An Absolute Quantification Method for Pharmacological MRI

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Introduction:

Pharmacological MRI (phMRI) studies utilize dynamic imaging methods to observe the drug induced hemodynamic response. Conventionally, the relative cerebral blood volume (rCBV) was obtained from the time-intensity curve after administration of iron oxide nanoparticles, and the synaptic function provoked by pharmaceutical compounds can be estimated [1,2]. Nevertheless, ΔrCBV could only be extracted, which is an altered percentage of baseline rCBV. However, for drug-addiction investigation, absolute quantification of phMRI could benefit inter-subject comparison and longitudinal follow-up. In this study, we aim to combine a modified Vascular-Space Occupancy (VASO) method [3] and the phMRI technique to acquire high-resolution multi-slice absolute quantification of cerebral blood volume (aCBV), and applied for methamphetamine (mAMPH) challenged phMRI on a rat model.

Materials and Methods:

In this study, six male Sprague Dawley rats (mean weight 311±29 g) were anesthetized with 1.5% Isoflurane and scanned in a 4.7T animal MRI scanner (Bruker Biospec 47/40). For each subject, single slice IR-RARE images were acquired before and after injection of 0.2 mL of Gd-DTPA. The imaging parameters were RARE factor=8, TI=590 ms, matrix 256x128, FOV 29 mm, thickness 1.5 mm, TE_{eff}/TR = 48/1600 ms. According to the VASO technique, the absolute CBV can be calculated from signal difference and calibrated by the signal in sagittal sinus. We optimized a short TR and corresponding TI for the IR-RARE to further reduce the interference of tissue signal. After a 30min rest to allow Gd-DTPA to excrete, 30 mg/kg monocrystalline iron oxide nanoparticles (MION) was administered. Multi-slice gradient echo images were then acquired to calculate ΔR_2* as rCBV maps. After correlating the relative value with the absolute value of VASO in the brain region of overlapped slice, a converting factor was found and applied to all slices. The parameters of gradient echo imaging were matrix 128x128, slice number=9, TE/TR=10/400 ms, and identical FOV and slice thickness as IR-RARE. The phMRI was then conducted by 150 consecutive gradient echo images, and 3 mg/kg of mAMPH was injected through tail vein after five baseline scans. All gradient echo images were then converted to aCBV maps. The acquisitions after mAMPH injection were last 2 hours.

Results:

The multi-slice aCBV colormaps with resolution of 0.23x0.23x1.5 mm were shown in Fig.1. The mean aCBV value in brain region from six rats is 2.5±1.0 mL/100mL, which is consistent with literature. The aCBV time curve in whole brain was shown in Figure 2. The time of mAMPH administration was at 5th min (red arrow). Note that the maximum aCBV increase was about 0.7 mL blood per 100 mL brain tissue. And the time to reach the maximum was 17 mins after mAMPH injected. The ΔaCBV in all rats are 0.40±0.29 mL/100 mL. The multi-slice ΔaCBV map of one rat was shown in figure 3.

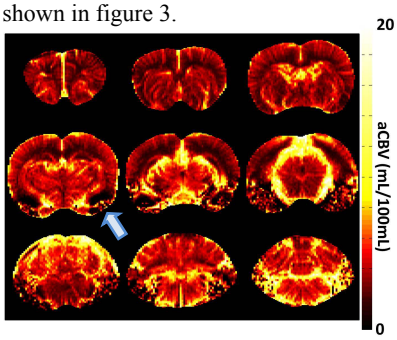

Figure 1 The multi-slice aCBV maps with resolution of 0.23x0.23x1.5 mm.

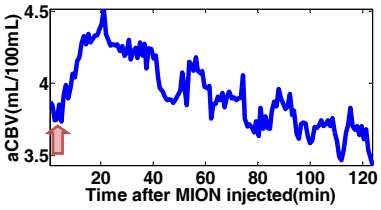

Figure 2 The aCBV time curve in whole brain of one rat. The time of mAMPH administration was at 5th min (red arrow).

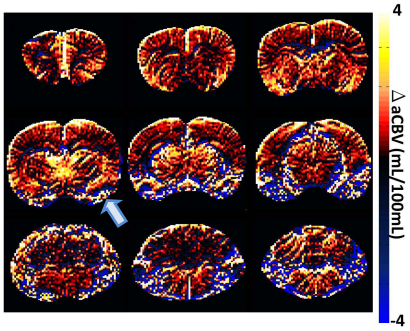

Figure 3 The multi-slice ΔaCBV maps after mAMPH administration of one rat.

Discussion and Conclusion:

In this study, we demonstrated the feasibility of absolutely quantified phMRI by combining VASO and iron oxide techniques. High-resolution multi-slice aCBV maps were achieved by this simple imaging strategy. Single slice VASO imaging can avoid quantification problem induced by T1 relaxation. Besides, the SNR of ΔR_2* induced by MION was substantial and with long half-life. The excretion of MION and Gd-DTPA may cause deviation of measured aCBV. It was corrected by fitting the baseline drift. The aCBV increased in most of the brain regions. In the bottom of brain especially toward the caudal slices, gradient echo images suffered from the signal loss by the susceptibility effect of air-tissue interface. Underestimations of ΔaCBV were found in these specific regions (blue arrows). In conclusion, this technique may provide valuable quantitative information for phMRI studies.

References:

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