Cerebral Blood Flow and CerebroVascular Reserve of the brain in diabetes

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Introduction: Stroke risk in type-2 Diabetes Mellitus (T2DM) is 2-3 times that in the non-diabetic population. Following a cerebrovascular accident, people with diabetes show poorer outcomes with slower recovery rates. Arterial cerebral blood flow (CBF) and, in particular, the ability to increase blood flow to the parenchyma when under vascular stress (cerebrovascular reserve or CVR) are vital in the context of potential cerebral ischemia. This study sought to assess CBF and any response to a stress test provided by a potent carbonic anhydrase inhibitor, acetazolamide (ACZ), in a group of neurologically asymptomatic patients with T2DM and to compare their microvascular cerebral status to that of a neurologically normal group of volunteers without T2DM.

Method: The cohort comprised 8 T2DM patients with no history of cerebrovascular abnormality (mean age 54.3±15.2yrs) and 7 age-matched normal controls (mean age=59.0±7.5yrs). Arterial CBF was determined at 3T (Achieva, Philips) using the QUASAR arterial spin labelling (ASL) technique (1). One dataset was acquired prior to intravenous infusion of 1000mg ACZ (Diamox sodium perenteral, Wyeth Laboratories) over 10 minutes. Four further ASL datasets were then acquired post ACZ, approximately 7 minutes apart. The length of the ASL bolus crusher gradients was reduced following ACZ by adjusting the Q2-TIPS crusher pulses to account for possible increases in blood velocity in large vessels. CBF quantification was performed using analysis software from the Test-Retest study (1). Group analyses of resultant gray matter CBF obtained before and the mean of the CBF obtained after administration of ACZ were performed using paired-T-tests. CVR = [(CBFpost-CBFpre)/CBFpre]x100 was compared using an independent-samples T-test.

Results: The estimated arterial CBF and CVR for the 2 groups are summarised in table 1

Group	CBF_{preACZ} (ml/100g/min)	$CBF_{postACZ}$ (ml/100g/min)	CVR
T2DM (n=8)	42.3±8.2	52.7±10.3	26.8±26.5
HV (n=7)	47.6±10.2	64.2±11.9	36.7±18.4

Table 1. CBF obtained before and after administration of ACZ and the resultant CVR for the 2 study groups (means ± 1 standard deviation). The mean CBF after ACZ was significantly higher than that measured before ACZ in both healthy volunteer (HV) [P=0.002, T=-5.0] and T2DM [P=0.021, T=-3.0] groups. The mean cerebrovascular reserve (CVR) was not statistically significantly different between HV and T2DM groups (P>0.05).

Discussion: This study demonstrates significant increases in gray matter CBF, using ASL, following administration of a pharmacological stress agent. Although the differences in mean CVR are not significantly different between the 2 study groups, a trend can be seen together with larger variance and higher T-statistic within the T2DM group following the statistical comparison. All of the HV's demonstrated an increase in gray matter CBF due to the stress test whereas 3/8 T2DM subjects did not. This suggests that there may be a subset within the neurologically, clinically normal T2DM group who have sub-normal gray matter CVR characteristics (see fig. 1) and this warrants further investigation.

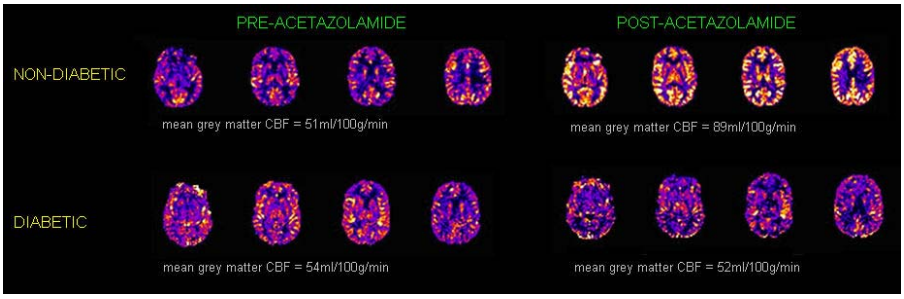

Fig 1. Example arterial CBF maps from a HV showing marked increase post ACZ and a diabetic who did not show vasodilatory / flow response.

Reference: 1. Petersen E.T. et al. The QUASAR reproducibility study, Part II: Results from a multi-center Arterial Spin Labeling test-retest study. NeuroImage 2009; 49:104-113.