliosis (arrow). The surrounding white matter integrity is also different in the AD and RD maps.

Results

Compared to the normal control rats, clear vascular malformation is seen in the MRA at the confluence of sinus (upper panel, Fig. 1) in the hydrocephalic rats. SWI revealed paucity of vasculature in cortex in the AVM rats (lower panel, Fig. 1) in comparison to controls. The DTI parameter maps denote that the hydrocephalus greatly changes the anatomy of AVM rats by dilating their ventricles (Fig. 2). Examining from the CC, AVM rats had significantly lower FA, higher MD, AD, and RD, suggesting the white matter integrity was congenitally different in the rats with hydrocephalus (Fig. 3). The micro-CT image affirms the exceptional connection between veins and arteries in the AVM rats (Fig. 4). The abnormal tangle of blood vessels in the brain is disclosed and suggests the AVM type of vascular malformation congenital exists in these hydrocephalus rats.

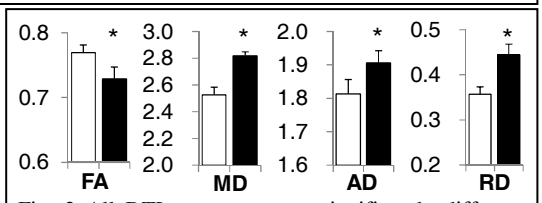

Fig. 3 All DTI parameters are significantly different between the normal (□) and AVM (■) rats. *p < 0.01.

Discussions and Conclusions

This study confirms the presence of congenital hydrocephalus in Wistar rats along with the presence of AVM in up to 60% of animals. The aberrent vasculature in these rats observed on MRI and micro CT possibly contributed to the increased insterstitial preasure and the lack of SWI detected vessels resulting in obstructive hydrocephalus. Our preliminary histology (data not shown) reveals excessive gliosis existing around the dilated ventricle, corresponding to increased FA[2]. The DTI results indicate that the increase of water content could significantly alter the DTI parameters resulting in false interpretations of pseudo-increase of axon and pseudo-decrease of myelin integrity. Behavioral observations (data not shown) indicate that the rats with congenital hydrocephalus and AVM tend to be much more docile than normal Wistar rats. Baseline scans are strongly suggested to prevent the accidental use of these AVM animals in the study of neurological disease, especially when testing any therapeutic intervention.

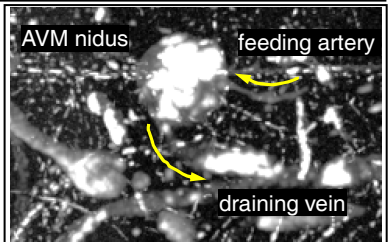

Fig. 4 CT image discloses an AVM nidus draining into a dilated vein. This representative image was acquired near the Circle of Willis in an AVM rat.

References (1) Koto et al., Jikken Dobutsu, 1987; 36:157-62; (2) Budde et al., Brain, 2011; 134:2248-60