Cerebral blood flow velocity and white matter changes in type 2 diabetes mellitus

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Introduction

Diabetes mellitus (DM) increases the risk for cerebrovascular disease, through the effects on cerebral microvasculature and blood flow regulation. The aim of the study is to assess the effects of type 2 DM on cerebrovascular responses to CO_2 challenges and to determine the relationship between white matter changes (WMC) on MRI and cerebral blood flow velocity.

Materials and method

We examined cerebral vasoregulation in 28 type 2 DM and 22 control subjects (age 62.3 ±7.2 years old) using transcranial Doppler ultrasound of the middle cerebral arteries during four breathing exercises: baseline, CO_2 rebreathing of air and 5% CO_2, hyperventilation and a second baseline. Beat-to-beat cerebral blood flow velocity (BFV) was averaged over each breathing exercise from the envelope of the arterial flow waveforms. Blood pressure (BP) was also continuously monitored. Cerebrovascular resistance (CVR) was calculated as the mean BP/mean BFV. Anatomical images and MR angiography were acquired in a GE 3 Tesla Vhi scanner with quadrature head coil. All patients had routine fluid-attenuation inversion recovery (FLAIR) ($T_I/T_E/T_R$ = 2250/161/11000 ms, 24 cm ×24 cm FOV, 256 ×160 matrix size, 5 mm slice thickness), dual T_2-weighted fast spin echo (FSE) ($T_{E1}/T_{E2}/T_R$ = 25/117/4000 ms, 24 cm ×18 cm FOV, 256 ×256 matrix size, 3 mm slice thickness) and 3D time of flight angiography (TOF) (T_E/T_R = 3.9/38 ms, 20 cm ×18 cm FOV, 384 ×224 matrix size, 2 mm slice thickness). FLAIR images were scored using a scale[1] from 0 to 3 (0: no lesions; 1: focal; 2: beginning confluence; 3: diffuse involvement of the entire region). Periventricular WMC and punctuate lesions were graded on all slices in the anterior, middle and posterior cerebral artery distributions for both hemispheres and quantified as a sum, mean and maximum grade. FSE images were reviewed for perivascular spaces. FLAIR images were also segmented to assess WMC volume. After extraction of a 3D region of interest (ROI) for the whole brain using the Brain Extraction Tools algorithm[2], WMC seeds were identified using the thresholding of hyperintense pixels. WMC borders were detected using a region growing method applied on each of the seeds. This method allowed an accurate WMC detection without expertise. The WMC volume was normalized for the whole brain ROI volume.

Results

The DM group demonstrated lower BFV and increased CVR during baseline, hypocapnia and hypercapnia. Figure 1 is an example of WMC segmentation on axial FLAIR slices at the level of the ventricles, for a control (Figure 1 A, B, C) and a DM subject (Figure 1 D, E, F). The distribution of continuous WMC sum grade differed between the DM and control group ($p < 0.0001$) and among the frontal, temporal, and parieto-occipital regions areas ($p < 0.0001$). Mean WMC grade in the frontal area was greater in the DM group compared to the control (mean 0.09 ± 0.3 vs. 1.8 ± 0.4, $p = 0.01$) and was borderline greater in the parieto-occipital area in the DM group ($p < 0.07$). Global WMC volume that included continuous and punctuate WMC (5.9 ± 5.5 vs. 6.7 ± 5.4 cm^3) and WMC volume normalized for brain volume (0.8 ± 0.7 vs. 0.8 ± 0.7%) were not different between the control and DM groups. MR angiography evaluations were normal for all subjects. WMC volume was negatively correlated with baseline BFV. A regression model revealed that DM diagnosis and WMC were significantly associated with reduced BFV.

Discussion - Conclusion

DM is associated with cerebral microvascular disease, affecting cerebral blood flow velocity and manifesting as white matter abnormalities on MRI. Interventions to enhance cerebral blood flow velocity may play an important role in preventing cerebrovascular complications of DM.

References

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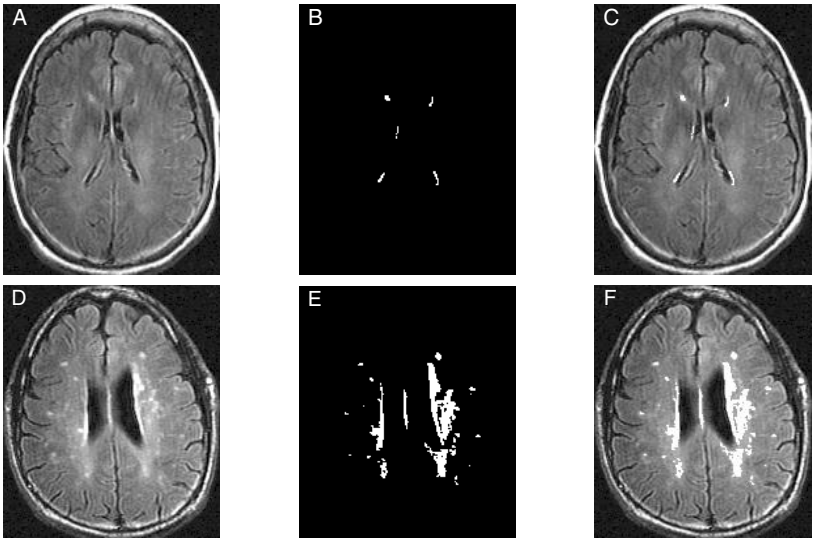

Figure 1: Axial slices at the level of the ventricles for a control (A, B, C) and a DM subject (D, E, F). The three columns represent the fluid-attenuation inversion recovery (FLAIR) image (A, D), the white matter changes (WMC) segmentation (B, E) and the overlay of the segmentation on the FLAIR image (C, F). Visual rating scale for continuous WMC for the control subject was 1 and for the DM subject was 3.

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