

## Regional effects of type 2 diabetes mellitus on cerebral blood flow and brain anatomy using MRI and Continuous Arterial Spin Labeling MRI at 3 Tesla

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### Introduction

Cerebral vasoregulation reflects the ability of cerebral microvasculature to adapt to metabolic demands and systemic blood pressure fluctuations and to maintain steady cerebral perfusion. Continuous Arterial Spin Labeling (CASL) perfusion magnetic resonance imaging (MRI) has already proven its ability to measure cerebrovascular reserve<sup>[1]</sup>. The goal of this study was to determine the regional effects of type 2 diabetes (DM) on cerebral blood flow and on brain anatomy using CASL MRI at 3 Tesla.

### Materials and method

Twenty-six healthy subjects (13 men, 13 women, mean age  $\pm$  SD:  $60.0 \pm 8.6$  years) and twenty-six subjects (13 men, 13 women,  $61.5 \pm 6.3$  years) with type 2 DM (for  $13 \pm 11$  years) were studied. Controls were not treated for any systemic disease; DM subjects with strokes, cardiac, renal or carotid disease were excluded. MR imaging was performed using a whole-body 3 T MRI scanner (GE Signa Vhi) with quadrature head coil. All subjects had routine T<sub>1</sub>-weighted inversion-recovery fast gradient echo (IR-FGE) (T<sub>1</sub>/T<sub>E</sub>/T<sub>R</sub> = 600/3.3/8.1 ms, 24 cm  $\times$  19 cm FOV, 256  $\times$  192 matrix size, 3 mm slice thickness) and fluid-attenuation inversion recovery (FLAIR) (T<sub>1</sub>/T<sub>E</sub>/T<sub>R</sub> = 2250/161/11000 ms, 24 cm  $\times$  24 cm FOV, 256  $\times$  160 matrix size, 5 mm slice thickness). Tagged and control images were collected over 5 minutes during: baseline, CO<sub>2</sub> rebreathing (RB) of air and 5% CO<sub>2</sub>, hyperventilation (HV) and a second baseline. End-tidal CO<sub>2</sub> (CO<sub>2</sub>) was continuously monitored and averaged over 15-second intervals for all conditions. CASL MRI<sup>[2,3]</sup> was performed with an echo planar imaging sequence (T<sub>E</sub> = 31 ms, 24 cm  $\times$  24 cm FOV, 64  $\times$  64 matrix size, 5 mm slice thickness). Images were obtained every 8 seconds and averaged for each condition. A perfusion map (PM) was then reconstructed for all conditions. On each image, a region of interest (ROI) corresponding to the brain was extracted using the Brain Extraction Tool algorithm<sup>[4]</sup>. The IR-FGE was segmented into three classes, CSF, gray (GM) and white matter (WM) using the expectation-maximization algorithm<sup>[5]</sup>. White matter changes (WMC) were extracted from the FLAIR image using a simple region growing algorithm. On each slice of each ROI (for IR-FGE, FLAIR, and PM), an ellipse was fitted using the non-linear least squares method. The medial axis of the smallest rectangle including the ellipse was then computed. This allowed the definition of eight regions corresponding to the left (L) and right (R) sides of the parieto-occipital (PO), temporal (T), frontal (F) and cortex (C) areas. On each of these regions, perfusion (in ml/100 g/min) for each of the four breathing exercises and WMC volume were respectively computed from PM and FLAIR. CSF, GM and WM volumes were extracted on the segmented IR-FGE. All volumes were normalized to the ROI volume. Cerebrovascular reserve (%BF) was computed as the percent of blood flow augmentation during RB compared to blood flow reduction during HV. The percent of CO<sub>2</sub> change between RB and HV (%CO<sub>2</sub>) was also computed. One-way ANOVA was used for statistical comparisons.

### Results

Figure 1 presents the method that was used to define the regions and to assess the spatial distribution of WMC on a FLAIR slice. Perfusion and CO<sub>2</sub> were significantly different between breathing exercises ( $p < 0.0001$ ), but were not between healthy subjects and DM groups. %CO<sub>2</sub> was not different between the groups. %BF was preserved in both sides of C and in T-R but was significantly reduced in DM compared to healthy subjects in F (L:  $p = 0.05$ , R:  $p = 0.03$ ), PO (L:  $p = 0.05$ , R:  $p = 0.01$ ) and T-L ( $p = 0.02$ ). WMC distribution was different between the regions ( $p < 0.0001$ ), but volume was not different between groups. For the DM, CSF volume was higher in all regions ( $p < 0.04$ ) except in PO-R and in both C regions. For the whole brain, GM and WM volumes were lower in the DM compared to the control group ( $p < 0.03$ ).

### Discussion - Conclusion

Regions could be computed on all images; this approach allows spatial distribution comparisons without using any registration step, providing significant advantage for comparisons of images with low spacial resolution (i.e. for the perfusion map). Anatomical changes associated with type 2 DM are indicative of brain atrophy and may contribute to the decrease of the vascular reserve. Association between WMC and perfusion warrants further investigations.

### References

[1] Detre JA, Samuels OB, Alsop DC, Gonzalez-At JB, Kasner SE, Raps EC. Noninvasive magnetic resonance imaging evaluation of cerebral blood flow with acetazolamide challenge in patients with cerebrovascular stenosis. *J Magn Reson Imaging* 1999; 10:870-875. [2] Alsop DC, Detre JA. Reduced transit-time Sensitivity in noninvasive magnetic resonance imaging of human cerebral blood flow. *J Cereb Blood Flow Metab* 1996; 16:1236-1249. [3] Alsop DC, Detre JA. Multisection cerebral blood flow MR imaging with continuous arterial spin labeling. *Radiology* 1998; 208:410-416. [4] Smith SM. Fast robust automated brain extraction. *Human Brain Mapping* 2002; 17:143-155. [5] Wells WM, Kininis R, Grimson WEL, Jolesz F. Adaptive segmentation of MRI data. *IEEE Trans Med Ima* 1996; 15:429-442.

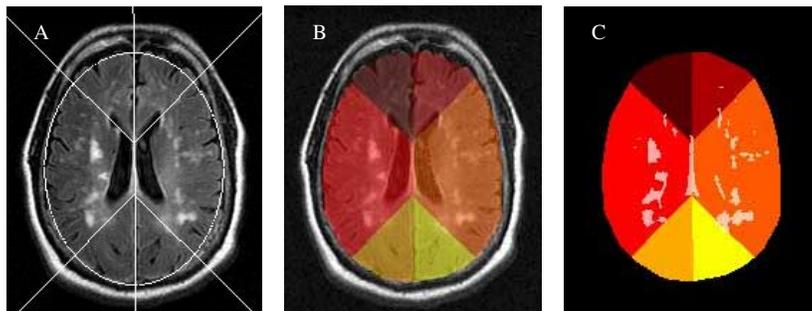


Figure 1: Definition of the anatomical regions on a FLAIR slice. An ellipse is fitted on the brain ROI (A). The medial axis of the smallest rectangle including the ellipse was then computed allowing the delineation of 8 regions. In B, 6 regions were defined on the ROI: left and right sides for the frontal (the 2 darkest ones), temporal (the 2 intermediate ones) and parieto-occipital (the 2 brighter ones) regions. The WMC segmentation corresponding to slice A is shown on C. The WMC volume could be computed on each region to assess its spatial distribution. The same protocol was used for the IR-FGE and for the perfusion maps.

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