Assessment of Water Diffusion Compartmentation in the Non-Human Primate Brain

Ramesh Paudyal1, Chun-Xia Li2, Edward J. Auerbach2, and Xiaodong Zhang

1Yerkes Imaging Center, Yerkes Regional Primate Research Center, Emory University, Atlanta, GA, United States, 2Center for MR Research, University of Minnesota, MN, United States

Introduction: Arterial spin labeling (ASL) perfusion MRI techniques have gained wide acceptance because ASL measures the cerebral blood flow (CBF) by magnetically labeling blood water molecules without the use of a paramagnetic contrast agent (CA) [1, 2]. ASL techniques combined with diffusion-weighted (DW) - MRI have also been employed to measure permeability-surface product (PS) of the capillary wall in brains [3, 4]. Estimates of the capillary permeability evaluate the status of blood brain barrier (BBB) in cerebrovascular diseases [5, 6], whereas apparent diffusion coefficient (ADC) evaluates the mobility of water molecules in normal and pathological tissues [7, 8]. Recently, DW-ASL perfusion technique detailed elsewhere [4] was applied to measure the capillary wall permeability in the human brain. Herein, we employed DW-ASL perfusion method in the non-human primate’s brain. In the present study, ASL signals evolving from the vascular and tissue compartments acquired via DWI-ASL perfusion method were fitted to biexponential diffusion decay for the fast and slow diffusion components to identify differences in diffusion compartmentation in white and gray matter in the non-primates brain using DWI-ASL perfusion data.

Material and Methods: Three healthy female rhesus monkeys (n=3, 7-11 years old) were utilized. All procedures followed the protocols approved by the Institutional Animal Care and Use Committee (IACUC) of Emory University. The DWI-ASL perfusion images were acquired using a Siemens 3.0 T Trio whole body scanner MR system (Siemens Medical, PA, USA) with an 8-channel high resolution knee coil (Invivo, Inc.) [9]. All the physiological parameters such as O2 saturation, blood pressure, heart rate, respiration rate, body temperature etc. were monitored continuously in each scan session and were recorded and maintained in normal ranges of anesthesia (0.7-1.0 % Isoflurane). The DWI-ASL perfusion data were collected at b = 0, 10, 25, 50, 105, and 190 s/mm2. The other MRI parameters were: TR/TE = 410/43 ms, FOV = 96 mm × 96 mm, data matrix = 256 × 256, 16 slice with slice thickness = 1.5 mm. Regions of interest (ROIs) were selected in the white matter and gray matter on the first b = 0 s/mm2 image in the series with weak diffusion weighting (Fig.1A). For all three subjects, a total of 24 ROIs were placed in the white matter and gray matter with a mean area of 72 pixels. For each ROI, the average DWI-ASL perfusion values of the monkey brain were fitted to biexpoential diffusion decay for the fast and slow diffusion components to identify differences in diffusion compartmentation in white and gray matter using DWI-ASL perfusion data.

Results and Discussions: A typical DWI-ASL image of a normal non-human primate brain with b= 0 s/mm2 is shown in Fig. 1A. Fig.1B and C represent the DWI-ASL cerebral blood map generated at b = 0 and b = 190 s/mm2. Fig.2 represents the signal decay curve as a function of b value for the white and gray matter ROIs (Fig.1A). The biexponential fitting yielded the following fitting parameter for the white matter: a = 0.055, \(D_f = 0.112 \times 10^{-3} \text{mm}^2/\text{s}\); for gray matter: a = 0.065, \(D_f = 0.193 \times 10^{-3} \text{mm}^2/\text{s}\). Table 1 summarizes the values of ADCs: \(D_f\), \(D_s\), and fractional weights: a and a; averaged over all the gray and white matter ROIs. Comparison of the fitted parameters a and a did show the differences but were not significant (p=0.26) for white and gray matter, whereas the slow diffusion component \(D_s\) showed a significant difference (p<0.01) for white and gray matter. The average, a and a differed by about 40% and 20% in white and gray matter, whereas \(D_s\) and \(D_f\) differed by about 10% and 14% in white and gray matter, respectively. The correlation coefficients (R2) for the biexponential fits were about 0.99, p < 0.0001.

Discussion and Conclusion: The DWI-ASL perfusion data of the monkey brain were compatible with a biexponential model in all white and gray matter ROIs studied (i.e., \(R^2 = 0.99\), p < 0.0001). In this study, it was found that white matter \(D_f\) was smaller than gray matter \(D_f\), while white matter \(D_s\) was larger than gray matter \(D_s\). The white matter \(a\) was smaller than the gray matter \(a\), whereas the white matter \(a\) was slightly larger than the gray matter \(a\). The estimated fast diffusion coefficients \(D_f\) showed relatively large intersubject variability, whereas the \(D_f\) was quite stable. Biexponential fitting of the signal decay data with diffusion sensitization gradient values can reveal \(a\) and \(a\), \(D_f\) and \(D_s\) as well as the rate constant of water exchange across the capillary wall (i.e., \(PS/V_c\)), where \(V_c\) is the volume of the capillary. \(P\) is the permeability of the capillary wall, and \(A\) is the surface area of the capillary. In conclusion, DWI-ASL methodology for the water diffusion compartmentation is clearly an attractive method to further our understanding of tissue water diffusion dynamics and for assessing BBB integrity in the progression of pathologies such as strokes in animal studies.