Hippocampal blood flow and vascular reactivity in normal aging

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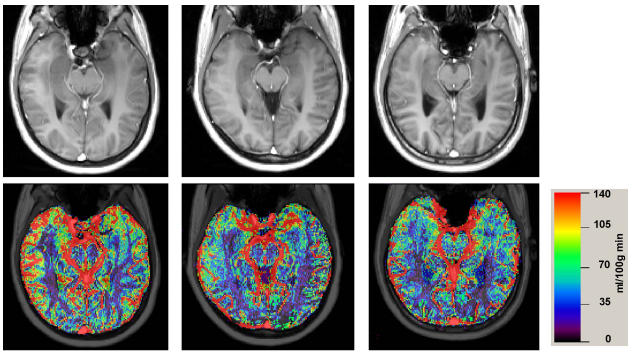
Due to methodological difficulties related to the small size, variable distribution of hippocampal arteries, and the location of the hippocampus in the proximity of cranial fossa, little is known about hippocampal blood flow. Hippocampus is supplied by branches of the posterior cerebral artery, the anterior choroidal artery, and by numerous arterioles arising from both of these vessels. Pathology studies often demonstrate collateral circulation, making it difficult to distinguish "through-flow" from tissue perfusion. Current arterial spin labeling (ASL) techniques suffer from severe signal loss and image distortions. To overcome these limitations, Fernandez-Seara et al [1] recently optimized an ASL sequence based on single shot 3D GREASE at an isotropic 4 x 4 x 4 mm^3 resolution. We present promising results obtained in normal subjects using pulsed 3T ASL based on FAIR and segmented TrueTFISP, with spatial resolution able to resolve small blood vessels (***see figure***).



Left column: 30 year old woman, **middle column**: 51 year old woman, **right column**: 68 year old man. Top: TrueFISP images; bottom: CBF images.

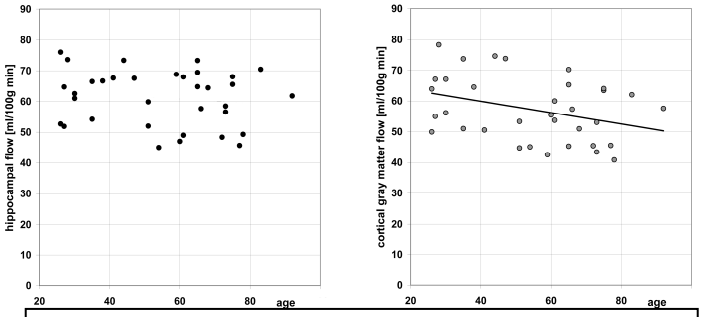
Methods

Mouthpiece, nose clip, and a rebreathing tube used to generate mild hypercapnia.

We studied 34 normal volunteers aged 26-92 years, 17 women, 17 men, on a 3T Siemens TIM Trio. All subjects above 55 years old received a battery of neuropsychological tests to confirm normal functioning. Pulsed 2D ASL images were acquired through the long axis of both hippocampi. TrueFISP readout was based on interleaved acquisition of 3 segments of the k-space, 53 lines (217.3 ms) per segment. TR/TE/TI=3.4/1.7/1200 ms, FA = 50^O, 256 x 168 matrix, 30 x 19.7 cm FOV, voxel size = 1.2 x 1.2 x 6 mm^3, NEX = 8, acquisition time 2:10 mins/slice.

CO_2 challenge was achieved using a partial rebreathing technique (***see figure***). Subjects were fitted with a mouthpiece, nose clip, and a respiratory tube. The expired air was sampled continuously by an infra-red capnometer via a 3 m long cannula attached to the mouthpiece. The length of rebreathing tube was individually adjusted in a training session that took place before each exam. Tube length was selected to raise end-tidal CO_2 by 7 mm Hg over the baseline level. The training session also served to familiarize each subject with the protocol and to reduce their level of anxiety.

Results and Discussion



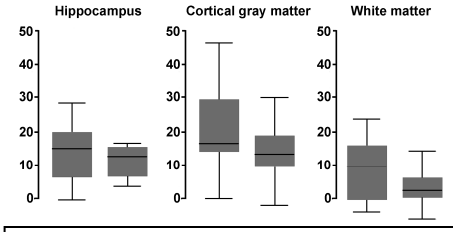
Resting hippocampal flow (left) and cortical flow (right) vs age.

Test-retest studies on 13 volunteers indicate good reproducibility of hippocampal CBF, with absolute difference averaging 3.6 ml/100g/min (5.4%) and intra-class correlation ICC = 0.90. Head motion, measured via automated signal sampling in the ring-shaped air region, was not correlated with either age (R=0.14, p=0.46), gender (t-test, t=0.26, p=0.79), or hippocampal CBF (R=0.21, p=0.30). However, in 13 test-retest studies the head motion was associated with the absolute difference between two successive CBF measures (R=0.57, p=0.04).

Resting hippocampal blood flow averaged 61.2 ± 9.0 ml/100g min. There was no statistically significant effect of age (***see figure***). The cortical flow averaged 57.2±10.4 ml/100g min and there was a significant linear relationship with age: CBF"= -0.18*age+67.3, p=0.04. There was no gender effect for resting cortical or hippocampal CBF.

For each patient a steady-state level of end-tidal CO_2 was achieved within about 30 seconds after breathing through the tube. Partial rebreathing yielded CO_2 increase of 6.8±1.9 mg Hg over the baseline level. Hypercapnia resulted in a significant CBF increase in all brain tissue (***see figure***). The neocortical flow response was 18.0±12.2 ml/100g min and the hippocampal flow response was 14.1±10.8 ml/100g min. Both hippocampus and neocortex responses were larger than 5.4±7.8 ml/100g min change in the white matter. There was no association between age and CBF response to CO_2 challenge. Cortical flow increase among the women was significantly larger than in the men (t-test, t=1.67, p=0.05) (***see figure***), confirming numerous prior studies.

Most of existing observations of hippocampal perfusion are based on low resolution studies and results have been inconsistent for SPECT, PET and ASL modalities. 3T TrueFISP ASL technique combines good spatial resolution, minimal susceptibility distortions, and high sensitivity for detecting subtle changes in this important brain region.



Flow response to mild hypercapnia challenge was greater in female than in male volunteers. Plotted is the change in CBF in ml/100g min. The horizontal line indicates the median value, the box represent two middle quartiles, and the whiskers the range.

[1]. Fernandez-Seara MA et al.. *Human Brain Mapping* 2007;28:1391-1400.